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RELATIONSHIP BETWEEN PROINFLAMMATORY AND ATHEROGENIC MARKERS AND VESSELS REMODELING IN PATIENTS WITH HYPERTENSIVE DISEASE

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Kharkiv National Medical University, Ukraine

Abstract. The article presents clinical data that shows the relationship between proinflammatory markers (IL-22) and atherogenic markers (indices of lipid spectrum) in the formation of structural and functional changes in the carotid arteries, which can be considered as early subclinical markers of atherosclerotic vascular damage in the cohort of patients with comorbidity of hypertension and obesity. Such a combined pathology can be considered a trigger of metabolic events adversely affecting the lipid profile and directing these patients to a high cardiometabolic risk group.

Key words: *atherogenesis, hypertension, interleukin-22, lipid profile, proinflammatory status, remodeling of carotid arteries.*

Introduction. Hypertensive disease (HD) is one of the most common diseases having clinical and social significance. All over the world, the number of HD patients is increasing and today on the average is 44% of the general population, but in some countries, these figures are notably higher and reach 50% [1]. Throughout Europe, Ukraine has the highest mortality rate due to cardiovascular diseases, namely 772.1 cases among men and 440.9 cases among women per 100.000 of people. Circulatory diseases are the most common disorders among Ukrainian population (24.2%). HD ranks first (55.8%) in the structure of blood circulatory system morbidity rate [2].

One of the most frequent and most dangerous comorbid conditions of the HD are obesity and lipid storage disease [3–5]. Early systemic manifestations of HD include carotids remodeling. Immune inflammation is the pathophysiological basis for these pathological conditions. Proinflammatory cytokines, involved in the pathogenesis of obesity, dyslipidemia formation, and architectural distortion of blood vessels, are the mediators of this immune inflammation. Recently, the role of interleukins in the pathogenesis of hypertensive disease and its complications has been actively studied. Thus, there have been studies on the biological effects of interleukine-22 (IL-22) being a member of IL-10 family with proinflammatory properties. IL-22 has various effects and is engaged in many physiological and pathophysiological processes, such as inflammation, tissue regeneration, etc. [6]. IL-22 is a proinflammatory cytokine, a homodimer with a molecular weight of 25 kD belonging to IL-10 family. It is mainly produced by activated Th17, in particular, phenotype memory cells and mast cells, is also produced by monocytes, T- and B- cells, NK cells, congenital lymphoid cells [7]. IL-22 stimulates the production of proinflammatory cytokines in human keratinocytes [8]. However, its role in the cardiovascular disease pathogenesis is poorly studied. That is why it is important to determine and analyze the influence of IL-22 upon elastic arteries remodeling through the example of common carotid (CC) in patients with HD and obesity.

2. Purposes, subjects and methods:

2.1. Purpose – is to study anthropometric parameters, peripheral hemodynamic findings, lipid spectrum, as well as structural and functional changes of the common carotid in HD patients with obesity depending on the level of IL-22 and apolipoprotein B (Apo B).

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2.2. Subjects & Methods.The study involved examination of 84 HD patients (33 men and 51 women) at the age from 41 to 78 years, the median age was 58.0 years.

The HD diagnosis was verified using the recommendations of the European Society of Hypertension (ESH) for the management of arterial hypertension (2013). The excessive weight or obesity was established by calculating the body mass index (BMI) according to the classification of the World Health Organization (WHO, 2006). The abdominal obesity was established if waist measurement (WM) for men was more than 102 cm and for women was more than 88 cm, according to the Ukrainian Association of Cardiology as of 2012 [9].

There were the following exclusion criteria: symptomatic arterial hypertension; thyroid gland pathology; autoimmune diseases; oncology; exacerbation of chronic inflammatory processes or acute inflammatory diseases; acute myocardial infarction or stroke, acute failure of left or right ventricular; traumatic injury of the central nervous system; coexisting mental illness, and diffuse connective tissue diseases.

Blood samples for biochemical and immuno-enzymatic analysis were taken from the cubital vein in the morning on an empty stomach.

Determination of lipid metabolism findings, namely total cholesterol (TC), triglycerides (TG), high density lipoprotein cholesterol (HDLC) in blood plasma on an empty stomach was made by enzymatic method using standard sets with further calculation of low density lipoprotein cholesterol (LDLC), very low density lipoprotein cholesterol (VLDLC), atherogenicity coefficient (AC) and non-HDLC. The level of Apo B was determined using the immunoenzyme method with Assay Max® Human Apolipoprotein B ELISA Kit.

Determination of the level of IL-22 in blood plasma was carried out by the enzyme-linked immunosorbent assay using the Bender Medsystems® Human IL-22 Platinum ELISA Kit.

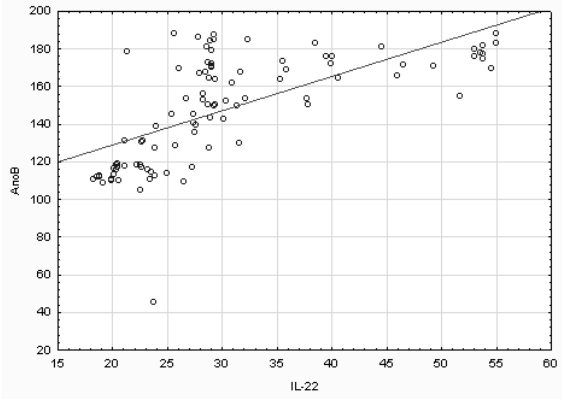
Also the patients underwent an ultrasound investigation of the carotids. The intima-media complex thickness (IMC) was measured in the middle third of the common carotid on the back wall using P. Pignoli method, as the distance between the characteristic echo zone, created by the surfaces of lumen-intima and media-adventitia in the cross-section [10]. The diameter of the common carotid lumen was measured at the same point. The blood flow velocity was also assessed. The relative wall thickness and arterial segment mass were calculated according to the recommendations of the European Society of Cardiology [11]. The common carotid remodeling type was assessed according to the classification offered by O.V. Ahafonov et al. [12].

Statistical analysis of data implied application of nonparametric statistics methods. In samples with nonparametric data distribution, the results were given in the form of Me (Q25; Q75), where Me was median (50th percentile), Q25 and Q75 were 25th and 75th percentile, accordingly. The results were compared by the Mann–Whitney U test. The Spearman correlation analysis was used to measure the degree of dependence. The null hypothesis was refused at the confidence level ($p < 0.05$).

Conflict of interests

There is no conflict of interests.

3. Results and discussion. Comprehensive study of the relationship between IL-22 and Apo B levels and anthropometric parameters, peripheral hemodynamics parameters, lipid metabolism, as well as the thickness of the IMC implied clustering of HD patients into 4 clusters based on the contents of IL-22 and Apo-B in blood serum (*Figure*).



Results of HD patients clustering based on interleukin-22 and apolipoprotein B levels

The first cluster included patients with the lowest IL-22 and Apo B levels, and the second cluster included patients with the highest IL-22 and Apo B levels. The third and the fourth clusters included patients with intermediate IL-22 and Apo B levels.

Characteristics of the first cluster of patients were as follows: levels of systolic blood pressure (SBP) and diastolic blood pressure (DBP), BMI and WM were within normal limits, lipid spectrum findings were within normal limits, the IMC level was also within normal limits (*Table 1*). The second cluster, which included patients with the highest IL-22 and Apo B levels, showed increased

Table 1

General characteristics of hemodynamic, anthropometric, lipid parameters and intima-media complex in clusters

Indices	Cluster 1 N=21	Cluster 2 N=20	Cluster 3 N=23	Cluster 4 N=20
SBP, mm Hg	120 (120; 150)	140 (140; 150)	160 (150; 165)	130 (130; 140)
DBP, mm Hg	80 (80; 90)	80 (80; 90)	100 (90; 100)	80 (80; 80)
BMI, kg/m^2	23 (21; 29)	31 (28; 36)	29 (27; 34)	28 (25; 30)
WM, cm	80 (70; 92)	97 (91.5; 109)	97 (89; 112)	94 (89; 97)
TC, mmol/l	5.2 (4.5; 6.2)	6.67 (5.65; 7.36)	5.80 (4.76; 6.60)	5.97 (4.93; 6.90)
TG, mmol/l	1.87(1.69;2.20)	2.11 (1.85; 2.87)	2.09 (1.75; 2.24)	1.94 (1.56; 2.07)
LDLC, mmol/l	3.01(2.31;3.47)	4.90 (4.64; 5.37)	3.90 (3.75; 4.60)	4.31(2.68; 4.71)
VLDLC, mmol/l	0.85(0.76;1.00)	0.96(0.84; 1.30)	0.95 (0.79; 1.01)	0.88(0.71; 0.94)
non-HDLC	3.8 (2.9; 5.1)	5.4 (4.6; 6.6)	4.65 (3.7; 5.5)	4.65 (3.6; 5.6)
HDLC, mmol/l	1.42(1.09;1.67)	1.05 (0.86; 1.34)	1.05 (0.87;1.26)	1.30(0.93; 1.76)
IMC, mm	0.9 (0.8; 0.9)	1.1 (1.0; 1.15)	1.0 (0.9; 1.1)	1.0 (0.85; 1.0)
D CC, mm	7.1 (6.6; 7.4)	5.8 (5.2; 6.8)	6.0 (5.5; 6.4)	5.7 (5.4; 6.5)

SBP to 140 (140; 150) mm Hg. At normal DBP 80 (80; 90) mm Hg, there was a significant increase in BMI and WM. Lipid metabolism findings in this cluster demonstrated proatherogenic changes, that is why the TC level of 6.67 (5.65; 7.36) mmol/l was above the norm for this cohort, the level of TG of 2.11 (1.85; 2.87) mmol/l was also above the norm, and significantly increased the level of LDLC with median 4.90 (4.64; 5.37) mmol/l, at the same time the level of VLDLC and HDLC of the second cluster patients remained within normal limits.

In the setting of high levels of blood pressure, BMI and WM, and atherogenic dyslipidemia in patients of this cluster there were abnormal findings of IMC 1.1 (1.0, 1.15) mm. IMC changes in the setting of chronic hemodynamic load of high blood pressure and atherogenic dyslipidemia being induced by the improved IL-22 activity (the fundamental for cluster formation) was due to the fact that oxidative stress potentiated the vascular wall inflammation processes, causing increased fibrosis of vessels, proliferation of smooth muscle cells secondary to the reduced endothelium-dependent vasodilation, gradually decreasing elasticity of the arteries and making them stiff. Previous studies have shown the role of proinflammatory cytokines (IL-1, IL-6, IL-17, tumor necrosis factor-α (TNF-α)) in the arterial stiffness pathogenesis [13]. There are also some suggestions that a biologically active TNF-α is produced in response to hemodynamic load created by vascular smooth muscles and endothelial cells. Being a strong inflammatory mediator, TNF-α provides vascular wall hypertrophy and vessels remodeling [14, p. 37].

Assessment of findings in the third and the fourth clusters (with intermediate figures of IL-22 and Apo B) showed the most substantial differences in the third cluster. Patients of this cluster had the highest levels of SBP and DBP, namely 160 (150; 165) and 100 (90; 100) accordingly. Lipid spectrum findings tended to increase above the norm of TC, TG and LDLC, which corresponded to clinical studies, showing that changes in hemodynamic conditions in the case of HD provided vessels remodeling due to the influence upon the vessel walls of blood flow velocity (shear stress), internal pressure of vessels and pressure by the surrounding tissues (transmural stress) [15]. One more study showed that high blood pressure was a triggering mechanism for the development of vessel wall hypertrophy and fundamental for structural arteries change [16]. Lipid storage diseases found in the second and the third clusters in patients with high and intermediate IL-22 and Apo B levels probably reflected additional pathogenic role of lipids in the vessels remodeling, which corresponded to the literature, which showed that IMC changes tended to progress more quickly in dyslipidemia [17, 18].

To better understand the features of vessels remodeling that were peculiar for different clusters, we analyzed the distribution of examined patients by classification of types of geometry of the common carotid according to O.V. Ahafonov (*Table 2*).

Assessment of morphofunctional parameters of the CC showed normal geometry of the CC and the concentric hypertrophy of the CC in the first cluster (*Table 2*). The second cluster was found to have an increase in the proportion of patients with concentric hypertrophy of the common carotid, the third cluster had more patients with concentric CC remodeling, and the fourth cluster had equal number of patients with normal geometry and concentric remodeling.

This cluster analysis showed a possible relationship between the peculiarities of

Table 2

Cluster analysis of the types of geometry of the common carotid

Types of geometry of common carotid arteries	Cluster 1 N=21	Cluster 2 N=20	Cluster 3 N=23	Cluster 4 N=20
Normal geometry CC, absolute (%)	18 (85.7)	6 (30)	7 (30.4)	9 (45)
Concentric remodeling CC, absolute (%)	3 (14.3)	3 (15)	10 (43.5)	7 (35)
Concentric hypertrophy CC, absolute (%)	-	9 (45)	3 (13.05)	3 (15)
Eccentric hypertrophy CC absolute (%)	-	2 (10)	3 (13.05)	1 (5)

distribution of IL-22 and Apo B levels and the nature of structural and functional changes of the CC, in particular the formation of concentric CC hypertrophy and concentric remodeling in patients with the highest levels of hyperinterleukinemia and hypercholesterolemia, which corresponded to a similar clinical study, showing that changes in proinflammatory cytokine IL-33 were associated with CC remodeling and hypertrophy of the vessel wall with mainly concentric variant [19].

The analysis of the correlates of the first cluster with the lowest IL-22 and Apo B levels demonstrated the following IL-22 and BMI relationship ($r = 0.76$; $p < 0.05$), WM ($r = 0.52$; $p < 0.05$), hip width (HW) ($r = 0.52$; $p < 0.05$); TG ($r = 0.44$; $p < 0.05$), HDLC ($r = 0.40$; $p < 0.05$), VLDLC ($r = 0.44$, $p < 0.05$), AC = 0.63; $p < 0.05$), non-HDLC ($r = 0.53$; $p < 0.05$), establishing the relationship between the activity of this cytokine and anthropometric data and changes in lipid metabolism. At the same time positive correlations of IL-22 with the atherogenic pool of lipids and a negative connection with the anti-atherogenic fraction of HDLC attracted more attention.

When analyzing correlations in the second cluster with the highest IL-22 and Apo B levels, the IL-22 level positively correlated with the SBP level ($r = 0.61$; $p < 0.05$), BMI ($r = 0.90$; $p < 0.05$); WM ($r = 0.63$; $p < 0.05$); WM/HW ($r = 0.74$; $p < 0.05$); TC ($r = 0.53$; $p < 0$) , 05%), TG ($r = 0.58$; $p < 0.05$), LDLC ($r = 0.58$; $p < 0.05$), VLDLC ($r = 0.58$; $p < 0.05$), AC ($r = 0.46$; $p < 0.05$) and non-HDLC ($r = 0.58$; $p < 0.05$). In summary, there were similar correlations between anthropometric data and atherogenic pool of lipids; also there was additional relationship between IL-22 and SBP level.

When assessing correlations in the third and the fourth clusters with intermediate IL-22 and Apo B figures no significant differences were found; there continued a similar trend of clearly valid relationship between peripheral hemodynamics data, anthropometric parameters and atherogenic lipid fractions. The third cluster was found to have the relationship between IL-22 and SBP ($r = 0.58$; $p < 0.05$), pulse pressure (PP) ($r = 0.58$; $p < 0.05$), BMI ($r = 0.83$, $p < 0.05$), WM ($r = 0.86$; $p < 0.05$), HW ($r = 0.64$; $p < 0.05$), WM/HW ($r = 0.87$, $p<0.05$), TC ($r=0.74$; $p<0.05$), LDLC ($r=0.75$; $p<0.50$, VLDLC ($r=0.77$; $p<0.05$), CA ($r = 0.78$; $p < 0.05$), non-HDLC ($r = 0.78$; $p < 0.05$). Thus, there was similar relationship; IL-22 also correlated with PP data.

The fourth cluster of IL-22 showed interrelations between IL-22 and BMI ($r = 0.82$; $p < 0.05$); WM ($r = 0.90$; $p < 0.05$); WM/HW ($r = 0.61$; $p < 0.05$), TC ($r = 0.58$; $p < 0.05$), LDLC ($r = 0.61$; $p < 0.05$), CA ($r = 0.58$; $p < 0.05$), non-HDLC ($r = 0.63$, $p < 0.05$).

