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ASSESSMENT OF THE LEVEL OF ORGANOTROPIC AUTOANTIBODIES IN NEWBORNS WITH LOW BODY WEIGHT

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The urgency of the problem. The frequency of preterm birth is variable, but in most developed countries in recent decades it has been quite stable and amounts to 5-10% of the number of children born[18,29,35]. The frequency of adverse outcomes among surviving children born before 28 weeks of gestation reaches 40–50%, rising to 70–90% for children weighing 500.0–750.0 g[30,32,34,36]. In children born with low body weight, mortality reaches 30% [8,30]. The current level of development of perinatology makes it possible to increase the survival of these children, but the peculiarities of their subsequent growth and development require no less attention. [8]. The fact of premature birth of children in women with a burdened obstetric-gynecological and somatic history is associated with perinatal CNS damage and often with a change in the vegetative status of a child in the first years of life. [9,37,41]. In early childhood and in subsequent periods of development, these children show psychosomatic abnormalities, in particular nocturnal enuresis, prolonged low-grade fever, tics and obsessive movements, attention deficit hyperactivity disorder, tension cephalalgia, arterial hypertension, arterial hypotension, biliary dyskinesia, bronchial asthma, atopic dermatitis[27,39]. An inverse relationship has been shown between low birth weight and adult blood pressure levels, the likelihood of developing type 2 diabetes, cardiovascular disease, and an excessive response to stress [26,38]. Lack of motor development in children at 16 years of age is associated with body weight less than 2 kg at birth. [31]. IQ tests showed that 41% of children born at the 7th month of pregnancy had worse performance compared to their healthy peers and had learning problems [41]. Early preterm birth can negatively affect puberty and increase the chance of adolescent depression [16], as these children may slow down the process of myelination of the frontal lobe of the brain, which is responsible for motivation, satisfaction, short-term memory and vision. [35]. Studies conducted among adolescents born prematurely revealed anomalies in their brain development, namely, a lack of gray matter in the temporal brain and cerebellum [37].

The birth of children with low body weight is not only a problem of perinatology, since the prerequisites for many diseases in adults begin in childhood. Discharged home from the second stage of nursing, a premature and underweight child has, according to various sources, an average of 4.1 to 5.5 diseases and belongs to the second - fifth health groups [3]. Most of these children (up to 68%) form the third health group, characterized by the presence of chronic compensated pathology [4]. A number of studies have shown that low weight is fixed at the epigenetic level, that is, not at the DNA level, but at the level of control of genes responsible for metabolism [6]. The fact is that a person inherits not a trait, but the norm of a trait's reaction: how a specific gene can manifest itself under specific conditions[15,21].

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The maturation of the fetus is a consistent implementation of genetic capabilities in the specific conditions of the existence of the organism, and the physiological, psychological and social characteristics of a person depend on a combination of influencing factors, including neuroimmune ones [14]. The development of the fetus is largely dependent on the state of the mother's immune system and is regulated by many interleukins, interferons and embryotropic antibodies of the IgG class. [20]. If pregnancy occurs against the background of altered immunoreactivity, this may be the reason for stopping the development of pregnancy, or a trigger for neurological, somatic or endocrine disorders in the child[15,20,40].

Identification of predisposition to somatic pathology in low birth weight newborns is relevant in terms of prognosis and targeted prevention of these conditions. At the same time, a promising direction in preclinical diagnostics is the determination of organ-specific antibodies. Considering that somatic pathology of mothers is of great importance among the causes of preterm pregnancy, it seems appropriate to screen newborns for the level of organotropic autoantibodies.

The aim of the study was to assess the level of 24 types of organotropic autoantibodies in newborns with low body weight.

Material and research methods. From 2019 to 2020, we examined 64 newborns who were born at a gestational age of 32-37 weeks with low body weight - 1500.0-2499.0 g. All newborns were divided into 2 groups: those born with a body weight of 1500.0-1999.0 g at a gestational age of 32-34 weeks (n=26) and those born at a gestational age of 35-37 weeks with a body weight of 2000.0-2499.0 g (n=38). The comparison group consisted of healthy full-term newborns weighing more than 2500.0 g, born at 38-40 weeks of gestation (n=12). All children underwent a standard clinical examination, as well as a study of the level of autoantibodies to 24 autoantigens - components of the tissues of the brain, heart, liver, intestines, lungs, kidneys, endothelium, thyroid gland, pancreas, adrenal glands, as well as an immunoreactivity index. Autoantibodies were determined by solid-phase ELISA on a Rayto analyzer (China), with ELI-Viscero-24-Test test systems (Immunculus, Russia). To conduct the entire panel of tests, 0.5 ml of the child's blood serum was required, blood sampling was performed on the 5th-7th day of life. Note that the deviation of the level of autoantibodies from the average level in the standard serum, expressed in%, is taken as a conditional norm; the conditional norm lies in the range from (- 20%) to + 10% (green zone). If the level of autoantibodies in the subject exceeds that in the standard by 10-20% ((+11) - (+15%) / (-21%) - (-35%)), then this is interpreted as a relative deviation (yellow zone), if the level of autoantibodies exceeds the standard by 20% or more (+15% or more; (-35) or more), then this is a significant deviation (red zone) [9].

Results. The average age of mothers of low birth weight newborns did not differ significantly in both groups and amounted to 23.4±1.2 and 25.8±0.9 years, respectively. The study of the anamnesis and the presence of somatic diseases in mothers showed that IDA was observed in 8 (30.8%) and 12 (31.6%) women - respectively in the 1st and 2nd groups ($p>0.05$); preeclampsia was significantly more

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common in mothers of the second group: 24 (63.1%) versus 10 (38.5%) ($p<0.05$); somatic diseases during pregnancy were detected in 8 (30.8%) and 14 (36.8%) women of the first and second groups, which was not statistically significant ($p>0.05$). Of the transferred somatic diseases, diseases of the thyroid gland and upper respiratory tract were most common, while diseases of the cardiovascular system (arterial hypertension, arrhythmias) were detected in 7.6% and 10.5% and mothers of groups 1 and 2, respectively, in In general, somatic diseases were in history in 10-12% of the examined mothers of underweight children, in the control group this figure was 8.3% (table 1).

Table 1.

Postponed somatic diseases of mothers of low birth weight newborns

	Control group	general group, n=64	Mothers of newborns of the 1st group (n=26)	Mothers of newborns 2 groups (n=38),
Diseases of the cardiovascular system	1 (8,3%)	6 (9,3%)	2 (7,6%)	4 (10,5%)
Respiratory diseases	1 (8,3%)	8 (12,5%)	3 (11,5%)	5 (13,1%)
Diseases of the stomach and intestines	1 (8,3%)	7 (10,9%)	3 (11,5%)	4 (10,5%)
Diseases of the liver and gallbladder	0	6 (9,3%)*	2 (7,6%)*	4 (10,5%)*
Diseases of the kidneys and urinary tract	0	7 (10,9%)*	3 (11,5%)*	4 (10,5%)*
Diabetes 2 types	0	1 (1,5%)	0 (%)	1 (2,6%)
Thyroid diseases	0	8 (12,5%)*	4 (15,3%)*	4 (10,5%)*
CNS diseases	0	0	0	0
Diseases of the reproductive system	1 (8,3%)	7 (10,9%)	3 (11,5%)	4 (10,5%)

Note: *-differences are statistically significant relative to the control group

Diseases of the kidneys and urinary tract, liver, thyroid gland were significantly more common among mothers of low birth weight newborns. There were no organic diseases of the nervous system in the anamnesis of mothers of underweight children, however, 6 (23.1%) and 8 (21.1%) women complained of frequent mood swings, nervousness - respectively in the 1st and 2nd groups ($p>0.05$).

The study of general immunoreactivity in terms of the level of total autoantibodies revealed that in low birth weight newborns there is a significant decrease in this indicator below the threshold of -35% relative to standard serum. Based on this, we

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can conclude that the immaturity of the immune system and hyporeactivity, polyclonal immunosuppression, which is typical for chronic intoxication, latent intracellular infections, immunodeficiency. The value of the average immunoreactivity in low birth weight newborns not only went beyond the reference interval, but was also significantly lower than in the control group, although there was no difference between groups 1 and 2 ($p>0.05$), which indicates that the overall Immunoreactivity in newborns after 32 weeks is reduced regardless of gestational age and birth weight.