Thus, all four clusters demonstrated similar clear relationship between IL-22 and blood pressure level, anthropometry, and atherogenic lipid fractions. The relationship between IL-22 and SBP and PP levels was due to the fact that in conditions of hemodynamical "shear stress", occurring in high blood pressure, there was proinflammatory cytokine response to the tissue injury, in which the IL22 was engaged.

The analysis of IL-22 relationship with lipid metabolism figures showed that this proinflammatory cytokine actively correlated with atherogenic lipid spectrum fractions. This analysis allowed to assume that endothelial dysfunction induced by the improved IL-22 activity influenced the increase in the content of adverse lipid fractions and might form a higher potential, which, along with endothelium dysfunction, might ensure the progression of the formation of fatty streaks and further receptor wall damage; this, it its turn, could boost tissue intercellular mechanisms of dystrophy of the smooth muscle layer of the vessel wall.

Assessment of Apo B correlates in the four analyzed clusters showed the following relationship. In the first cluster, Apo B correlated with BMI ($r = 0.72$; $p < 0.05$); in the second cluster, Apo B strongly correlated with BMI ($r = 0.66$; $p < 0.05$); WM ($r = 0.77$; $p < 0.05$); HW ($r = 0.64$; $p < 0.05$); WM/HW ($r = 0.76$; $p < 0.05$); HDLC ($r = -0.58$; $p < 0.05$), AC ($r = 0.45$; $p < 0.05$). The third cluster, having intermediate IL-22 and Apo B findings, had strong relationship between Apo B and BMI ($r = 0.50$; $p < 0.05$), WM ($r = 0.6$; $p < 0.05$), HW ($r = 0.66$; $p < 0.05$), WM/HW ($r = 0.48$; $p < 0.05$), TC ($r = 0.52$; $p < 0.05$), TG ($r = 0.60$; $p < 0.05$), HDLC ($r = -0.47$; $p < 0.05$), LDLC

(r = 0.57; p <0.05), CA (0 , 69), non- HDLC (0.60). In the fourth cluster Apo B correlated with IMT (0.65), MW (r = 0.61; p <0.05), HW (r = 0.51; p <0.05), TC (r = 0, 47; p <0.05), TG (r = 0.58; p <0.05), HDLC (r = -0.56; p <0.05), VLDLC (r = 0.58; p <0.05), AC (r = 0.78; p <0.05), non-HDLC (r = 0.66; p <0.05). General analysis of the Apo B correlates in the clusters being studied showed general positive, valid relationship between Apo B with anthropometric data and atherogenic lipid fractions level. In the intermediate third and fourth clusters, Apo B more strongly correlated with an increased degree of correlation with a greater number of lipid fractions, that is why there were more distinct tendencies of Apo B correlation with non-HDLC, due to active transport intervention of Apo B in the atherogenic processes of blood lipids disorders thus increasing the cardiometabolic risk in patients with HD and obesity triggering additional adverse metabolic lipid disturbances.

The isolated analysis of IL-22 and Apo B activity in the cluster analysis of our study showed clear relationship between IL-22 and anthropometric data and blood pressure levels; Apo B correlated both with anthropometric parameters and atherogenic pool of lipids, however, no relationship between Apo B and peripheral hemodynamics data was found.

4. Conclusions. The cluster analysis revealed a possible relation between the characteristics of the distribution of IL-22 and Apo B level and the nature of structural and functional changes of the common carotid, in particular formation of concentric hypertrophy of the common carotid and concentric remodeling in patients with the highest levels of hyperinterleukinemia and hypercholesterolemia. Based on the clinical features of the common carotid remodeling in HD patients it is possible to assume that IL-22 participates in the development of endothelial dysfunction and atherogenesis in patients with HD and obesity; at the same time Apo B is engaged in lipid disorders, being transported from the increased atherogenic fractions.

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INTESTINAL INVAGINATION OF ADULTS

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Authors present literature review on incidence, etiology, pathogenesis, presentation and management of intestinal intussusception in adults, rare form of acute intestinal obstruction. The study involved assessment of a case history of a patient with intestinal intussusception.
Key words: *intestinal obstruction, intestinal intussusception, acute peritonitis, emergency surgery.*

Introduction. Acute intestinal blockage (AIB) is more difficult for diagnosis in acute surgical diseases of the abdominal organs and it is characterized by severe clinical course, the highest mortality in patients operated on due to acute peritonitis.

Objective. An important feature noted recently is the redistribution of the frequency of individual forms of intestinal obstruction. Thus, such forms as nodulation and intussusception became much less common.

2. Purposes, subjects and methods:

2.1. Purpose – is to study individual forms of intestinal obstruction.

2.2. Subjects & Methods. Intussusception in adults is one of the rare and poorly diagnosed forms of acute intestinal blockage (AIB). Its incidence ranges from 10 to 18 % among all forms of AIB. Intussusception of the cecum occurs in 45–63 %, of the colon in 15 %, of the ileocolon in 12–17 %, of the small intestine in 10.7 % cases. Multiple intussusception develops in 0.4–3.6 % cases (*Fig. 1*), complex (multi-cylindrical) in 8.3 % [1–5].

Rare forms of intussusception:

• Intussusception of cupola, lateral walls of the cecum;

• Intussusception of appendix, diverticula of intestine;

• Intussusception of appendiceal stump;

• Intussusception of haustrum of colon;

• Multiple intussusception of different parts of intestine;

• Intussusception of tumors and hematomas;

• Retrograde intussusception;

• Multi-cylindrical intussusception.

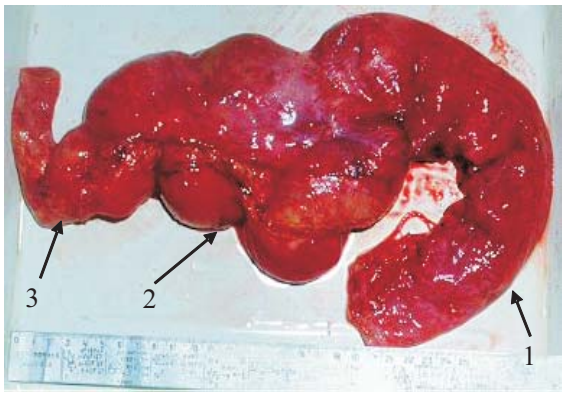

Fig. 1. Macro-preparation. Plural invagination of the small intestine (actually observe). 1 – leading loop; 2 – invaginate – 10 sm; 3 – taking loop of the small intestine

Any fixed mechanical obstacles or local morphological changes of the intestinal wall can be involved to the intestinal lumen, then advance into the intestine by peristaltic wave. Most frequently intussusception in adults trigger development of tumors, particularly peduncular polyps in 25–33 % cases.

Intussusception can develop secondary to infectious diseases, causing lesions and inflammatory infiltrations in the intestine, (dysentery, typhoid fever). They cause discoordination of peristalsis, a reinforcement of segmental peristalss in an attempt of the intestine to get rid of the foreign

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mass. This is the pathogenic mechanism, triggering the process of intussusception. A similar mechanism for the development of intussusception occurs in hemorrhages in its wall (intramural hematomas of various origin: spontaneous, posttraumatic, Shonlein–Henoch's disease, etc.).

High intussusception, as other forms of acute intestinal obstruction of this localization, is characterized by metabolic disturbances. Presentation of the disease is determined by the age of the patient, the speed with which the intestine is intussuscepted, the type of intussusception, the length of intussusception, the nature of the intestinal contents at the time of intussusception, and changes in the intussuscepted intestine.

Conflict of interests. There is no conflict of interests.

3. Results and discussion. In rapid introduction and necrosis of intussusceptum, spasms may be absent. Only acute, then subsiding pain with the subsequent development of the second stage (phase) of intoxication and peritonitis. The classic symptoms of intussusception are known to be the following triad:

1) Acute, then recurring pains in the form of contractions. They are immediately localized, usually in the place where the intussusception occurred, but then, as the intussusception advances, they move along the intestine and radiate to the epigastrium, as typically mesenteric;

2) The presence of a tight-elastic, mobile, painful formation palpable through the abdominal wall or rectum (Rush's symptom). With palpation pain may increase. Intussusceptum is palpable in intussusception of the small intestine in 60 %, of the colon in 40 %;

3) Anal bleeding (Cruveiller's symptom) in bowel movements, or presence of blood in the wash water after an enema. It is observed in 70–80 % of patients. Vomiting of blood, coffeeground vomiting in high (gastrointestinal) intussusception is a late syndrome;

One of the clinical masks of intussusception is ischemia, which is clinically very close to acute impairment of blood circulation in one of the visceral vascular pools (upper, lower mesenteric, celiac). Both diseases are characterized by acute, sudden pain, initially intensified, then subsiding peristalsis, flatulence, presence of palpable intestinal compaction (heart attack in case of acute intestinal obstruction, Mondor's syndrome), discharge of blood during a bowel movement or tenesmus. Hemodynamics and metabolism are disturbed with the development of thrombosis, intoxication increases. However, in acute intestinal obstruction pain is constant, increasing, not cramping. Painful induration appears much later. Blood discharge is a late and inconsistent symptom. Swelling of the intestine as one of the symptoms of acute intestinal obstruction appears earlier and involves significant areas of the intestine (symmetrical swelling). At the same time, vomiting, as one of the main symptoms of acute intestinal obstruction, is not typical. Dysentery is a general symptom in both diseases, seasonally increasing, up to attacks of pains, being false defecation, diarrhea with mucus and blood. The dysenteric bleeding, as a rule, is moderate, traces of blood in the mucous intestinal contents. In tenesmus, it is called "blood spitting". Pain is felt on palpation of the large intestine, mainly of its left half. Infiltrates are not detected. Dysentery is an infectious disease, so intestinal symptoms are accompanied by symptoms of a general inflammatory reaction, hyperthermia, changes in the blood formula, early intoxication. Intestinal paresis develops with especially aggressive forms of the disease. Conservative treatment of intussusception, medication, physical attempts to reduce intussusception through the abdominal wall in adults, especially in elderly, are not allowed.

The loss of time for attempts at conservative treatment is directly proportional to the amount of time lost to an emergency operation for life reasons. Moreover, retrograde, jejunogastric (postoperative), complex intussusception, intussusception of the appendix and Meckel's diverticulum do not respond to conservative treatment.

Reduction of intussusception is allowed only in the early stages, with recent, small and non-fixed intussusceptum.

Reduction of intussusception should be carried out in combination, by squeezing the intestine entering the intussusceptum and pushing the intussusceptum head out, having previously performed a novocainic blockade of the mesentery of both intestines – the invasive and ingested intussusceptum. If resistance is felt, the reduction should be stopped.

If the reduction is successful, it is not necessary to transfer the contents accumulated over the intussusceptum to the loop withdrawn from the intussusceptum by "squeezing", since the "massage" of the intestine by squeezing can lead to thrombosis in both mesenteric vessels and microvascular bed. In addition, reduction results in long-term paresis of the intestine.

If the reduction is not indicated or impossible, resection of the invasive intestine and the "casing"

intestine is carried out according to the technical standards adopted for mechanical intestinal obstruction.

We present the following case to illustrate the difficulties in diagnosis and errors in the treatment of intussusception in adults.

A 34-year-old patient C/H 15561/1005 on 07.08.2015 was urgently ad-mitted to the Department of Emergency Surgery of Andijan State Medical Institute with acute intestinal obstruction.

Complaints: abdominal pain, flatulence, stool retention, vomiting, general malaise.

Present history: *disease started 4 days ago.*

On examination: state of moderate severity. Consciousness is clear. Skin is palepink. Breath is vesicular, 26 breaths per minute. Heart tones are dull, tachycardia. BP is 120/80 mmHg, pulse is 96 beats per minute. Tongue is dry, cov-ered with dirty-grey plaque. Stomach is bulging, tender on palpation. Deep palpation showed pain in the right iliac region, and clearly detected a densely elastic, slow-moving infiltrate.

Common blood analysi:s Hb – 118 ã/ë; RBC – 4.02; CP- 0,8; WBC – 4.5; stab cells – 7; seg-mented – 68; eos – 1; lymph – 27; blood sedimentation rate – 38. Urine analysis: protein-abs, ep – 0-1-3, L – 5-5-6.

ECG- Right sinusoid rhythm.

X-ray showed cups of Kloyber.

*Ultrasound detetcted considerable formation in the right abdominal side with the size of 12*8 cm (may be intussusception). Loop of ileum is widened, full with liquid contents.*

On 07.08.2015 the patient underwent operation No.301, middle-median laparotomy under endotracheal anesthesia.

An increase and a thickening of the walls of the small intestine were estab-lished, with a further revision, intussusception of a part of the small intestine into the small intestine was revealed. Reduction of intussusception of the small intestine was unsuccessful.

The patient underwent resection of the small intestine with intussusception followed by anastomosis side to side.

Sanation of the abdominal cavity. Drainage tube was administered into the area of the anastomosis. The surgical wound was sutured in layers.

In the postoperative period, the patient was given antibacterial therapy, infusion therapy. On day 10 after surgery, the patient was discharged without complications.

The diagnosis after surgery is intestinal intussusception (*Fig. 2*).

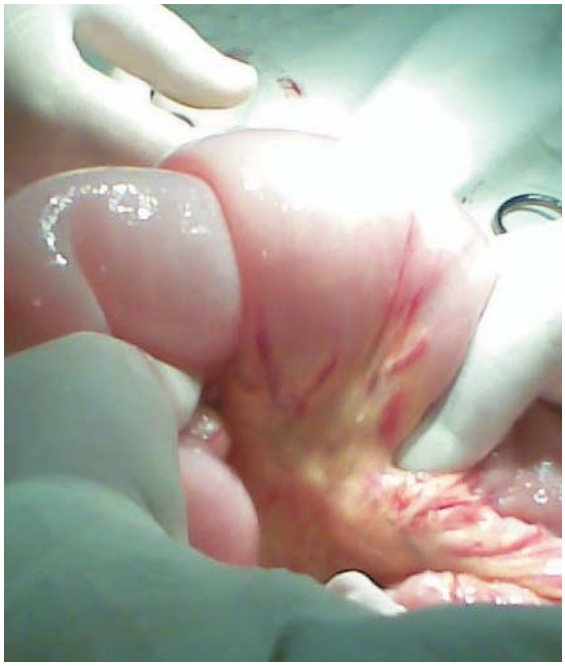

Fig. 2. Invagination the small intestine into the jejunum

A bunch of polyps was determined when dissecting intussusceptum on the mucous membrane of the small intestine. Given the presence of small intestinal polyposis, the patient was diagnosed with Pate-Eggers syndrome, multiple small intestinal polyposis.

Conclusion. The main cause of intestinal intussusception in adults are tumors. The younger the patient, the more severe intussusception is. The older the patient, the more likely the presence of the tumor, as the causes of intussusceptio. The older the patient, the faster the circulatory disorders in the intussuscepted intestine develop, the wider the zone of their spread, the higher the risk of circulatory necrosis after surgery. The larger the size of the intussuscepted intestine, the more the mesentery is involved in it, the more the blood circulation in the intussuscepted intestine is impaired, the faster the necrosis occurs. The higher the intussuscepted intestine is located, the more prevalent is presentation of high obstruction, the more complicated the course. The faster intussusception develops, the faster and deeper circulatory disorders occur in the intussuscepted intestine. During the operation for intussuscepted intestine, it is necessary to revise the entire intestine, intussusceptions may be multiple and unrecognized.

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PEUTZ–JEGHERS–TOURAINE' SYNDROME (CASE REPORT)

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Authors present two clinical observations of Peutz-Jeghers' syndrome, which is hereditary and is also called periorificial lentiginosis, multiple polyposis of the small intestine (jejunum mainly) with complications such as intestinal ob-struction intussusception associated with intra-colonic bleeding. The authors concluded that abdominal surgeons should know and remember about Peutz-Jeghers' syndrome, in order to avoid diagnostic and tactical errors and promptly provide expert surgical treatment.
Key words: *syndrome, emergency surgery, perioficial lentinginosis, intussusception, intestinal obstruction.*

Introduction. Peutz-Jeghers-Touraine's syndrome (synonym: periorificial lentiginosis) was first described by J. Hutchinson in 1896. A more detailed description was given by L. L. A. Peutz in 1921. A. Touraine called this condition Lentigo poliposis. H. Jeghers et al. in 1949, described 10 cases of this disorder and emphasized the characteristic triad: polyposis of the gastrointestinal tract, the hereditary nature of the disease, pigment spots on the skin and mucous membranes. Since then, this condition has been described as Peutz–Jeghers–Touraine's syndrome. This syndrome is found on all continents. Women develop this condition more often than men. The fact that the syndrome occurs in several members of the same family testifies in favor of its hereditary origin. Autosomal dominant inheritance.