Of all the 24 parameters studied, the average values of autoantibodies of 7 types out of 24 were at a level exceeding the limits of the "red zone", i.e. a decrease of more than 35% and an increase of more than 15% relative to standard serum: these are autoantibodies to components of the nervous tissue - protein S-100, GFAP, myelin basic protein, native DNA, platelet membrane antigens, antigens to colon cell membranes , mitochondrial antigens of liver cells (Table 2).

Table 2.

The content of organotropic autoantibodies in low birth weight newborns

Type of autoantibodies	Marker function of autoantibodies	Control group	group 1 (n=26), p1	group 2 (n=38), p2
Index of immunoreactivity		- 12,2±1,1	-35,3 2,7**	-38,3 2,7**
A / t to S100 - a protein - apoptosis regulator, trophic factor of serotonergic neurons	Marker of changes in the central and peripheral nervous system. An increase in autoantibodies is accompanied by disturbances in the emotional and volitional sphere, in some cases this increase initiates the human papillomavirus	7,4±1,0	54,7± 2,6**	48,6±1,8**,*
A / t to GFAP - Brain-specific glial fibrillar acidic protein of the intermediate filaments of the astrocyte cytoskeleton system	Marker of astroglial proliferation, including reactive astrogliosis.	5,7±0,3	45,9± 9,4**	62,8±8,8*,**

A / t to MBP - myelin basic protein	Marker of demyelinating processes	5,2±0,6	50,3±5,4**	39,7±2,3*,**
A/t to double-stranded DNA	It characterizes the state of the immune system, a marker of infectious-inflammatory and autoimmune processes, general immunoreactivity	8,0±2,1	17,1± 2,9**	16,4 ±1,54**
A / t to TrM-03 - antigens of platelet membranes	Autoantibodies to platelets, markers of changes in the hemostasis system	13,0±3,0	29,4 ±1,9**	30,3 ±3,2**
A/t to ScM	Marker of changes in the walls of the thick intestines	9,4±0,6	15,7 ±1,3**	16,8 ±1,6**
A / t to HMMP - antigens of liver mitochondria	Marker of changes in liver tissue	5,6±0,4	18,7 ±2,4**	20,6 ±2,7**
A/t to LuM-02+LuS-06 – membrane and cytoplasmic components of lung tissue	Markers of changes in lung tissue	-15,0± 4,1	-21,4± 3,9	-19,7 ±2,5
A/t to b2-glycoprotein I	Characterizes the state of the immune system, a marker infectious-inflammatory and autoimmune processes, cicatricial adhesive processes	5,1±1,2	8,1± 1,2**	9,05± 1,42**
A/t to the Fc-fragment of IgG	It characterizes the state of the immune system, the intensity of the production of immunoglobulins, a marker of infectious-inflammatory and	-2,8±1,5	-3,1± 1,03	-2,17± 0,61

	autoimmune processes			
A/t to collagen	Characterizes the state of the immune system, a marker of connective tissue destruction, cicatricial adhesive changes	-7,2±2,7	-6,7± 1,3	-7,2± 1,2
A / t to CoM-02 - membrane antigens of myocardial cells	Marker of changes in the heart muscle	-9,0±1,0	-14,5± 2,1	-15,8± 1,6
A / t to b1-adrenergic receptors	Marker of changes in the heart muscle	-12,1±2,4	-18,1 ±2,0**	-15,5 ±2,8
A / t to ANCA - anionic proteins of vascular endothelium	Autoantibodies to the endothelium, a marker of vascular changes similar to vasculitis	-9,0±1,3	-8,4± 1,5	-10,0 ±1,1
A/t to KiM-05+KiS-07 – membrane and cytoplasmic components of kidney tissue	Markers of changes in kidney tissue	-2,0±0,4	-6,6± 2,3	-6,2± 1,3
A / t to GaM-02 - membrane antigens of the gastric mucosa	Marker of changes in the walls of the stomach and small intestine	7,4±1,8	8,3 ±2,4	12,4 ±2,1
A / t to ItM-07 - membrane antigens of cells of the small intestine mucosa	Marker of changes in the walls of the stomach and small intestine	-5,8±1,1	-8,7 ±2,7	-8,5 ±1,6
A / t to HeS-08 - cytoplasmic antigens of hepatocytes	markers of changes in liver tissue	-2,5±1,1	-6,4 ±1,2**	-5,6 ±0,5**
A / t to Ins - insulin	Islet Change Marker Langengars and peripheral insulin receptors	-9,0±1,0	-9,7 ±2,0	-9,9 ±1,7
A / t to Ins-R - insulin receptors	Change marker in islets of Langengars and peripheral insulin receptors)	-9,5±3,0	-6,8± 1,6	-7,53± 1,4

A/t to thyroglobulin	Marker of thyroiditis and changes in thyroid gland)	-9,0±0,5	-8,7 ±2,2	-7,7 ±1,1
A / t to TSH-R - TSH receptors	Marker of thyroiditis and changes in thyroid gland	7,0±0,4	5,8± 1,9	6,0± 1,5
A / t to AdrM-D / C-0 - membrane antigens of the cells of the cortical layer of the adrenal glands	Marker of changes in the adrenal glands	8,6±3,3	8,9 ±1,85	7,5± 1,8
A / t to Spr-06 - membrane antigens of spermatozoa	Marker of changes in the prostate gland in men and endometrium in women	- 17,0±5,6	-18,8 ±2,5	-18,2 ±2,3

Note: *- differences are statistically significant between groups 1 and 2 at $p<0.05$.
**-differences are statistically significant from the control group at $p<0.05$

The level of autoantibodies to the S100 protein exceeded the values in the control group by 7.3 times and 6.6 times in newborns of groups 1 and 2, respectively, and in children weighing 1500.0-1999.9 g, this indicator was significantly higher than in newborns with weighing 2000.0-2500.0g. A similar trend was noted for the MBM, GFAP. These results show a fairly high degree of damage to the nervous tissue in low birth weight newborns against the background of a decrease in the elimination of products of incomplete catabolism and apoptosis of brain cells. This is also confirmed by the high level of autoantibodies to double-stranded DNA in low birth weight newborns, the content of which was increased by 2.1 times relative to the control group in children of groups 1 and 2. An increase in autoantibodies to double-stranded DNA indicates the activation of apoptotic processes in low-weight newborns in all tissues, when there is a powerful release of excess phospholipid components of the membranes of destroyed cells and fragments of nuclear DNA, which is the source of autoantibodies[22]. The increase in these autoantibodies is the result of catabolism, apoptosis, and reduced elimination of biodegradation products of various molecules in low birth weight infants. In addition to impaired clearance from intermediate and end products of catabolic processes against the background of an increase in their intensity, the accumulation of autoantibodies can have a cytopathic effect. It is known that antinuclear antibodies against the nuclear structures of cells have a pronounced pathogenic potential, disrupting gene transcription [24], which can contribute during the perinatal period in small children, reducing the adaptive capacity of their body.

An analysis of the spectrum of elevated autoantibodies shows that the most vulnerable organs in low birth weight newborns are the central nervous system, the large intestine (increased autoantibodies to ScM), and the liver (increased

autoantibodies to HMMP). This predisposition to autoaggression to these tissues in newborns may explain the high incidence of perinatal CNS damage, necrotizing enterocolitis in these children [8,25], as well as a high tendency to disturbances in the hemostasis system and a prolonged course of transient conditions - neonatal jaundice.