Differential diagnosis is carried out with other intestinal tumors: diffuse familial polyposis, juvenile polyposis, multiple and single adenomatous and hyperplastic polyps, pseudo-polyps in ulcerative colitis and Crohn's disease. It is also performed with freckles, senile lentigo, LEOPARD syndrome, hereditary forms of lentiginosis, especially systemic and with mastocytosis. Often the disease is accompanied by cancer of the ovaries and the body of the uterus, breast and pancreas [1–7].

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These circumstances indicate the complexity and difficulty of diagnosis, as well as the unresolved issues of surgical treatment of Peutz–Jeghers–Touraine's syndrome.

Case

Patient B., was born in 19, was urgently admitted to the Department of Clinical Surgery No.3 of Andijan State Medical Institute on 01.06.2009 at 6.40 pm with acute intestinal obstruction.

Presentation: dry mouth, aching and cramping pain throughout the abdomen, nausea, vomiting, gas and stool retention, as well as general weakness and indisposition.

Present history: considers himself ill for a week. She does not associate his disease with anything. According to the parents, 3 years ago she was operated on acute intestinal obstruction at the Department of Pediatric Surgery of the Republican Scientific and Practical Center for Cardiovascular Surgery of Andijan branch. In addition, she was repeatedly consulted by various specialists on the lack of appetite and retardation in physical development and the presence of moderate painful sensations in the abdomen without the proper effect.

On examination: on admission the patient's condition was of moderate severity. There were signs of retardation of physical development. Height – 150 cm, weight – 38 kg. The skin and visible mucous were of pale color. Around the upper and lower lips there was dark brown pigmentation with a diameter of 2–3 mm, lined in

one row at the border of the transition to the skin of the labial surface (*Fig 1*).

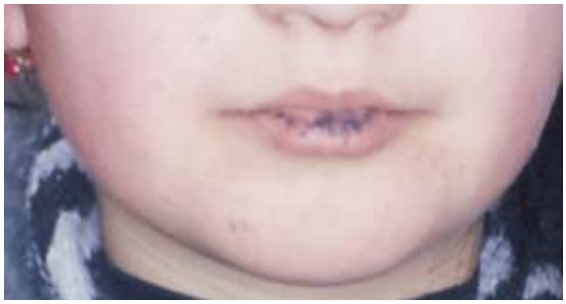

Fig. 1. Patient B. There are dark-brown color pigmentation around upper and downer lips, diameter 2–3 mm, lined one row with border to the lips skin

Tongue was wet and coated. Respiration rate was 20 per minute. Above the lungs: breathing in all departments, no wheezing. Heart rate was 100 beats per minute, blood pressure was 110/70 mmHg The abdomen was of the usual form, soft, moderately tender in all departments on palpation. Symptoms of peritoneal irritation were absent. Absence of defecation for 3 days. Flatulence. Urination was without difficulties, regular.

ECG findings: sinus tachycardia. The horizontal position of electric axis of the heart. Hypertrophy of the left atrium and ventricle. Diffuse changes in the myocardium.

Plan radiography of the chest and abdomen: the pulmonary fields are clean, the sinuses are not blocked, the heart and aorta are without abnormalities. There are no signs of free gas in the abdominal cavity; there are single cups of Kloyber. Urine tests did not show any pathology.

Complete blood count: erythrocytes 3.42×1012, hemoglobin 61 g/l, hematocrit number 26, CP 0.7, leukocyte count 8.1×109, ESR 12 mm/h.

Diagnosis: acute mechanical intestinal obstruction.

The patient underwent complex preoperative preparation (nasogastric probe with gastric lavage, parenteral administration of electrolytes, preventive antibiotic therapy, etc.).

On 01.06.2009 middle-median laparotomy was performed with excision of the old postoperative scar under endotracheal anesthesia after appropriate treatment of the skin with hemostasis along the wound.

Revision of the abdominal organs showed the presence of 3 and 4-cylinder intussuscept (*Fig. 2*).

After their reduction, the viability of the intestines was preserved. Palpation in these places detected glandular polyps on the pedicle with a diameter of 2.0 to 3.5 cm, which due to the

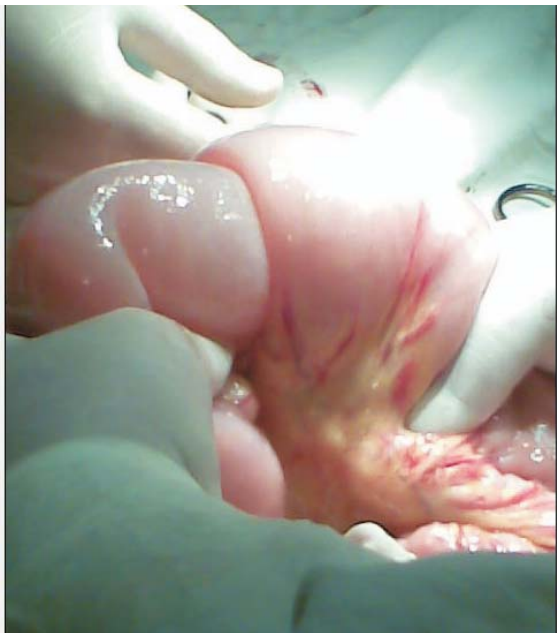

Fig. 2. Sight invagination intestinal obstruction, patient B

overhanging contributed to the formation of intussuscepta. Excision of polyps was performed by longitudinal enterotomy, followed by closure of the bowel defect in the transverse direction, in order to avoid narrowing of its lumen.

Upon further revision, the presence of a multiple polyps was established in the jejunum and single polyps in the ileum with a diameter of 0.7–1.0 to 3.0–4.0 cm, which could further prevent the passage of its contents and the absorption of nutrients. In addition, enterotomy, excision of polyps and suturing of the defect were performed in 14 places in the same way (*Fig. 3*).

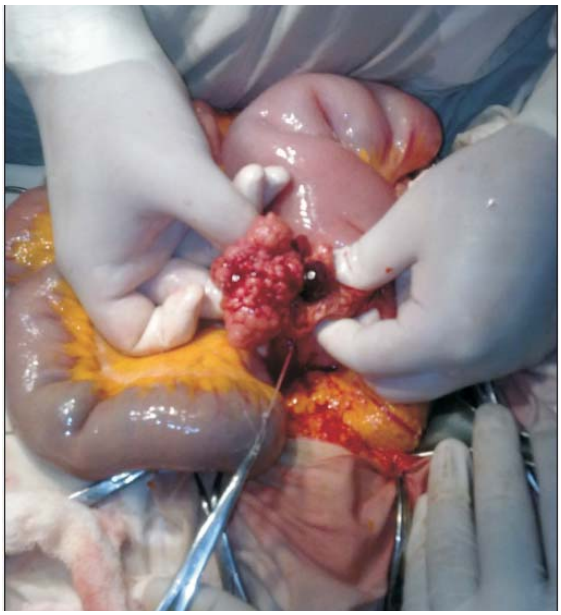

Fig. 3. Sight polyps in enterotomy, patient B

The patient was administered nasogastroduodenal decompression probe, expansion of the anus according to Payr, as well as thorough reorganization of the abdominal cavity with antiseptic solutions. Drainage of the abdominal cavity was performed for control. Laparotomy wound was closed by layer-by-layer suturing with aseptic dressing.

Gross specimen: glandular-villous polyps of the small intestine in the amount of 27, with a diameter of 1.5–2.0 to 3.5–4.0 cm. Of them, 3 polyps had signs of hemorrhage. Histological findings: smooth muscle polyps (*Fig. 4*).

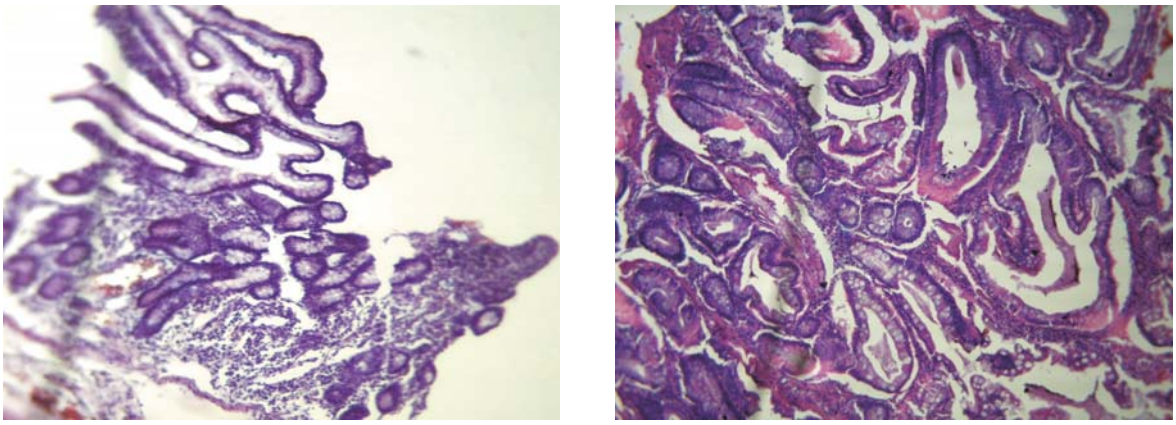

Fig. 4. Micro-preparation of patient B. Polyps tenia of the smooth muscle.
Color hemotoxilin eosinum. Enlarged with Leits Biomed microscope. Î B: 40. Î Ê: 10

The postoperative period was uneventful, without complications. On 09.06.2009 the patient was discharged from the hospital in a satisfactory condition. At the same time, the patient was recommended a follow-up every 6 months.

The patient was monitored every 6 months. After 2 years, she gained 15 cm in height, 17 kg in weight (height 151 cm, weight 38). She felt well, there were no signs of retardation of physical development. Intestinal function was normal.

After reviewing the literature data and assessing this case, we concluded that there was a triad of signs of Peutz–Jeghers' syndrome: perioral hyperpigmentation, multiple small intestinal polyposis (mostly jejunum) and the presence of intussuscepted jejuno-jejunal obstruction. Moreover, when performing the first operation (reduction of intussusception), its cause was not eliminated. This contributed to the recurrence of acute intestinal obstruction in the form of intussusception, as well as preservation of signs of retardation of physical development and chronic anemia of moderate severity.

This confirmed the complexity of diagnosis and surgical tactics in this disease.

After 1.5 years, we had an opportunity to observe the 2nd case. We present the second observation.

Patient X, born in 1997, was urgently admitted to the Department of Clinical Surgery No.3 of Andijan State Medical Institute on 02/02/2012 at 10.35 am with acute intestinal obstruction, total polyposis of the small intestine.

Present history: from 10/08/2011 to 10/13/2011, she was hospitalized for a palpable abdominal tumor projected in the surgical department of the RCEME of the Andijan branch. She was also consulted by an oncologist. As a result of a comprehensive study, a diagnosis of total intestinal polyposis was established. After conservative treatment she was discharged in a relatively satisfactory condition.

On 8 January 2012 she was repeatedly hospitalized for acute intestinal obstruction, with signs of moderate anemia in the surgical department of the RCEME of the Andijan branch. The laparotomy, reduction of jejuno-jejunal intussusceptum was made. She was also found to have polyposis of the small intestine without intervention on it. She was discharged from the hospital on 15.01.2012 year in a relatively satisfactory condition. Two days prior to admission she complained of cramping and rumbling all over the abdomen, nausea, vomiting, gas and stool retention, as well as lack of appetite, general weakness and malaise.

She was admitted to the Department of Clinical Surgery No.3 on 02.02.2012.

On admission the patient's condition was of moderate severity. There were signs of retardation of physical development. Height 162 cm, weight 47 kg. The skin and visible mucous were of pale color. Around the upper and lower lips there was

dark brown pigmentation with a diameter of 1–2–3 mm, lined in one row at the border of the transition to the skin of the labial surface (*Fig. 5*).

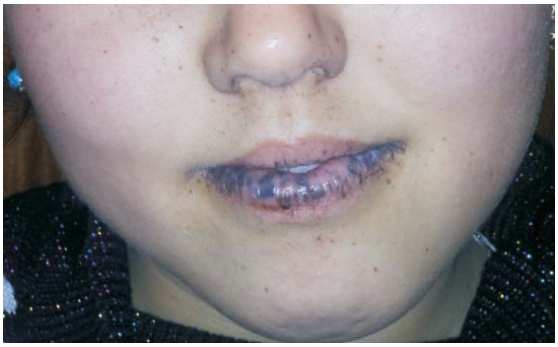

Fig. 5. Patient B. There are around upper and lower lips dark-brown color pigmentations with diameter 1–2–3 mm, covered in one row on border of the transition to skin of the labial surface

Tongue was wet and. Respiration rate was 20 breaths per minute. Above the lungs breathing is carried out in all departments, no wheezing. Heart rate was 100 beats per minute, blood pressure 110/70 mmHg. The abdomen was of usual configuration, with a postoperative scar in the mid-midline, the abdomen was soft on palpation, moderately tender in all departments. Symptoms of peritoneal irritation were absent. Her last defecation was 4 days ago. Flatulence. Urination was without difficulties, regular.

ECG findings: sinus tachycardia. The normal position of the electrical axis of the heart. Diffuse changes in the myocardium.

Plan radiography of the chest and abdomen: the pulmonary fields were clean, the sinuses were not blocked, the heart and aorta were without abnormalities. There were no signs of free gas in the abdominal cavity; there were single cups of Kloyber. Urine tests did not show any pathology.

Complete blood count: erythrocytes 3.0× 1012, hemoglobin 74 g/l, hematocrit count 26, CP – 0.7, leucocytes 4.2×109, ESR – 5 ì ì /h.

Diagnosis: Peutz–Jeghers' syndrome.

The patient underwent complex preoperative preparation (nasogastric probe with gastric lavage, parenteral administration of electrolytes, preventive antibiotic therapy, etc.).

On 03.02.2012 at 10.14 pm middle-median laparotomy was performed with excision of the old postoperative scar under endotracheal anesthesia after appropriate treatment of the skin with hemostasis along the wound.

Revision of the abdominal organs showed the presence of 3 and 4-cylinder jejuno-jejunal intussuscepta. After their reduction, the viability of the intestines was preserved. Palpation in these places detected glandular polyps on the pedicle with a diameter of 2.0 to 3.5 cm, which contributed to the formation of intussuscepta. Excision of polyps was performed by longitudinal enterotomy, followed by closure of the bowel defect in the transverse direction, in order to avoid narrowing of its lumen.

Upon further revision, the presence of a multiple polyps was established in the jejunum and single polyps in the ileum with a diameter of 0.7–1.0 to 3.0–4.0 cm, which could further prevent the passage of its contents and the absorption of nutrients. In addition, enterotomy, excision of polyps and suturing of the defect were performed in 22 places in the same way. The patient was administered nasogastroduodenal decompression probe, expansion of the anus according to Payr, as well as thorough reorganization of the abdominal cavity with antiseptic solutions. Drainage of the abdominal cavity was performed for control. Laparotomy wound was closed by layer-by-layer suturing with aseptic dressing.

Gross specimen: glandular-villous polyps of the small intestine in the amount of 42, with a diameter of 1.5–2.0 to 3.5–4.0 cm. Of them, 3 polyps had signs of hemorrhage. Histological findings: smooth muscle polyps.

The postoperative period was uneventful, without complications. On 15.02.2012 the patient was discharged from the hospital in a satisfactory condition. At the same time, the patient was recommended a follow-up every 6 months.

Results. After reviewing the literature data and assessing this case, we concluded that there was a triad of signs of Peutz–Jeghers' syndrome: perioral hyperpigmentation, multiple small intestinal polyposis (mostly jejunum) and the presence of intussuscepted jejuno-jejunal obstruction. Moreover, when performing the first operation (reduction of intussusception), its cause was not eliminated. This contributed to the recurrence of acute intestinal obstruction in the form of intussusception, as well as preservation of signs of retardation of physical development and chronic anemia of moderate severity.