It is known that the S100 protein is involved in the development of the nervous system, regulates the migration of neuroblasts in the brain and spinal cord and their functional differentiation, regulates the processes of intracellular calcium metabolism and protein phosphorylation, organization of the cytoskeleton, gene transcription, growth and differentiation of glial cells and neuronsю Its high level in the first 72 hours of life is a marker of a poor prognosis in children with asphyxia of the severity of cerebral disorders. The growth of antibodies to GFAP-specific protein of astrocyte filaments - accompanies the proliferation of astroglia in response to inflammation, damage and oxidative stress

The involvement of the CNS and intestines in damage in preterm infants is also associated with the presence of a hypoxic component, to which these tissues are particularly sensitive. [28]. The involvement of liver mitochondria with the development of oxidative stress and endogenous intoxication during fetal hypoxia was confirmed by us earlier in the experiment, and disturbances in the phospholipid spectrum of membranes of microsomal and mitochondrial liver fractions were detected, which were observed both at birth and up to 21 days of observation of rat pups that underwent intrauterine hypoxia and premature births with low birth weight[2, 28]. This once again proves that protein-energy deficiency, along with hypoxia, is a trigger for an increase in ROS production in the liver, when mitochondria are the most vulnerable and are the first to turn on, which can provoke an increase in the production of autoantibodies to them. The presence of autoantibodies to the components of liver mitochondria (cardiolipin), as well as to the nervous tissue and intestines, is perhaps another of the mechanisms that contribute to the damage to organs and tissues in low birth weight newborns long before the clinical manifestation

We also found an increase in autoantibodies to platelets, the level of which exceeded the control level by 2.2 times, and, regardless of the gestational age after 32 weeks. The presence of antiplatelet antibodies indicates a predisposition to increased adhesion and aggregation of platelets and potential microcirculatory disorders, which play a key role in hypoxic-ischemic lesions of the brain and intestines in preterm infants both in the early neonatal period and later.

As our results showed, the average values of autoantibodies to 3 tissues: lung, heart and reproductive system were slightly reduced, in some cases to the threshold of the "yellow zone", while there were no significant differences between the control and experimental groups, and the incidence of mothers with diseases of these systems was also identical in both control and experimental groups. It is possible that the presence of somatic pathology of the mother leads to insufficient synthesis of autoantibodies to the affected organs, which may reflect both the insufficient development of these organs and increased vulnerability to damage. [1,13]. Autoantibodies have a protective property, tk. bind the degradation products of

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biomolecules, so their decrease is undesirable, it, along with an increase in autoantibodies, can cause the onset of pathological changes in tissues.

Thus, autoantibodies to the membrane and cytoplasmic components of the lung tissue in low birth weight newborns were in the "yellow zone", indicating subthreshold changes that can be realized in bronchopulmonary dysplasia in newborns, or frequent colds of the upper respiratory tract in children of the first years of life. Subthreshold changes in these autoantibodies in newborns were combined with the incidence of bronchopulmonary pathology in mothers of underweight children. At the same time, as our observations showed, the frequency of diseases of the upper and lower respiratory tract was the same in mothers of the control group and groups 1 and 2, and the level of autoantibodies in their newborns also did not differ significantly between the control and two observation groups. This suggests a maternal origin of autoantibodies to lung tissue in newborns.

Also, the maternal origin of autoantibodies is indicated by the fact that newborns have a subthreshold level of a decrease in autoantibodies to the Spr-06 antigen. This is a common antigen of the membranes of spermatozoa and human prostate cells, which is not expressed by the cells of the woman's body (gender-specific antigen). The production of autoantibodies to it occurs in women with inflammatory diseases of the endometrium and genital tract, a pathological change in the level of autoantibodies is an indicator of inflammatory diseases in the pelvic organs in women [22]. It should be noted that the level of autoantibodies to Spr-06 in newborns did not differ significantly between the control group, groups 1 and 2, and the frequency of diseases of the reproductive system was also identical in the experimental and control groups.

The level of cardiospecific autoantibodies to membrane antigens of myocardial cells and to b1-adrenergic receptors in low birth weight newborns was characterized by their moderate deficiency in the range of -15% - -18%. Pathological changes in the level of antibodies to the membrane antigen of cardiomyocytes CoM-015-15 and b1-adrenergic receptors are markers of the onset of destructive changes in the myocardium and the conduction system of the heart. It is known from the literature that a significant deviation of the level of autoantibodies from the reference values may be associated with metabolic disorders, causing myocardial dysfunction; and inhibition of the production of cardiospecific autoantibodies was associated with arrhythmias in children[10,11].

The average level of autoantibodies to the IgG fragment, collagen, anionic proteins of the vascular endothelium, kidney tissue, stomach, hepatocytes, islets of Langerhans, insulin and insulin receptor, as well as to thyroglobulin and TSH receptors were within the reference values and data of the control group. At the same time, a comparative assessment of the number of children with a pathological level of autoantibodies in the control group and observation groups 1 and 2 showed that the number of children with a significant deviation of autoantibodies among low-weight children is statistically significantly higher than among children in the control group in almost all studied parameters. (Table 3). At the same time, the frequency of significant deviations was higher ($p<0.05$) in group 1 relative to group 2 for such

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parameters as autoantibodies to ScM, HMMP, beta-adrenergic receptors, ANCA, KiM-05+KiS-07, TSH-R, to AdrM -D/C-0, Spr-06.

Table 2.
The frequency of occurrence of a significant deviation from the conditional norm of organotropic autoantibodies in low birth weight newborns

	The nature of the deviations	1 group (1500-1999г), n=26, p1		2 group (2000-2500г), n=38, p2		Control group	
		n	**%**	**n**	**%**	**n**	**%**
Index of immunoreactivity	Conditional rate (-20 - +10)	0	0	0	0	10	83,3
	Relative deviation.	0	0	0	0	2	16,7
	significant deviation 35 +15	26	100	38	100	0	0
A / t to S100 - a protein - apoptosis regulator, trophic factor of serotonergic neurons	Conditional rate (-20 - +10)	0	0	0	0	10	83,3
	Relative deviation	0	0	0	0	1	8,4
	significant deviation.	26	100	38	100	1	8,3
A / t to GFAP - Brain-specific glial fibrillar acidic protein of intermediate filaments of the astrocyte cytoskeleton system	Conditional rate (-20 - +10)	0	0	0	0	12	100
	Relative deviation.	0	0	0	0	0	0
	significant deviation.	26	100	38	100	0	0
A / t to MBP - myelin basic protein	Conditional rate (-20 - +10)	0	0	0	0	12	100
	Relative deviation	0	0	0	0	0	0
	significant deviation..	26	100	38	100	0	0
A/t to double-stranded DNA	Conditional rate (-20 - +10)	5	19,2	5	13,2	9	75

	Relative deviation.	11	42,3	20	52,6	2	16,7
	significant deviation	10	38,5 *	13	34,2*	1	8,3
A / t to TrM-03 - antigens of platelet membranes	Conditional rate (-20 - +10)	3	11,5	5	13,2	8	66,7
	Relative deviation.	0,0	0,0	9	23,7	1	8,3
	significant deviation.	23	88,5 *	24	63,2*, **	3	25,0
A/t to ScM	Conditional rate (-20 - +10)	3	11,5	4	10,5	11	91,7
	Relative deviation.	10	38,5	27	71,1	0	
	significant deviation.	23	88,5 *	7	18,4*, **	1	8,3
A / t to HMMP - antigens of liver mitochondria	Conditional rate (-20 - +10)	3	11,5	4	10,5	12	100
	Relative deviation.	3	11,5	13	34,2	0	0
	significant deviation	20	76,9 *	21	55,3*, **	0	0
A/t to LuM-02+LuS-06 – membrane and cytoplasmic components of lung tissue	Conditional rate (-20 - +10)	16	61,5 *	20	52,6*	9	75
	Relative deviation.	0,0	0,0	4	10,5	2	16,7
	significant deviation	10	38,5 *	14	36,8*	1	8,3
A/t to b2-glycoprotein I	Conditional rate (-20 - +10)	18	69,2	20	52,6	12	100
	Relative deviation.	8	30,8 *	9	23,7*	0	0
	significant deviation	0,0	0,0	9	23,7*, *	0	0
A/t to the Fc-fragment of IgG	Conditional rate (-20 - +10)	26	100, 0	38	100,0	12	100
	Relative	0,0	0,0	0	0,0	0	0