The patient was recommended sparing diet, restricting physical exertion, medication, astringent agents (bismuth nitrate). Pigmentation of lips was treated with laser light. Follow-up every 6 month for 3 years.

After 1 year her height was 162 cm, weight 47 kg. She was in satisfactory condition, without signs of retardation of physical development. Function of the bowels was normal.

Conclusions

Abdominal surgeon should know about Peytz–Jeghers' syndrom to provide correct diagnosis and timely give qualified emergency surgical treatment, completely remove polyps, promote normalization of intestinal function, prevent relapsing of intussusception and obstruction of the intestine.

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GENERAL NUTRITIONAL PRACTICES IN SCHOOL-AGE CHILDREN OF KHARKIV REGION

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Abstract. Pediatric nutrition has become one of the cornerstones of global health due to its association with the most insidious non-communicable diseases. As part of the research "Assessment of the current nutritional status, nutrition-related health problems in school-age children in Ukraine", conducted at Kharkiv National Medical University, general nutritional habits and practices of school-age children of Kharkiv region were assessed for the further elaboration of educational programs. Current nutritional status was assessed by using original questionnaire (adapted from the FAO recommendations) in 392 school-age children, divided into 3 groups: primary school (75 children aged 6–9), middle school (202 children aged 10–14) and high school (115 children aged 15–18.), who were randomly selected in urban and rural areas of the region.

The study showed a trend for irregular nutrition, ascending with age. Family traditions for regular meals are still powerful. There is a decrease of this tendency in high-school age, when the quarter of children become less sure in exact impact factors on the choice of food. It was established that about 20 % of school-age children skipped their breakfasts, but understood possible health-related outcomes. Almost all children were found to have unhealthy snacks such as pastry, sweets and sugary beverages. Besides, 80 % of school-age children spend their pocket money on food and purchase it at the nearest groceries or school canteen. And this tendency is statistically higher in middle-school age. There is no particular involvement of parents in day-time nourishment as just 13 % of them give lunch-boxes to their children.

Conclusions:

1. Nutrition of school-age children is not balanced with incorrect energy distribution during the working day: tendency for skipping breakfasts and to have multiple unhealthy snacks between main meals (pastry, sweets, sugary drinks etc.).
2. Educational programs for school-aged children must be focused on the choice of healthy snacks and drinks as well as outcomes of inappropriate nutrition. Particular attention should be paid to the education of middle-school children.
3. Parents should be actively involved in the educational programs due to the significant influence of family traditions on the nutrition of school-age children.

Key words: *Nutrition, general nutritional practices, school-age children, educational programs.*

Introduction. Nutrition of children has become one of the most important problems of the international health policy. The WHO is a global leader, which has recently proclaimed: "In September 2017, we jointly launched The State of Food Security and Nutrition in the World, marking the beginning of a new era in monitoring progress towards achieving a world without hunger and malnutrition, within the framework of the Sustainable Development Goals" [1]. Beside the malnutrition breast feeding [2] and pediatric obesity are in the focus [3]. Moreover, overweight was stated as the one of the forms of malnutrition, which underlines the double burden of disease in low and low-middle income countries [4] due to endorsement of economic costs of the problem [5]. According to the global recommendations, the specific national data about state of nutrition are necessary to attain the goal.

2. Purposes, subjects and methods:

2.1. Purpose – was to assess general nutritional habits and practices of school-age children of Kharkiv region for further development of nutrition education programme.

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2.2. Subjects & Methods. This work is a part of research "Assessment of the current nutritional status, nutrition-related health problems in school-age children in Ukraine", conducted at Kharkiv National Medical University for the development and further implementation of social education program for prevention of non-communicable diseases.

A cross-sectional study was conducted in three different geographic regions of Ukraine. The present data provides survey results of Kharkiv region children (as a representative of eastern part of country).

For the survey the original questionnaire (adapted according to the FAO recommendations) was elaborated for the analysis of broader context (economic, social, environmental factors) that influences on nutrition.

Assessment of current nutritional status in school-age children of 3 age groups (aged 6–9, 10–14, 15–18), who were randomly selected in urban and rural areas of region, was performed.

The total number of participants was 392 school-age children. The high school group (aged 15–17) consisted of 115 children aged 15.28 ± 1.47 that included 29 (25.22 %) boys and 86 (74.78 %) girls.

The middle school group (aged 10–14) consisted of 202 children aged 12.55 ± 1.40 that included 95 (47.03 %) boys and 102 (52.97 %) girls.

The primary school group (aged 6–9) consisted of 75 children aged 8.20 + 1.27 that included 43 (57.33 %) boys and 32 (42.67 %) girls.

The study was approved by the institutional Committee in Ethics and Bioethics of Kharkiv National Medical University. Written consent from parents and children was obtained for every participant.

Standard statistics was used for the data analysis.

Conflict of interests. There is no conflict of interests.

3. Results and discussion. The survey results have shown that 83.16 % school age children have regular breakfast and vast majority of them (84.84 %) do it at home and 15.01 % at school.

Regular lunch is eaten by 93.31 % of children, 45.97 % of them have their lunch at home after school, 44.93 % at school and 9.83 % in other places. The study showed that the number of primary and middle-school children had their lunch more regularly (ð=0.03) than high school children.

Moreover, 13.26 % respondents (with no difference in groups) take the meal precooked by their parents, 31.67 % have their lunch in school canteen and 9.83 % purchase meal in different cafeteria with the pocket money. And the tendency for purchasing meal is age-dependent (from 5.5 % primary school to 18.64 % high school, p=0.03)

Dinner is usually eaten at home (93.18 %). But it is less regular (ð<0.01) for high-school (88.7 %) as compared to middle-school (97.02) and primary-school (95.9%) children.

Snacks between main meals are eaten by 76.53% children. The list of the most common snacks is as follows:

• 82.88 % – pastry, which is less typical for primary-school (18.9%) and the most common for middle-school (72.55 %) with a further decrease in high-school (54.12 %);

• 58.33 % – seasonal fruit (the tendency is the same);

• 50.33 % - sandwiches with cheese or sausages (the tendency is the same);

" 51.66 % – sweets, less common (p<0.001) for primary-school children (12.6 %) with no difference between middle- and high-school;

• 16.33 % – potato chips and crisps, more popular (p=0.02) between middle-school children (2.57 %)

The most favored drinks include tea (46.66 %), sweet sparkling beverages (mainly for middle age – 23.66 %), juice (32.33 %), coffee (mainly in girls from middle and high school – 16.99 %), energy drinks (3.66 %).

About 70 % of respondents spend their pocket money on meals and additionally to this 13 % do it when they have money.

The vast majority of children purchase their snacks in school canteen (53.41 %) and the nearest groceries (63.66 %). Meanwhile, 4.96 % buy street food. Only 37.26 % of children buy appropriate lunch and it is mainly (ð<0.01) middle-age children (66.18 %).

The family influence (59.94 %) is the most significant factor for choosing meals that children normally consume. This factor is more powerful in primary middle school (more than 60 %) and significantly (p<0.01) drops down in high-school (48.69 %). Impact of mass-media advertisement (10.2%) and peers (9.43 %) is relatively low. Alternatively, 21.93 % of respondents were unable to explain what exactly influences their food priorities. Interestingly, 25 % of high-school children are beside them.

Main meal together with two snacks is considered to be a good nutritional plan, which is easy to follow (for 75.51%).

Surprisingly, only 45.15 % of children reported that assorted nutrition was a good thing, 33.43 % were against this statement and 21.41 % were not sure. According to the responses, an assorted nutrition is available for 76.53 %.

Taking into account the fact that breakfast is a main meal that serves to the appropriate energy distribution during the day, we paid a particular attention to this meal in the frames of survey. Thus, 90.83 % of children consider breakfast to be an essential meal. But they become less sure in this in the middle-age ($p<0.01$ with primary and high school). It is not difficult to have regular breakfast for 64.41 % children and occasional difficulties are met by 26.53 %.

Assessment of "open questions" concerning health-related problems due to skipped breakfast has shown that they are aware of potential harm. Along these lines, 42.82 % of children are concerned about gastrointestinal disorders (abdominal pain, gastritis, ulcer, vomiting). The number of middle-school children is significantly (ð<0.01) higher beside them (57.42 %) as compared to the primary-school (29.33 %) and high-school (34.78 %).

Potential general problems (headaches, tiredness, fatigue, moodiness, low energy), directly related to school performance were reported by 53.01 % of participants. Markedly general problems were more frequently ($p<0.0001$) reported by high-school (59.13 %) and middle-school (57.92 %) children versus primary-school ones (30.66 %). Relation to the overweight, underweight or diabetes was marked just by 1 % of responders.

Summarizing the obtained data, 20 % of school-age children have no breakfast, but they are mainly aware of health-related outcome.

The tendency to irregular nutrition decreases with age, but it is not dramatic due to powerful influence of family traditions, which decreases in high school age, when the quarter of children become less sure in exact impact factors on the choice of food.

Nutritional pattern of school-age children during the working day attracts particular attention. On the one hand almost half children have their lunch after school at home and one third of them in school canteen. On the other hand, there is no particular involvement of parents in day-time nourishment as only13 % of them give lunch-boxes to their children.

The study showed that almost all children had unhealthy snacks such as pastry, sweets and sugary beverages. And this tendency is statistically higher in middle-school age. Eighty percent of school-age children spend their pocket money on food and purchase it at the nearest groceries or school canteen.

Conclusions:

1. Nutrition of school-age children is not balanced with incorrect energy distribution during the working day: tendency for skipping breakfasts and to have multiple unhealthy snacks between main meals (pastry, sweets, sugary drinks etc.).

2. Educational programs for school-aged children must be focused on the choice of healthy snacks and drinks as well as outcomes of inappropriate nutrition. Particular attention should be paid to the education of school-children to prevent nutrition-related problems in middle-school.

3. Parents should be actively involved into the educational programs due to the significant influence of family traditions on the nutrition of school-age children.

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DISEASES OF THE RESPIRATORY SYSTEM WITH THE SUBSEQUENT FORMATION OF CARDIOVASCULAR PATHOLOGY IN CHILDREN

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Diseases of the respiratory system are one of the most frequent causes of the treatment of children in hospital facilities. The younger the child, the more often these diseases occur and the more severe it can be. Cardiovascular disorders with bronchopulmonary pathology develop slowly, potentially reversible in childhood, which requires a correct assessment of the risk of their development for a particular patient and timely correction of therapy. The presence of dyspnea, prolonged exhalation, pale skin, cyanosis of the nasolabial triangle and acrocyanosis, swelling of the nose (symptoms common to cardiac and respiratory failure) indicate the reaction of the cardiovascular system in diseases of the respiratory system. We examined 14 children: among them 7 boys and 7 girls. Ten children were diagnosed with acute obstructive bronchitis, and 4 with pneumonia. In the course of the study, the parameters were assessed, reflecting the linear dimensions of the heart cavity and the main vessels, followed by the calculation of central hemodynamics, diastolic transmittal blood flow by the method of L.K. Hattle, B. Angelsen.

Key words: *bronchopulmonary pathology, children, electrocardiography, doppler echocardiography of the heart.*

Introduction. Respiratory diseases are one of the most common causes for the treatment of children in hospitals. The younger the child, the higher the incidence of these diseases and the more severe it may develop [1, 2]. Cardiovascular disorders in broncho-pulmonary pathology develop slowly, are potentially reversible in childhood, requiring a proper assessment of the risk of their development for a particular patient and timely correction of therapy tactics [3].

Toxicosis, as well as frequent concomitant diseases and oxygen deficiency cause profound changes in tissue metabolism, decrease in the processes of energy formation, disturbance of the regulatory function of central and autonomic nervous systems. All these factors affect the activity of the heart and the circulatory system as a whole, developing both compensatory, adaptive and pathological reactions [4].

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The reaction of the cardiovascular system in diseases of the respiratory system is characterized by dyspnea, prolonged vision, pallor of the skin, cyanosis of the nasolabial triangle and acrocyanosis, inflammation of the nasal wings, a decrease in the ratio of respiratory and pulse rates [5], tachycardia that does not correspond to body temperature, accent of tone 2over the pulmonary artery, muffling of the tone of the heart, systolic murmur of soft tone (general symptoms of cardiac and respiratory failure) [6].

Assessment of literature data showed that bronchopulmonary diseases, which begin their pathological path in early childhood, may lead to irreversible changes in adults with the development of complications and early mortality [7, 8]. Thus, children with frequent respiratory diseases may potentially replenish the population of adults with chronic obstructive pulmonary diseases, which is a very significant problem, requiring a combination of efforts of different specialists [9, 10].

2. Purposes, subjects and methods:

2.1. Purpose – to study the development of cardiovascular disorders in children from 1 month to 3 years with bronchopulmonary disorders.

2.2. Subjects & Methods. The research was carried out at the Department of Pediatrics No.1 and Neonatology of KhNMU, at the Department of Infectious Diseases of Kharkiv Regional Children's Clinical Hospital. The study implied the assessment of histories, clinical and instrumental data. The features of bioelectric activity of the heart in the examined children were assessed by the results of electrocardiography. In the course of the study, we evaluated the indices reflecting the linear dimensions of the cardiac cavity and major vessels with subsequent calculation of central hemodynamics, diastolic transdermal blood flow by the method of L.K. Hattle and B. Angelsen following Doppler echocardiography of the heart ("AU 3 Partner" by "Esaote Biomedica" (Italy).

Conflict of interests. There is no conflict of interests.

3. Results and discussion. We examined 78 children aged from 1 month to 3 years, who were divided into 3 groups: Group 1 included 28 (35.8 %) children with acute obstructive bronchitis and pneumonia, Group 2 comprised 27 children (34.6 %) with acute simple bronchitis, Group 3 was the control group of 23 children (29.6 % of healthy children). The average age of children was 1.5 ± 1.6 years. The groups were representative and comparable by gender and age.

Assessment of family histories showed that most children (75 %) were the first child in the family. First-degree relatives of 28.6 % children had cardiovascular disorders, namely arterial hypertension. Mothers of 37.5 % children had pains or discomfort in the area of the heart on exertion and stress, which resolved spontaneously or after taking sedative.

Parents of 62.5 % children were overweight, due to insufficient motor and sedentary lifestyles. During pregnancy mothers of 87.5 % children were examined for TORCH infections, of whom 50 % were infected with herpes virus or rubella. Parents of 62.5 % children often drank alcohol or low-alcohol beverages; fathers of 87.5 % smoked, and both parents of 25 % smoked. Mothers of 12.5 % children have focal points of chronic infection (chronic tonsillitis).

Assessment of children and their relatives' complaints on admission showed the following data. Cough and dyspnea were observed in all children. In this case, 75 % of mothers described the cough as dry or non-productive. Elevated body temperature was observed in 87.5 % of children. Besides, 62.5 % of children had nasal congestion or mucous discharge from the nose, and 50 % had distant wheezing. Features of bioelectric activity of the heart in the examined children were determined by ECG.

There were 8 (12 %) patients with no ECG changes.

In other 88 %, morphological and functional features were registered. The violation of ventricular myocardial repolarization was prevalent in 73.8 %, and nomotonic rhythm disturbances in the form of sinus tachycardia in 40.5 %. Also, overload and hypertrophy of the right chambers of the heart were observed in 18 % and a decrease in bioelectric activity of the heart (voltage) in 14.3 %.

The control group children were also found to have a significant difference in numbers. Thus, violation of ventricular myocardial repolarization and nomotonic rhythm disturbances in the form of sinus tachycardia occurred much less commonly, in 14 and 19 % respectively. And such changes as overload and hypertrophy of the right chambers of the heart and a decrease in bioelectric activity of the heart were not recorded at all.

The study of morphology of the heart, functional state of the myocardium and indices of central hemodynamics implied an assessment of Doppler echocardiography findings. Doppler echocardiography (DopECHOCG) of the heart showed an increase in mean pressure on the pulmonary artery (PA) to 20 mmHg (63 %), which significantly exceeded the norm ($p<0.05$) in comparison with the control group, 1st degree regurgitation of the tricuspid valve (14 %) and 1^{st}–2^{nd} degree of the PA valve (23 %), which was significantly increased in comparison with the control group (ð<0.05); an increase in the diameter of the right atrium and right ventricle (30%), which significantly differed in patients of the control group ($p<0.05$). Mild structural anomalies of the heart were recorded with the same frequency and the rates did not exceed the average incidence in the population.

A comprehensive cardiac examination using ECG, Doppler echocardiography of the heart made it possible to detect early changes in the cardiovascular system in the form of sinus tachycardia, an increase in average pressure on the airway, an increase in the diameter of the right atrium and right ventricle, etc. Acute inflammatory process in the respiratory tract is accompanied by disturbances of microcirculation, which in turn can lead to systemic disruption of the functioning of the whole organism. But most often it affects the cardiovascular system.

4. Conclusions. In order to prevent the development of cardiovascular complications in the cardiovascular system in young children, it's necessary to provide:

– timely detection and appropriate treatment for children with acute broncho-pulmonary pathology;

– dynamic monitoring with ECG and DopECHOCG.

These data should be taken into account when monitoring children to identify the risk group for the development of cardiovascular complications with possible administration of antihypoxic agents.

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FEATURES OF FORMATION AND PROGRESSION OF CHRONIC KIDNEY DISEASE IN CHILDREN WITH PYELONEPHRITIS AND VESICOURETERAL REFLUX

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Vesicoureteral reflux (VUR) is observed in 40 % of children with pyelonephritis and is one of the leading causes of its recurrent course, which subsequently leads to chronic kidney disease. The purpose of this study was to determine the peculiarities of the formation and progression of chronic kidney disease in children with pyelonephritis and vesicoureteral reflux. The clinical material from 141 children aged from 6 months to 17 years with grade I–V VUR in the period of clinical and laboratory remission of pyelonephritis was analyzed. The study showed that the risk of developing scarring of renal parenchyma in children with high-grade VUR was 8 times higher than in children with grade I-II VUR. And the risk of developing scarring of the renal parenchyma in patients with grade V VUR is 3.8 times higher than in children with grade III–IV VUR. In recurrent pyelonephritis, the risk of scarring of the renal parenchyma is 1.8 times higher than in one episode of inflammation. In patients with a high grade of reflux, the risk of recurrent pyelonephritis is 2.6 times higher than in children with grade I-II VUR. In patients with pyelonephritis and high-grade VUR, with signs of systemic undifferentiated connective tissue dysplasia, the risk of developing scarring of the renal parenchyma is 33.9 times higher. Depending on the grade of VUR and the presence of signs of scarring of the renal parenchyma, the degree of CKD increases, which reflects the functional state and severity of pathological changes in the kidneys.
Formation and progression of chronic kidney disease in children with pyelonephritis and VUR depends on the course of pyelonephritis, the grade of VUR and presence of signs of scarring in the renal parenchyma.
Keywords: *Vesico-ureteral reflux, renal scarring, pyelonephritis, children.*

Introduction. Vesicoureteral reflux (VUR) is observed in 40% of children with pyelonephritis and is one of the leading causes of its recurrent course [1, 2]. Recurrent course and chronic interstitial inflammation of the kidneys, especially secondary to VUR, initiates the development and progression of nephrosclerosis in 30–60 % of patients, leading to chronic kidney disease, and subsequently chronic renal failure in 25–60 % of patients [3–6]. Despite the fact that VUR has been studied for more than a century, no pathognomonic symptoms have yet been detected. It is for this reason that VUR is often diagnosed and treated at late stages, as late as in the presence of signs of scarring of the renal parenchyma. A lot of studies have been carried out over the last decade to find early diagnostic criteria for kidney damage in children with VUR [7, 8]. However, there is a lack of information on the peculiarities of the formation and progression of chronic kidney disease in children with pyelonephritis and vesicoureteral reflux.

2. Purposes, subjects and methods:

2.1. Purpose – is to determine the peculiarities of the formation and progression of chronic kidney disease in children with pyelonephritis and vesicoureteral reflux.

2.2. Subjects & Methods. The study involved assessment of clinical material from 141 children aged 6 months to 17 years with grade I–V VUR in the period of clinical and laboratory remission of pyelonephritis (more than 3 months after the last episode of exacerbation). Taking into account the grade of VUR and the method of its correction, the examined children were divided into three groups: Group 1 (n=24) included patients with pyelonephritis and grade I–II VUR after or at the stage of conservative treatment,

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Group 2 (n=87) comprised children with pyelonephritis and grade III–IV VUR after endoscopic correction, Group 3 (n=30) included children with pyelonephritis and grade V VUR after surgical correction of VUR. Statistical analysis was performed using Stat Soft STATISTICA Version 7 (Tulsa, OK). The planned clinical trial was approved by the Medical Ethics Committee of Kharkiv National Medical University and was conducted in accordance with the guidelines of Helsinki Declaration. All participants and/or their parents gave written informed consent to participate.

Conflict of interests. There is no conflict of interests.

3. Results and discussion. Assessment of age distribution showed that the number of children of junior and preschool age ($p < 0.001$) (*Table*) was statistically more significant, which corresponded to world statistics on the age distribution of patients with VUR [9–13].

Physical examination of patients with pyelonephritis and VUR did not show any probable differences between accelerated or delayed physical development according to individual components. The study showed that 33 ((24.40 ± 3.56) %) patients of the main group had a tendency to allergic reactions, 82 ((58.16 ± 4.15) %) patients had chronic foci of infections of ENT organs, 47 (33.33 ± 3.97) % in the oral cavity, which can significantly affect the protective forces of the body and contribute to the subsequent relapse of pyelonephritis. In 110 ((78.01 ± 8.45) %) patients, pyelonephritis

Distribution of patients with pyelonephritis and VUR by age and gender

Age / Gender	6 months – 6 years		7–11 years		12–17 years		Total	
	n	p%±$s_{p\%}$	n	p%±$s_{p\%}$	N	p%±$s_{p\%}$	N	p%±$s_{p\%}$
Boys	19	13.5±2.9	14	9.9±2.5	5	3.6±1.6	38	26.9±3.7
Girls	65	46.1±4.2	22	15.6±4.3	16	11.4±2.6	103	73.1±3.7
Total	84	59.7±4.1*	36	25.5±3.6*	21	14.9±2.9*	141	100.0±0.0

Notes: n is the number of observations; p% is sample share in percent; sp% is statistical error of the sample share in percent; * is percent from the total number of patients.

This may be a reflection of the fact that the debut of pyelonephritis secondary to VUR most often occurs at an early age. Gender distribution analysis showed that, regardless of age, in all groups of children with pyelonephritis and VUR, the number of girls was statistically more significant than boys ($p < 0.001$), which does not contradict the data of the European Association of Urologists (EAU, 2012) [7].

According to the European Registry, provided by the EDTA (European Dialysis and Transplant Association), the incidence of congenital and hereditary kidney diseases has increased in recent decades, contributing to the development of CKD. The progressive increase in the number of patients with VUR is attributed to the pathology of antenatal development [14–16]. Chronic intrauterine fetal hypoxia has been found to be a risk factor for the development of renal dysembryogenesis. Assessment of medical records concerning the course of pregnancy and labor, heredity and premorbid background testify to the negative influence of adverse factors on the formation of congenital malformations of urinary organs, which does not contradict the literature data [17]. The researchers provide evidence that the incidence of chronic pyelonephritis and VUR is accompanied by a high genealogical index [18]. Family histories of the patients under examination showed the presence of congenital malformations of the urinary organs, pyelonephritis and urolithiasis in parents and / or close relatives of 55 ((39.01 ± 9.95) %) patients.

manifested at a younger age ($p < 0.0001$). Patients of all groups with the same frequency came for examination with changes in clinical analysis of urine in the form of leukocyturia and fever of unknown origin. Hyperthermia as the first manifestation of pyelonephritis was observed predominantly in young children, in rare cases, fever was combined with dysuric signs, but no significant intergroup differences were observed. Pain syndrome and dysuric signs in manifestation of pyelonephritis were predominantly observed in adolescents. In one child, the reason for nephro-urological examination, in addition to hyperthermia, was an urgent surgical intervention due to carbuncle of the left kidney.

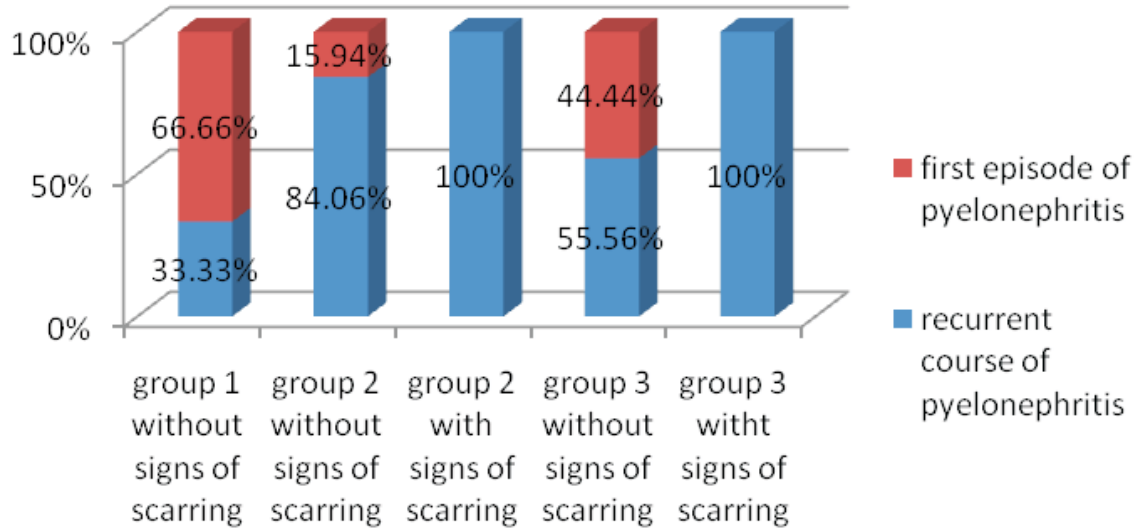
According to the results of voiding cystography, higher grades of VUR (III, IV, V) ($p<0.0001$) were observed more frequently, without a statistically significant difference between the lesion side or bilateral localization (total $p<0.05$), but unilateral lesion was more frewent than bilateral in all grades of VUR ($p=0.0001$). In 39 (27.66 ± 3.77 %) of the subjects with pyelonephritis and VUR, there were signs of scarring of the renal parenchyma. The risk of

developing scarring of the renal parenchyma in children with high grades of VUR (III, IV, V) is 8 times higher than in children with grade I–II VUR (RR = 8.00 [1.16; 55.44]). And the risk of developing scarring of the renal parenchyma in patients with grade V VUR is 3.8 times higher than in children with grade III–IV (RR=3.38 [2.11; 5.43], p<0.05), which does not contradict the literature [19, 20].

In the vast majority of subjects (68.79 ± 3.90 %, p <0.0001), pyelonephritis secondary to VUR had a recurring course with the number of episodes from 2 to 6 (*Figure*). In recurring course of pyelonephritis, the risk of scarring of the renal parenchyma is 1.8 times (RR=1.81 [1,50; 2,18]) higher than in one episode of inflammation. The risk of recurrent pyelonephritis in children with a high reflux rate is 2.6 times (RR = 2.55 [1.35; 4.80]) higher than in children with grade I–II VUR.

Besides, 54.61 ± 10.16 % patients were found to have concomitant kidney disease secondary to VUR. Namely: 68 (48.23 ± 10.19 %) children had dysmetabolic nephropathy, which was caused not only by metabolic disorders, but also by the presence of VUR, which created an obstacle to the outflow of urine. Carbuncle of the kidneys, as a purulent-inflammatory disease, was observed in 1 child with a bilateral grade III VUR. Urolithiasis was observed in isolated cases, but in children with grade III–V VUR and mainly in patients with signs of renal parenchymal scarring, which may be due to reflux nephropathy, as also confirmed by other studies [21]. Refluxing megaureter and hydronephrosis were predominantly (p<0.0001) observed in patients with grade V VUR without a significant difference between patients with signs of scarring of the renal parenchyma and without them (p=0.1063, p=0.77345, respectively). Other congenital renal abnormalities, such as doubling of pyelocalyceal system, Fraley syndrome, were diagnosed in all groups of the children under examination without intergroup differences.

In the vast majority of patients, 76 (53.90 ± 4.26 %) had signs of connective tissue dysplasia, which, according to literature data, contributes to the recurrence of pyelonephritis [22]. Statistically more often (p<001) signs of undifferentiated



The ratio of patients with different grades of VUR depending on the course of pyelonephritis

connective tissue dysplasia were observed in patients with signs of scarring of kidney parenchyma, which scientists are paying attention to. The calculations showed that in children with pyelonephritis and high grade of VUR with signs of systemic undifferentiated dysplasia of the connective tissue, the risk of developing scarring of the renal parenchyma was 33.9 times higher (RR=33.87 [4.78; 239.82]). The study detected a tendency to an increase in the percentage of children with recurrent pyelonephritis, depending on the grade of VUR and the presence of signs of scarring of the renal parenchyma.

It is noteworthy that, depending on the grade of VUR and the presence of signs of scarring of the kidney parenchyma, the number of patients with a deflection of GFR from the normative indexes increases. According to the results of the analysis of indices of the state of glomerular filtration and tubular renal function, it was found that in the subjects of Group 1, renal function was not disturbed; Group 2 and 3 had a significant

number of patients with a deflection of the GFR from normative indices and with a decrease in concentration kidney function, with the highest specific gravity among patients with signs of renal parenchyma scarring. Thus, depending on the grade of VUR and the presence of signs of scarring of the kidney parenchyma in the affected patients, the degree of CKD increases, which reflects the functional state and severity of pathological changes in the kidneys.

Conclusions. Pathological course of pregnancy, aggravated heredity on the part of kidney diseases in parents and close relatives, high grades of VUR, recurrent pyelonephritis and signs of systemic undifferentiated connective tissue dysplasia were identified as risk factors for the formation and progression of chronic kidney disease in children with pyelonephritis and vesicoureteral reflux. This gives an opportunity to identify them as a risk group for nephrosclerosis, which is the cause of progression of chronic kidney disease towards the terminal stage of chronic renal failure. Thus, the formation and progression of chronic kidney disease in children with pyelonephritis and VUR depend on the course of pyelonephritis, the degree of VUR and the presence of signs of scarring of the renal parenchyma.

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MEDICAL AND SOCIAL ASPECTS OF OPTIMIZING THE NUTRITIONAL STATUS OF CHILDREN DEPRIVED OF PARENTAL CARE

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Summary. The study deals with investigation of the content of amino acids by thin layer chromatography in blood serum of 109 children in orphanage with atopic dermatitis or dysplasia of connective tissue. It showed elevated levels of tryptophan in children with atopic dermatitis, as well as the levels of proline, glycine, lysine in children with connective tissue dysplasia, which confirmed the importance of amino acid metabolism disorders in pathogenesis of these conditions. The authors elaborated an algorithm for diet correction of metabolic and intestinal disorders developing in early childhood.
Key words: *atopic dermatitis, connective tissue dysplasia, amino acid composition of the blood, dietary correction.*

Introduction. Nutrition is known to be the most important environmental factor determining the health of the child and basic preventive measures of premorbid alimentary-dependent states that most frequently occur in the early age.

Especially important is the organization of rational nutrition in orphanages, where the children come from the first days of life, often with different disorders of the central nervous system, genetically determined metabolic disorders, and conditions of irrational nutrition with an ongoing food sensibilization.

The first three years of life are a special period for the development of health and depend on the rational nutrition of children, because a relatively high level of metabolism, a significant rate of growth and development, as well as physical activity determine the highest and qualitatively distinctive nutritional requirements, adequate provision of which is an important medical and social challenge.

It has been proved that characteristics of early age nutrition not only plays an important role in the formation of physical health and optimal intellectual development of the child, but may define a significantly higher risk of morbidity in the adult. If we consider prevention of cardiovascular diseases (coronary heart disease, arterial hypertension) in population, ranking first among the causes of death of the adult population in Ukraine, as well as the prevalence of endocrine pathology (obesity, diabetes, metabolic syndrome), then the need for rational recommendations for optimal nutrition for this category of children is a priority and is strategically important for the healthcare system as a whole.

The problems of optimization and rationalization of nutrition of children deprived of parental care are dealt with pediatricians, geneticists, nutritionists, managers of children's custodial institutions [1–6].

2. Purposes, subjects and methods:

2.1. Purpose – is to investigate amino acid composition of blood serum in children in orphanage in order to identify pathochemical profile underlying to the disease, and identify ways to its dietary correction.

2.2. Subjects & Methods. The study involved examination of 109 children aged from 4 months to 3 years in orphanage, 18 of whom were diagnosed with atopic dermatitis (AD) in various stages, and 26 children with connective tissue dysplasia (STD), mainly dysplastic cardiomyopathy. The vast majority of children had retardation of psychomotor and speech development.

In addition to a comprehensive clinical examination of children amino acid composition

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of the blood of the observed children was analyzed by thin layer chromatography (TLC) in collaboration with Kharkiv interregional center for clinical genetics and prenatal diagnosis.

Conflict of interests. There is no conflict of interests.

3. Results and discussion. The study results indicated increased levels of both nonessential and essential amino acids in children with atopic dermatitis and connective tissue dysplasia (*Figure*).

However, children with AD were more regularly and continuously found an increase in the content of tryptophan, which indicated a violation of its metabolism and effects on the body of excess concentration.

In addition, children suffering from STD were shown to have increased levels of proline, glycine and lysine. Thus, the presented data demonstrate the importance of tryptophan metabolism disorders in children`s pseudoallergic skin diseases and proline, glycine and lysine metabolism disorders lead to connective tissue dysplasia due to collagen complex dysfunction.

Therefore, persistent and recurrent changes in the skin in history accompanied by delayed psychomotor development, despite of ongoing dietary correction and drug therapy can be explained by the impairment of amino acid metabolism, in particular tryptophan. It was confirmed by a successful use in children with severe tryptophan acidemia diet with restriction of protein content in the diet, and exception of tryptophan-containing products.

The positive effect consisted in reduction of exudative rash, dry skin, itching, and repeated measurements showed a decrease in tryptophan level. Dietary correction of nutrition depending on the etiologic factor causing the disease was suggested due to etiological ambiguity in the identity of clinical symptoms of pathochemical and allergic skin lesions.

The study established the difference between etiological factors in atopic dermatitis in the identity of clinical manifestations of the disease and in this regard we individualized the most unified nutrition model of children in custodial institutions, without exceeding the fixed financial budget. Solving the problem of optimization of the nutritional status of children in orphanage more globally, we proposed an algorithm for the diet of these children depending on age and probability of possible enzymopathy, food sensitization, malabsorption syndrome, dysbiosis, etc., guided by the principles of evidence based medicine.

Thus, the children of the first month of life were administered prebiotic and probiotic mixtures e.g. Nutrilon 1.

These mixtures have value for the prevention of food allergy in newborns. The addition of probiotics provides metabolic optimization of bifidobacteria and lactobacilli bacteria in the intestinal flora, improves digestion, accelerates the formation of intestinal microbiocenosis. The mixtures were used for feeding healthy infants since birth.

Considering the most probable enzymopathy of the first months of life, lactase deficiency, children with severe intestinal dysfunction should be administered NAN-lactose-free. This adapted lactose-free formula is enriched with nucleotides, which enhance the reparative processes in the intestine by selenium, contains all the necessary substances and trace elements in the amount necessary for proper growth and development of the child. Furthermore, the reduced content of phosphorous improves calcium absorption. Given the possibility of "maturation" of enzyme systems, dairy products were gradually added to the diet in which milk sugar undergoes partial fermentation splitting: acidophilic "Malyutka", acidophilic "Malysh", acidophilic "Vitalakt", as well as kefir and other acidophilus mixtures. It is possible to add all sugars except lactose. Meat, fish, eggs, vegetables and fruit should be timely added.

There are certain periods of the child life, when the first clinical symptoms of the disease are detected more frequently.

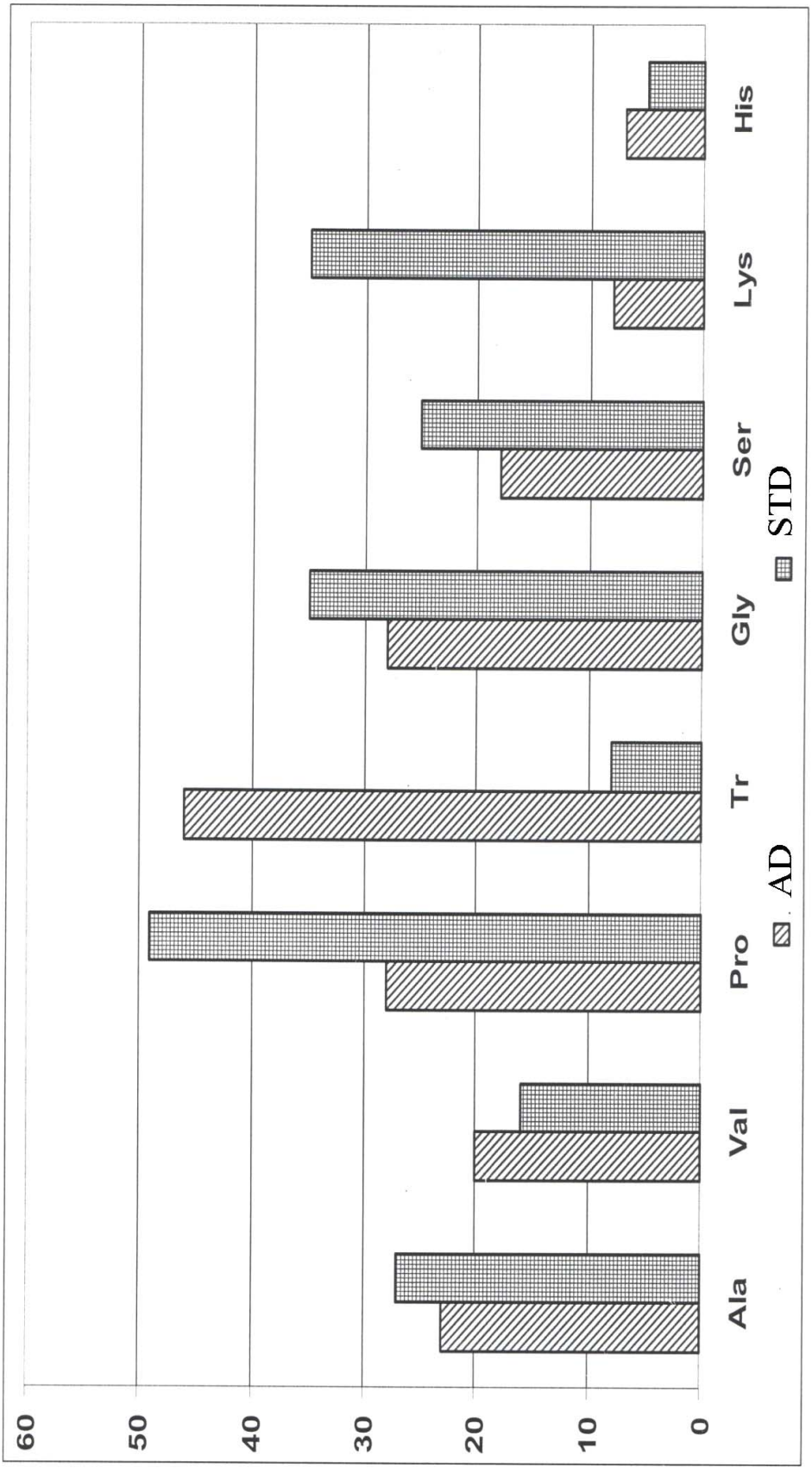
Food containing sucrose added into the child's diet triggers intestinal dysfunction (diarrhea syndrome characterized by persistent fermentation dyspepsia, flatulence, signs of dystrophy), which is not due to other reasons, the high probability of hereditary intolerance to glucose, fructose and other carbohydrates, which requires the use of elimination diet, i.e. complete exclusion of foods containing fructose, sucrose and other mono- and disaccharides [7].

There is a period when the food diet of the child includes gliadin-containing products (semolina, bread, milk formulas, which include wheat, oats, rye, barley). Under these circumstances, the child may be intolerant to cereals (celiac disease).

Proteins of cereals are represented by four fractions: albumin, globulin, prolamin and glutein.

The nutritional value of cereal proteins is defined by gluten protein fraction. Prolamin fraction is an inhibitor of cavernous hydrolases and among many intermediate protein hydrolysis products slows cavernous digestion.

Comparative characteristics of the amino acid content in children groups with AD and STD (% of cases) method TCX



List of abbreviations:
Ala – alanine; Val – valine; Pro – proline; Tr – threonine; Gly – glycine; Ser – serine; Lys – lysine; His – histidine.

Wheat, rye and millet have the highest content of prolamins, the lowest is in buckwheat and corn.

Malabsorption and loss of protein, lipids, electrolytes, vitamins, minerals and other substances necessary for normal life of the growing organism leads to dystrophy, anemia, rachitis, polyhypovitaminosis.

Gliadin diet is the basis of treatment of celiac disease in children. The diet excludes products containing wheat, barley, oats; it is advisable to use meals with rice, corn, buckwheat, soybeans.

A special place is occupied by the diet in the conditions of maldigestion due to functional and organic changes. These are malabsorption syndrome, primary and secondary enzymopathy, mucoviscidosis, dysbacteriosis, etc. These pathological conditions require a rather strict diet, which is not always possible in numerous groups of children.

In chronic non-specific diseases of the intestine the diet should have increased protein content, physiological intake of fat and a limited intake of carbohydrates. The diet should exclude milk, gluten, disaccharides, raw vegetables and fruit, fermented-milk mixture for infants.

An increase in the protein content is achieved by meat, fish, grated cheese, protein omelets, it is necessary to enrich food with polyunsaturated fatty acids (vegetable oil, butter).

Diet therapy is the main method of treatment of atopic dermatitis in children with food allergy.

Diet therapy for patients with food intolerance is the basis, sometimes the only effective treatment. In addition to its primary purpose, providing nutrients and energy, diet therapy offers great diagnostic possibilities and has a preventive value [8].

Therapeutic and preventive mixtures with partial protein hydrolysis are used in the presence of elementary signs of atopy (diaper rash, gneiss, cradle cap). Mixtures with dietary lectins have prebiotic activity. Oligosaccharides stimulate bifidobacteria and lactobacteria in the intestine, improve digestion and do not contain gluten. Such mixtures are Nutrilon HA 1, Nutrilon HA 2, Nutrilon-comfort-1, Nutrilon-comfort-2.

In manifestations of food allergy and malabsorption syndrome the diest should include therapeutic mixtures with a high degree of protein hydrolysis (half-elemental).

Protein components consisting of short peptides and free amino acids have hypoallergenic properties and high biological value and do not contain gluten, lactose. These are "NutrilonPepti", "Nutricia" (Holland), high-grade, highly adapted mixtures for feeding children from birth to the first year of life or older.

Focusing on the terms of adding complementary food, at this age it is necessary to add partially adapted protein milk mixtures with probiotics (galactooligosaccharides), optimal content of essential microelements (iron, zinc, manganese, copper) in necessary quantities (Humana Folgemilch-2). Galactooligosaccharides are energy substrate for populating the intestine with bifidobacteria and lactobacteria with the ability to bind and remove toxic substances from food.

"Bona" is a milk mixture, which protein fractions are distributed similarly to those in breast milk; therefore proteins are more easily and quickly digested.

The complementary food in atopic dermatitis should be administered at 4.5-5 months, vegetable puree excluding brightly colored products is recommended as the first complementary food.

At 6 months the diet should comprise cereals without gluten, such as rice, buckwheat, as part of hypoallergenic mixture or vegetable broth.

It is necessary to add to the porridge 1/4, 1/3, 1/2 of egg yolk as a source of vitamin D according to age. At 7 months the diet should include vegetable soup with butter or vegetable oil, kefir with cottage cheese as a source of protein and calcium. Minced meat (veal without hyperuricemia or chicken) should be added at 7.5 months, at 9 months it is recommended to add steamed cutlet.

Early artificial feeding of children with hereditary predisposition should not include corrective additives, the factors contributing to manifestation of atopic dermatitis. In this regard the delayed administration of corrective additives, using the highly adapted dairy mixtures, such as casein hydrolysates or mixtures based on soybean is a prerequisite in prevention and treatment of allergic diseases in infants.

In case of intolerance of cow's milk protein, the child's diet excludes whole cow's milk, and products prepared on its basis. Elimination diet is followed for one year, then it is possible to gradually add fermented-milk products, their volume should increase gradually.

Good effect is ensured by the use of adapted dairy-free mixtures based on soy milk "NAN-soy". The mixture used for children with allergies to cow's milk protein or its intolerance, lactase deficiency, including transitory intolerance to sucrose, galactosemia. "NAN-soy" is characterized by a high degree of purification, soy protein component has a complete amino acid

composition, is enriched with taurine, methionine and has the optimal content of L-carnitine.

Multiple causes of children`s diarrhea can include exudative enteropathy (intestinal lymph loss syndrome, protein diarrhea, intestinal lymphangiectasia). In this disease the diet should contain a high content of protein; it is advisable to limit the amount of fat to reduce stress of lymph circulation in the intestine; preference is given to fats which contain polyunsaturated fatty acids.

Hypoallergenic half-elemental mixture with low osmotic activity "Alfare" for feeding the children since neonatal period can reduce diarrhea, the severity of malabsorption syndrome and malnutrition.

The mixture is based on whey protein hydrolysate, which consists of 80 % of oligopeptides and 20 % of free amino acids, which prevents allergy to protein and secondary malabsorption. At the same time the child receives all the necessary micronutrients for normal growth and development. Creation of favorable conditions for active obligate growth of intestinal microflora is one of the major problems during the treatment of children suffering from intestinal dysbiosis.

It is necessary to use adapted milk products "Vitalakt", mixture "Malyutka", as well as dairy versions of adapted mixtures, such as acidophilic mixture "Malyutka", "Adapted biolact", sour milk "Vitalakt".

Administration of milk mixtures "NaN-new", "Bona", "Nestogen" has recently become common.

"NaN-new" is dairy mixture intended to feed children since neonatal period. Unique protein complex made it possible to approximate "NaN-new" to the quality of human milk. The mixture has lipid complex, enriched with fatty acids, a balanced combination of vitamins, minerals and microelements necessary for the child development. Children receiving complementary foods, should also be administered sour-milk unadapted mixtures, such as "Biolact", "Biolact-2", "Narine" (Armenia), "Mazzoni" (Georgia), etc. It is useful to administer "NaN-new" with bifidobacteria, dry mixture with bifidobacteria and Streptococcus thermophilus, which provide its probiotic activity in signs of dysbacteriosis.

The use of mixtures ensures optimal intake of basic food ingredients, vitamins, microelements, minerals for proper growth and development of children since 6 months.

In addition to the progressive increase of funding the costs for children's feeding, it is important to unify and, if necessary, personalize the nutrition of this category of children.

Due to probability of lactase deficiency among children of the first month of life, it is advisable to administer "NaN-new", "NaN-lactose-free" since neonatal period.

At 2 months it is recommended to add hypoallergenic monocomponent fruit juices, puree, at 3–4 months mixture "Bona", "Nestogen", acidophilic "Malyutka", acidophilic "Malysh", acidophilic "Vitalakt".

Therapeutic and prophylactic mixtures with partial protein hydrolysis are used in case of elementary signs of atopy. These are "Nutrilon HA-1", "Nutrilon HA-2", "Nutrilon-comfort-1", "Nutrilon-comfort-2". In manifestations of atopic dermatitis it is necessary to add mixtures with a high degree of protein hydrolysis (half-elemental). These are "Nutrilon Pepto", "Nutricia" (Holland), "Bona", "Alfare", etc.

Focusing on the terms of adding complementary food (4–5 months), at this age it is appropriate to add partially adapted protein milk mixtures with prebiotics (galactooligosaccharides) and optimal content of microelements. These are "Humana Folgemilch-2", as well as non-adapted dairy mixtures "Biolact", "Biolact-2", "Narine", "Mazzoni".

Considering the possibility of manifestation of intolerance to cereals at 5–6 months it is recommended to give porridge for all children without glutein "Bananen-Milchbrei", "Fruchxe Milchbrei", "Kirsch-Bananen-Mlchbrei" and hypoallergenic dairy mixtures "Humana S7-brei", "Yreis-Milchbrei" to children with allergic history.

Mixture "O-F-plus" should be administered to preterm infants and those born with low weight.

Conclusions

1. Medical-social aspects of optimizing nutritional status of children in custodial institutions must be under the constant supervision of the social services and healthcare institutions.

2. If the diagnosis of allergic disease was verified, hypoallergenic diet for such patients should be compiled taking into account the nosological form, age and gender. For this purpose, it is advisable to use established by us as a result of population studies the degree of allergy to foods for children at different age periods, as well as the possibility of correcting the diet equivalent for the ingredient composition of the product.

3. In initial manifestations of "atopic triad" (atopic dermatitis, asthma, allergic rhinitis) dietary restrictions should comply with nosologic form described in the methodological recommendations "Determination of etiologic spectrum of allergic diseases of children by gender and age by nomographic method".

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CLINICAL AND ANAMNESTIC FEATURES OF THE COURSE OF ACUTE BRONCHITIS IN CHILDREN

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Abstract. The purpose of the study was to detect clinical and anamnestic features of the course of acute obstructive bronchitis in children with a background of undifferentiated connective tissue dysplasia. Dynamic examination of 42 children with acute obstructive bronchitis was performed. The registration card for all children was developed and filled, it consisted of several sections: general information, family history, allergic history, life and past medical history, phenotypic assessment of undifferentiated connective tissue dysplasia. The results indicate that compromised allergic and genealogical history, as well as burdened obstetric history of the mother (threatened preterm delivery and gestosis) is significant risk factors.

Assessment of clinical manifestations of acute obstructive bronchitis in children showed that the severity of the disease, which is determined by the degree of severity and duration of symptoms, was associated with the number of signs of UCTD.

Keywords: acute obstructive bronchitis, children, undifferentiated connective tissue dysplasia, wheezing, phenotypic assessment.

Introduction. Acute obstructive bronchitis (AOB) in young children persists in contemporary pediatrics, despite the scientific and practical achievements in the field of etiopathogenesis of the disease and introduction of current therapies into the medical practice [1, 2, 3, 18].

The prevalence of AOB according to the authors listed ranges from 15 to 50 % [1, 2] and incidents of acute obstructive bronchitis in infants reaches 90 % [5, 6]. AOB is mostly manifested in infaants in their first year of life and depends on morphofunctional features of the respiratory system at this age: narrowness of the respiratory tract, weak cartilages of the bronchial tree, and insufficient development of smooth muscle of the bronchial tubes which is one of the proofs of the theory of relative immaturity of all organs and systems in early childhood [7, 4, 17].

A special place in the formation of increased bronchoreactivity in infants and development of AOB is occupied by neuroreflectory mechanisms which are based on dysfunction of autonomic nervous system stipulated by bronchospasms, vasodilation, hyperproduction of high secretion and triggering the development of AOB [3, 5, 19].

Results of many studies have been published recently. The authors consider bronchial dysfunction as a manifestation of autonomic dysfunction due to the disorder of the cartilage and connective tissue of the trachea and the bronchial tubes secondary to undifferentiated connective tissue dysplasia (UCTD) resulting in tracheobronchial dyskinesia [6, 9, 10, 12], and disorder of both drainage and ventilation functions of bronchial tubes.

Changes in connective tissue related to the disorder of synthesis and function of derivatives of collagen and elastic proteins are called connective tissue dysplasia. The definition was offered by P. Âeighton (1983) [5]. It is a polygenic multifactorial state, manifested by external and internal phenotypic features and clinically significant dysplastic-dependent disorders of organs and systems with progressive presentation.

The pathological state of connective tissue leads to the disorder of its functions, which is important for the development of many diseases because of the disorder of the functions of other tissues, for instance, dystrophy (protein, fat) and immune reactivity decreasing with the further development of allergic autoimmune reactions.

A change in almost all of the functions of the connective tissue secondary to a decrease in

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adaptive capacity of the organism leads to the development of different clinical variants in manifestation of connective tissue insufficiency.

Vegetative dysfunction is an important component of UCTD in children with obstructive bronchitis (OB). It is manifested by eructation, colics, low weight gain, and respiratory disorders with respiratory failure in young children secondary to UCTD. In these cases arrhythmic breathing is associated with gastroesophageal reflux (manifestation of UCTD). When brought together, these factors are important in the formation of relapses of acute obstructive bronchitis: disorder evacuation of the bronchial secretion, hyperkinesia, and the consequences of gastric reflux.

Mucostasis and disturbance of the drainage function of the bronchial tubes in OB provide favorable conditions for permanent colonization of the bronchial tree by microorganisms.

Relapses of acute obstructive bronchitis in young children, their anatomical and physiological features, and growing allergization of the modern society create a pathophysiological complex that promotes further development of bronchial asthma in children.

2. Purposes, subjects and methods:

2.1. Purpose – is to detect clinical and anamnestic features of the course of acute obstructive bronchitis in children secondary to undifferentiated connective tissue dysplasia.

2.2. Subjects & Methods. The study was a one-stage cohort, and the sampling method was continuous (during hospitalization). The key population was children admitted for examination and treatment at the Department of Pulmonology. Inclusion criteria were as follows: age 5 years and younger, obstructive bronchitis in history (one or more), and parental consent to participate in the study. Exclusion criteria were diagnosed bronchial asthma, chronic somatic diseases at the stage of exacerbation, malformations of internal organs, congenital and hereditary diseases of the bronchopulmonary system and gastroesophageal reflux.

As a part of a study only one program of clinical and laboratory examination has been used to evaluate the criteria for the selected parameters.

The registration card for all children was developed and filled, it consisted of several sections: general information, family history, allergic history, life and past medical history, phenotypic assessment of UCTD (according to T.I. Kadurina, L.N. Abakumova, 2008), and the results of examination at the specialized department [1, 7, 15, 20].

Statistical analysis of data was carried out using statistical software STATISTICA 10.0. Non-parametric Mann-Whitney U-test was used to assess the differences between the two groups in quantitative terms. The estimation of inter-group differences by qualitative features was carried out using the criterion $\chi 2$ and Fisher's exact criterion.

Conflict of interests. There is no conflict of interests.

3. Results and discussion. According to the inclusion/exclusion criteria, 42 children with OB were included in the study and the average age of children was 3.2 ± 1.3 years. The children were divided into the following groups: main Group 1 (n = 30) comprised children with acute obstructive bronchitis and phenotypic manifestations of undifferentiated connective tissue dysplasia, and control Group 2 (n=12) included children with acute obstructive bronchitis without phenotypic manifestations of UCTD. The observation was conducted in the acute phase of the disease throughout the whole course of hospital treatment. The diagnosis of bronchitis was based on generally accepted clinical criteria, for the comparative description of the diseases, depending on the presence of UCTD the severity of clinical manifestations was evaluated in points. Diagnosis of UCTD implied assessment of stigmatization levels (a conditional indicator including the total number of UCTD points with the extraction of low (up to 12 points), middle (13–24 points) and high (more than 24 points) levels (using the table "Value of indices in the assessment of the degree of connective tissue dysplasia severity" by T.I. Kadurina, L.N. Abakumova, 2008). Group 1 children comprised 11 girls (36.7 %) and 19 boys (63.3 %), and Group 2 included 3 boys (25 %) and 9 girls (75 %) (*Fig. 1*).

The findings showed ($p < 0.05$) that boys predominated among the examined children with AOB and UCTD.

According to the questionnaire, the compromised allergic history was significantly more frequent ($p < 0.05$) in main group children (22 children from Group 1 (73.4 %), and 4 children from Group 2 (33.3 %).

The genealogical history of probands included information about the health of relatives in three generations, with a significantly higher frequency ($p < 0.05$) of burdened family history of chronic bronchopulmonary diseases (bronchial asthma, chronic obstructive pulmonary diseases) in three

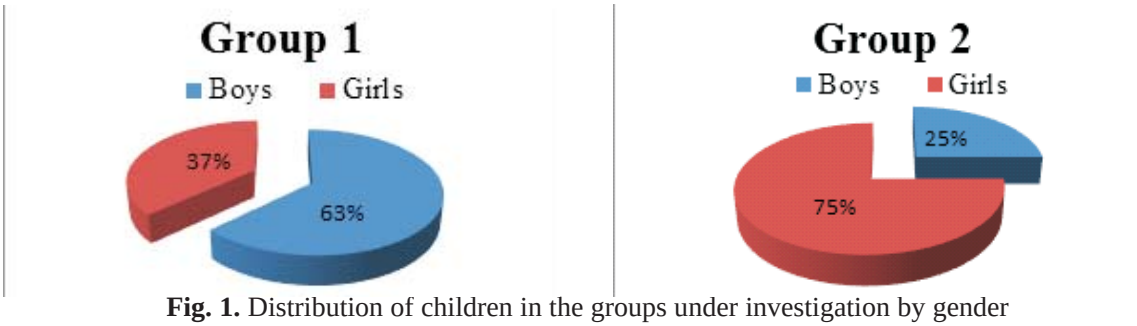

Fig. 1. Distribution of children in the groups under investigation by gender

generations of Group 1 children (16 children (53.4 %)) and only 2 children from Group 2 (16.7%) (*Fig. 2*).

External phenotypic manifestations of UCTD in patients of the main group were more common ($p < 0.05$) than in children of the other group,

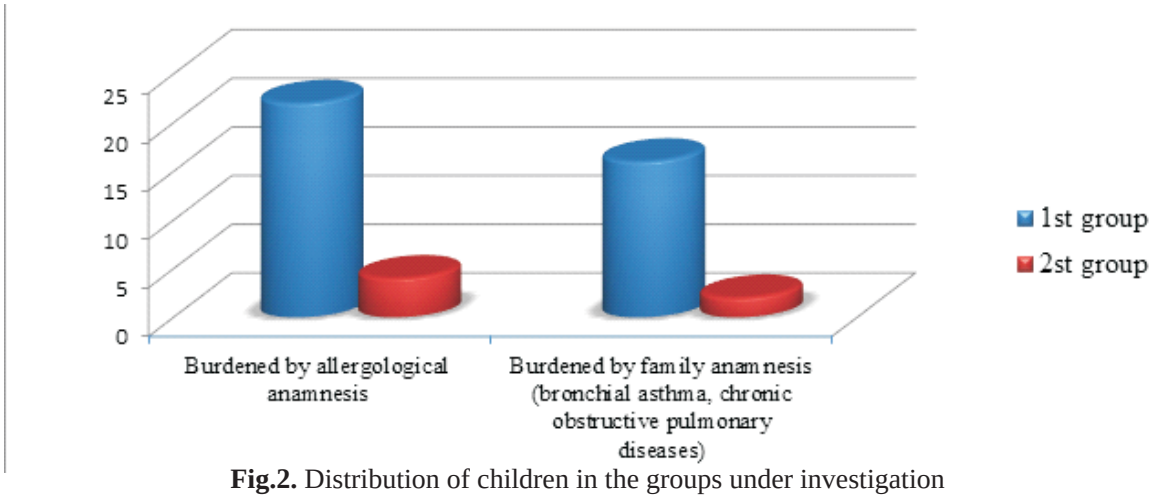

Fig.2. Distribution of children in the groups under investigation by burdened allergic and genealogical history

Among the mothers of the main group 19 mothers (63.3 %) had a risk of preterm delivery, which was significantly higher ($p < 0.05$) than in mothers of the other group (3 mothers, 25 %).

Also, the mothers of the control group had more manifestations of gestosis (70 %), among the other group only 4 women (30 %) had manifestations of gestosis (*Fig. 3*).

namely asthenic build, thin skin, soft and brittle nails, diastase of the abdominal muscles, fine and brittle hair and blue sclera (*Table*).

Examination of Group 1 children showed moderate degree of UCTD in 25 children (83.3 %), expressed as CTD in 5 (16.7 %) patients.

Assessment of clinical manifestations of AOB in children showed that the severity of the disease,

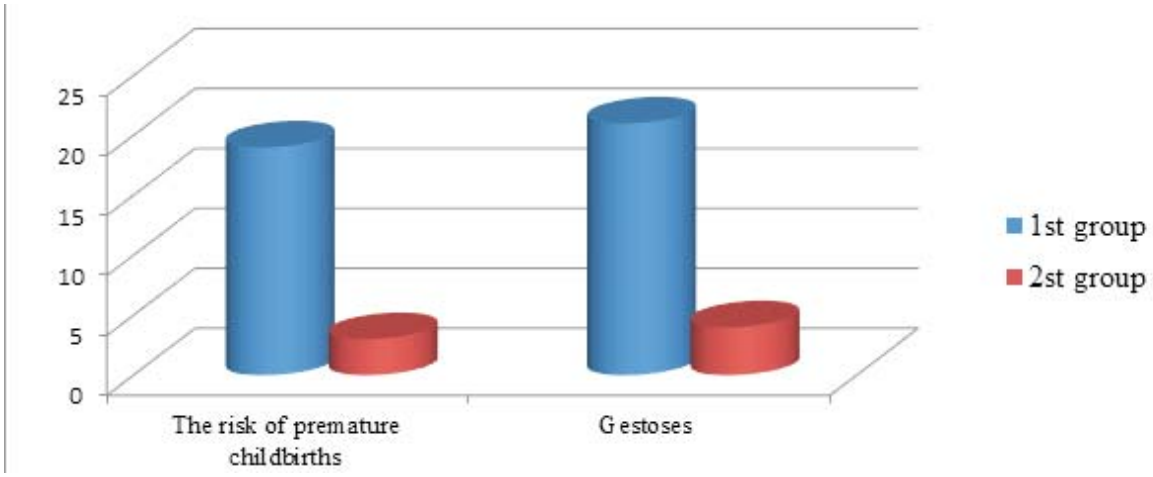

Fig. 3. Distribution of mothers of children in the groups under investigation according to burdened obstetric history (the risk of preterm delivery and gestosis)

Incidence of phenotypic signs of UCTD in patients of the groups under investigation

Phenotypic signs of UCTD	Group 1 (n=30)		Group 2 (n=12)	
	%	absolute	%	absolute
Asthenic body composition	53.3*	16	16.7	2
Dolichostomenoeia	16.7	5	8.35	1
Arachnodactyly	3.3	1	-	-
Hypermobility of the joints: moderate degree	50.0*	15	8.35	1
Velvet, soft skin	26.6	8	33.4	4
Thin skin (moderate venous mesh)	60.0*	18	16.7	2
Hyperelasticity of the skin: • low; • moderate.	 40.1 9.9	 9 3	 33.4 -	 4 -
Nails (soft / brittle / flaky)	53.3*	16	16.7	2
Ears (soft / folded in a tube)*	53.3*	16	16.7	2
Blue sclera	53.3*	16	8.35	1
Petechia / ecchymosis / nosebleeds	20.0	6	16.7	2
Myatonic syndrome / diastasis of the direct abdominal muscles	23.3	7	8.35	1
Hernias/prolapse of organs / postoperative hernias	9.9	3	16.7	2
Hair (thin / brittle / areas of alopecia)	63.3*	19	25.0	3
1st degree scoliosis	13.6	3	16.7	2
Flat-foot transverse / longitudinal	13.6	3	8.35	1
Pes valgus. Valgus deformation of the lower extremities.	9.1	2	8.35	1

Note. *p <0.05 when compared to Group 2 patients.

determined by the degree of severity and duration of symptoms, was associated with the number of UCTD signs. Thus, febrile fever in children of the main group was registered 3.5 times more often than in the other group (in 86.7 and 25.0 % of cases, respectively); p <0.05, while the terms of normalization of body temperature in 40.0 % of patients with UCTD were more than 5 days. Characteristics of cough in children of both groups did not have significant differences except in the long term perseverance of this symptom in patients with UCTD. Auscultatory changes were characterized by dry whistling and scattered damp melliferous wheezing secondary to prolonged exhalation. In children of the comparison group, the clinical symptoms of GBS lasted for 3.4 ± 1.2 days, while in Group 1 children clinical symptoms (dry whistling wheezing and prolonged exhalation) persisted for 5.2 ± 1.8 days.

Conclusions. Connective tissue dysplasia has a modifying effect on the course of acute bronchitis, resulting in greater severity and prolongation of the leading symptoms and syndromes, and the significant risk factors is the presence of a compromised allergic and genealogical history, as well as burdened obstetric history of the mother (threatened preterm delivery and gestosis). This emphasizes the need for the improvement of the program of examination of children with acute obstructive bronchitis for the prognosis of the course and optimization of treatment and rehabilitation measures.

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HEART RHYTHM DISTURBANCES IN NEWBORNS IN THE EARLY NEONATAL PERIOD

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Abstract. Neonatal arrhythmia is not a rare condition, and may occur both in patients with structural heart disease and in children with functional cardiovascular disorders as well as in a relatively small number of healthy newborns. The article presents the results of the study of basic parameters of electrical activity of the heart in newborns with administration of daily ECG monitoring. The study involved examination of 187 infants in the early neonatal period. Assessment of the data of obstetric and gynecological history and extragenital pathology of the mothers of the examined children, analysis of the data of Holter ECG monitoring of newborns showed the most frequently occurring types of neonatal arrhythmias and significant risk factors for their development.

Key words: *cardiac rhythm disturbances in newborns, neonatal arrhythmias, risk factors.*

Introduction. Childbirth and the early neonatal period are a combination of extreme impact on the child's body, requiring rapid adaptation at different levels of self-regulation. A cascade of compensatory and adaptive mechanisms, aimed at adapting organs and systems to the conditions of extrauterine life, is activated in the child's body immediately after birth. Restructuring of the circulatory system plays the most important role in this physiological process [1, 2].

It is reported that the incidence of neonatal arrhythmias and conduction disturbances ranges from 1 to 5 % among all newborns. Neonatal arrhythmias have variable clinical manifestations and are classified as both benign and those with adverse effects on the health and life of a newborn child [3]. That is why studying the range and nature of violations of cardiac rhythm and conduction in newborns remains an urgent area of development in neonatology.

The use of modern recorder devices does not significantly interfere with vital activity of the newborn and does not violate psycho-emotional state of the child, providing a possibility to register changes in the parameters of electrocardiography during normal functioning (sleep, feeding, anxiety, medical procedures, etc.) and obtaining important data on the time course of the cardiac rhythm in newborn during the day. Round-the-clock recording of electrocardiogram with the help of Holter ECG monitoring (HECGM) ensures the accuracy of measuring the basic parameters of electrical activity of the heart for a long period of time, followed by their analysis [4].

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2. Purposes, subjects and methods:

2.1. Purpose – to improve early diagnosis of cardiac rhythm and conduction disorders in newborns in the early neonatal period and identify significant risk factors for their development based on the analysis of the results of daily ECG monitoring.

2.2. Subjects & Methods. The study involved 187 newborns in the early neonatal period with cardiac rhythm disturbances at auscultation of the heart. All the newborns were administered daily ECG monitoring, following which they were divided into 2 groups. Group 1 (n=126) included newborns with heart rate and conduction impairment, Group 2 (n=61) comprised newborns with no rhythm and conduction disorders. Taking into account the gestational period, Group 1 and 2 newborns were divided into subgroups of full-term and pre-term infants: Group 1a with arrhythmia (n=34), Group 1b pre-term with arrhythmia (n=92), Group 2a full-term without arrhythmia (n=24), Group 2b pre-term without arrhythmia (n=37). The exclusion criterion was the presence of birth defects and/or the organic

pathology of the cardiovascular system. The study implied the assessment of obstetric and gynecological history data and extragenital pathology of mothers of the examined newborns and analysis of daily Holter ECG monitoring (HECGM) data. The recording and analysis of HECGM was performed using electrocardiographic hardware and software complex "ECGpro" (Holter monitor "EP810"), IMESC. Interpretation of findings was performed using ECGproHolter v.7.44.7-S12 software. The data obtained in the study was processed by Statistica 10.0 Microsoft software package using Mann–Whitney U test and analysis of conjugation tables using Pearson $\chi 2$ criterion.

Conflict of interests. There is no conflict of interests.

3. Results and discussion. The study of histories of mothers of the examined infants showed that 86.5 % of mothers of Group 1 newborns and 67.2% of mothers of Group 2 newborns had obstetric-gynecological complications, which became a significant risk factor for the development of cardiac rhythm disturbances in the groups of examined infants ($\chi 2$=9.641; p<0.002). Obstetric and gynecological pathologies of mothers of newborns of both groups mainly included gestosis of pregnant, the development of which is due to the inability of the adaptive mechanisms of the parent to adequately meet the needs of the developing fetus, resulting in the development of different degrees of severity of perfusion-diffusion insufficiency in the mother-placenta-fetus system [5]. This was confirmed by a rather high percentage of placental malfunctioning in mothers of the examined neonates (17.1 %). A significant number of complications during pregnancy was due to anemia of pregnant (24.0 %), infectious disorders of reproductive system in mother and fetal membranes of different etiologies (16.0 %), development of oligohydroamnion (16.0 %), multiple pregnancies with threatened miscarriage and preterm delivery (33.7 %) and premature rupture of fetal membranes (37 %). Assessment of incidence of a specific type of obstetric-gynecological disorder did not show any statistically significant difference between the groups of the examined children.

Assessment of the presence and structure of extragenital disorders showed impairments of the structure and / or function of different organs and systems in 60.3 % of mothers of Group 1 newborns and 42.6% of mothers of Group 2 infants, which was a significant risk factor for the development of cardiac rhythm disturbances ($\chi 2$=5.190; p<0.02). The most common disorders of organs and systems included cardiovascular (23 %), endocrine (21.4 %), gastrointestinal (10.7 %), urinary (16.6 %), nervous (3.7 %) and respiratory (0.5 %) diseases, but there was no significant difference between the groups regarding the prevalence of a specific type of disorder in any of the systems.

The examined infants were born from 2.57 + 0.16 delivery. Cesarean section was performed during the delivery of 57.9 % of Group 1 and 47.5 % of Group 2 infants.

Assessment of the groups of examined neonates by weight and gestational age showed that in the group of infants with cardiac arrhythmias (Group 1) the term of gestation at birth was lower than in the group of children without arrhythmia (32.5 weeks (30.0, 37.0) for Group 1 and 34.0 weeks (33.0; 39.0) for Group 2, p <0.0006). By weight criterion at birth, Group 1 infants also had lower rates (1900.0 g (1440.0; 2950)) than Group 2 neonates (2375.0 g (1940; 3125)), p<0.01.

The Apgar scores were lower both in the 1st minute in the group of children with arrhythmia (5 (4; 6) points) than in the group of infants without cardiac rhythm disturbances (6 (5; 8) points; p<0.000003); and on the 5th minute (7 (6; 7) and 7 (7; 9) respectively, p?0,000008).

Asphyxia at birth was diagnosed in 50 % of Group 1 newborns and 23 % Group 2 newborns ($\chi 2$=12.416; p <0.001). The presence of asphyxia in newborns was confirmed by a low Apgar score on the first and fifth minutes of life respectively, by acid-alkaline state of the umbilical blood (pH <7.15 and (or) base deficiency (BE) greater than 12 mmol / L) and the presence of diagnostic criteria for asphyxia at birth in the form of clinical symptoms of central nervous system damage and/ or signs of transient impaired function of the respiratory and cardiovascular system. Hypoxic-ischemic and hypoxic-hemorrhagic damage of the central nervous system was detected in 61.9 % of Group 1 and 37.8 % of Group 2 infants ($\chi 2$=9.691; p<0.002).

In the group of infants with arrhythmias diagnosed by HECGM (Group 1), 70.6 % had sinus tachyarrhythmia accompanied by signs of myocardial repolarization of the left ventricle. Sinus bradyarrhythmia was diagnosed in 7.1 %, supraventricular extrasystole in 33.3 %, ventricular extrasystole in 11.1 % (including 3 children with frequent ventricular arrhythmia (more than 60 episodes of ventricular ectopia per hour)). Atrioventricular (AV) nodal extrasystole was detected in 7.9 % of newborns with cardiac

rhythm disturbances, 1st degree transient atrioventricular blockade in 11.9 %, episodes of 2nd degree transient atrioventricular blockade in 8.7 %, migration of pacemaker from sinus node to the lower parts of atria in 27.8 %, transient QT prolongation in 28.6 % of newborns, rhythm pause in 11.1 %, disturbance of repolarization in left ventricle in 54 % of children.

Assessment of the prevalence of diagnosed neonatal arrhythmias showed that sinus tachycardia ($\chi 2=15.786$; $p<0.001$) and atrial extrasystole ($\chi 2=3.948$; $p<0.05$) were more common in pre-term infants than among full-term infants in the group of children with heart rhythm disturbances (*Table 1*).

The QT interval is one of the most clinically significant ECG parameters, since changes in the QT interval of any origin are a risk factor for ventricular tachyarrhythmias [6, 7]. In the groups of the examined infants transient QT prolongation was observed in 28.6 % of Group 1 newborns, therefore this parameter was considered in more detail.

QT interval analysis was performed by determining the following parameters: daily QT duration; daily mean corrected QT (QTc) which is a value independent of the heart rate; QT mode which is QT length, corresponding to the maximum number of complexes; SDQT (NN) which is a standard deviation of all QT intervals from normal complexes; SVQT (NN) is the coefficient of QT variation.

Detailed examination of QT interval parameters showed that only daily mean corrected QT (QTs) duration values were greater in Group 1 children ($p<0.01$) as compared to Group 2 infants. However, other QT parameters were higher in the subgroup of full-term Group 1 infants (with arrhythmia) as compared to pre-term infants of the same group, and the index of QT variation (SVQT (NN)) also had higher values in the subgroup of full-term Group 2 newborns (without arrhythmia) as compared to pre-term infants of the same group (*Table 2*).

Table 1

The prevalence of cardiac rhythm and conduction disturbances

Cardiac rhythm and conduction disturbances	Infants with arrhythmia (Group 1), % (n=126)	Full-term infants with arrhythmia (Group 1a), % (n=34)	Pre-term infants with arrhythmia (Group 1b), % (n=92)
Sinus tachyarrhythmia	70.6	44.1	80.4; **$P_{1a,1в}<0.001$**
Sinus bradyarrhythmia	7.1	11.8	5.4
Supraventricular extrasystole	33.3	47.0	28.3; **$P_{1a,1в}<0.05$**
Ventricular extrasystole	11.1	23.5	6.5
AB-nodular extrasystole	7.9	8.8	7.6
1st degree AV block	11.9	5.9	3.3
2nd degree AV block	8.7	17.7	5.4
Migration of pacemaker	27.8	17.7	31.5
QT prolongation	28.6	32.4	16.7
Rhythm pauses	11.1	14.7	9.8
Repolarization disturbances	54.0	41.2	58.7

A recent study of the variability of cardiac rhythm indices in newborns who were in the intensive care unit revealed a link between the incidence of changes in the characteristics of the cardiac rhythm of newborns with the development of systemic inflammatory response, infectious

Table 2

Daily QT intervals

QT indices	Group 1 (n=126)	Group 2 (n=61)	Group 1a (n=34)	Group 2a (n=24)	Group 1b (n=92)	Group 2b (n=37)
Mean QT, ms	294.5 (264.0; 326.0)	297.0 (275.0; 317.0)	309.0 (294.0; 356.0)	300.0 (288.0; 323.5)	284.0 (261.0; 318.0) **$p_{1a,1в}<0.001$**	295.0 (265.0; 309.0)
QTc, ms	435.0 (412.0; 475.0)	427.0 (415.0; 435.0) **$p_{1,2}<0.01$**	444.0 (424.0; 484.0)	430.5 (418.0; 436.5)	446.4 (411.0; 470.0)	426.0 (409.0; 435.0)
QT mode	289.0 (264.0; 320.0)	294.0 (273.0; 315.0)	303.5 (289.0; 335.0)	299.5 (282.5; 321.0)	281.5 (258.5; 316.0) **$p_{1a,1в}<0.01$**	279.0 (263.0; 312.0)
SDQT (NN)	29.0 (20.0; 45.0)	29.0 (23.0; 43.0)	42.0 (25.0; 55.0)	32.0 (28.0; 46.0)	26.0 (17.0; 39.5) **$p_{1a,1в}<0.0001$**	27.0 (18.0; 41.0) **$P_{2a,2в}<0.05$**
SVQT (NN)	9.6 (7.0; 13.0)	9.8 (7.0; 13.0)	12.0 (8.0; 16.0)	10.5 (8.0; 14.5)	8.5 (5.0; 12.0) **$P_{1a,1в}<0.001$**	9.0 (6.0; 12.0) **$P_{2a,2в}<0.05$**

diseases of the urinary tract, necrotizing enterocolitis, apnea and deterioration of external respiration rates [8]. As already outlined above, the violation of sinus node automatism, the main driver of the heart rate, in the form of sinus tachyarrhythmia was diagnosed in 70.6 % of Group 1 newborns. Therefore, we assessed heart rate parameters in detail.

Detailed analysis of heart rate indices showed that the levels of the mean daily and the mean maximum daily heart rate were higher both in Group 1 (infants with arrhythmia) as compared to Group 2 (infants without arrhythmia) and in subgroups of pre-term infants (Groups 1 and 2) as compared to subgroups of full-term newborns (Groups 1a and 2a). Indices of the mean minimum heart rate were also higher in the subgroups of pre-term infants (Groups 1b and 2b) as compared to subgroups of full-term infants (Groups 1a and 2a) of both main groups. Assessment of RR length parameters showed that the parameters of the minimum RR-interval were higher in Group 2 infants ($p<0.0001$), and the maximum RR-interval values were higher in Group 1 newborns ($p<0.01$). Indices of circadian index (the ratio of the mean daily to the mean nightly heart rate) were higher ($p<0.05$) only in the subgroup of full-term infants with arrhythmia (Group 1a) as compared to the subgroup of pre-term children (Group 1b) of the same group (*Table 3*).

Table 3

Daily heart rate parameters

Herat rate parameter	Group 1 (n=126)	Group 2 (n=61)	Group 1a (n=34)	Group 2a (n=24)	Group 1b (n=92)	Group 2b (n=37)
Mean heart rate, beats	148.0 (135.0; 158.0)	141.0 (132.0; 148) **$p_{1,2}<0.05$**	139.0 (123.0; 144.0)	127.5 (124.0; 141.0)	152.0 (142.0; 160.0) **$P_{1a,1в}<0.0001$**	146.0 (139.0; 155.0) **$P_{2a,2в}<0.00001$**
Minimum heart rate, beats	114.5 (102.0; 126.0)	111.0 (102.0; 123.0)	104.5 (94.0; 114)	103.0 (93.0; 113.0)	119.5 (106.5; 128.5) **$p_{1a,1в}<0.001$**	116.0 (108.0; 130.0) **$P_{2a,2в}<0.001$**
Maximum heart rate, beats	194.0 (182.0; 206.0)	189.0 (178.0; 200.0) **$p_{1,2}<0.05$**	187.0 (175.0; 203.0)	182.5 (171.5; 193.0)	197.0 (185.5; 206.5) **$P_{1a,1в}<0.05$**	194.0 (182.0; 202.0) **$P_{2a,2в}<0.01$**
Minimum RR-interval, ms	253.5 (226.0; 281.0)	281.0 (265.0; 304.0) **$P_{1,2}<0.0001$**	250.0 (203.0; 281.0)	292.5 (277.0; 312.0)	261.0 (230.0; 281.0)	265.0 (257.0; 281.0) **$P_{2a,2в}<0.01$**
Maximum RR-interval, ms	875.0 (718.0; 1085.0)	718.0 (648.0; 882.0) **$P_{1,2}<0.01$**	875.0 (757.0; 992.0)	726.0 (663.0; 867.0)	874.0 (714.0; 1085.0)	710.0 (632.0; 937.0)
Circadian index	1.0 (0.98; 1.03)	1.0 (0.97; 1.03)	1.01 (0.99; 1.03)	1.01 (0.98; 1.04)	0.99 (0.97; 1.03) **$P_{1a,1в}<0.05$**	0.99 (0.97; 1.02)

Conclusions:

1. The study showed a relationship between obstetric and gynecological disorders ($\chi2=9.641$; $p<0.002$), extragenital diseases in pregnant ($\chi2=5.190$; $p<0.02$), perinatal hypoxia ($\chi2=12.416$; $p<0.001$) and the development of neonatal heart rhythm disorders in the early neonatal period.

2. Newborns during this age period were more frequently found to have impairment of automatism and excitability of the sinus node with the development of sinus tachycardia and supraventricular extra systole ($\chi2=15.786$; $p<0.001$ and $\chi2=3.948$; $p<0.05$, respectively).

3. Considering the above, in further studies it is expedient to study the correlation of cardiovascular system disorders with the presence of cardiac rhythm and conduction disturbances in newborns at different gestation periods by comparing the state of electrical activity of the heart, central hemodynamics and the data of biochemical markers of hypoxic myocardial damage.

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