	deviation.						
	significant deviation	0,0	0,0	0	0,0	0	0
A/t to collagen	Conditional rate (-20 - +10)	26,0	100,0	38	100,0	11	91,7
	Relative deviation.	0,0	0,0	0	0,0	0	0
	significant deviation	0,0	0,0	0	0,0	1	8,3
A / t to CoM-02 - membrane antigens of myocardial cells	Conditional rate (-20 - +10)	13	50,0	29	76,3	10	83,3
	Relative deviation.	8	30,8	2	5,3	0	0
	significant deviation	5	19,2	7	18,4	2	16,7
A / t to b1-adrenergic receptors	Conditional rate (-20 - +10)	16	61,5	27	71,1	8	66,7
	Relative deviation.	2	7,7	2	5,3	4	33,3
	significant deviation	8	30,8*	7	18,4*,**	0	0
A / t to ANCA - anionic proteins of vascular endothelium	Conditional rate (-20 - +10)	23	88,5	34	89,5	12	100
	Relative deviation.	0	0,0	2	5,3	0	0
	significant deviation	3	11,5*	2	5,3*,**	0	0
A/t to KiM-05+KiS-07 – membrane and cytoplasmic components of kidney tissue	Conditional rate (-20 - +10)	23	88,5	34	89,5	12	100
	Relative deviation.	0	0,0	2	5,3	0	0
	significant deviation	3	11,5*	2	5,3*,**	0	0
A / t to GaM-02 - membrane antigens of the gastric mucosa	Conditional rate (-20 - +10)	21	80,8	26	68,4	11	91,7
	Relative deviation..	0,0	0,0	4	10,5	0	0

	significant deviation. - 35 +15	5	19,2 *	8	21,1*	1	8,3
A / t to ItM-07 - membrane antigens of cells of the small intestine mucosa	Conditional rate (-20 - +10)	23	88,5	35	92,1	12	100
	Relative deviation..	0,0	0,0	0	0,0	0	0
	significant deviation. - 35 +15	3	11,5 *	3	7,9*	0	0
A / t to HeS-08 - cytoplasmic antigens of hepatocytes	Conditional rate (-20 - +10)	23	88,5	36	94,7	12	100
	Relative deviation..	3	11,5	0	0,0	0	0
	significant deviation. - 35 +15	0,0	0,0	2	5,3	0	0
A/т к Ins – insulin	Conditional rate (-20 - +10)	23	88,5	34	89,5	12	100
	Relative deviation..	0,0	0,0	0,0	0,0	0	0
	significant deviation. - 35 +15	3	11,5 *	4	10,5*	0	0
A / t to Ins-R - insulin receptors	Conditional rate (-20 - +10)	26, 0	100, 0	34	89,5	12	100
	Relative deviation..	0	0,0	0	0,0	0	0
	significant deviation. - 35 +15	0	0,0	4	10,5	0	0
A/t to thyroglobulin	Conditional rate (-20 - +10)	23	88,5	38	100,0	12	100
	Relative deviation..	3	11,5	0	0,0	0	0
	significant deviation. - 35 +15	0,0	0,0	0	0,0	0	0
A / t to TSH-R -	Conditional	23	88,5	36	94,7	12	100

TSH receptors	rate (-20 - +10)						
	Relative deviation..	0	0,0	0	0,0	0	0
	significant deviation. - 35 +15	3	11,5 *	2	5,3*,**	0	0
A / t to AdrM-D / C-0 - membrane antigens of the cells of the cortical layer of the adrenal glands	Conditional rate (-20 - +10)	21	80,8	27	71,1	10	83,3
	Relative deviation..	2	7,7	9	23,7	0	0
	significant deviation. - 35 +15	3	11,5 *	2	5,3*,**	2	16,7
A / t to Spr-06 - membrane antigens of spermatozoa	Conditional rate (-20 - +10)	18	69,2	22	57,9	12	100
	Relative deviation..	0	0,0	0	0,0	0	0
	significant deviation. - 35 +15	8	30,8 *	16	42,1*	0	0

Note: *- differences are statistically significant from the control group at $p<0.05$
**- differences are statistically significant between groups 1 and 2 at $p<0.05$

The number of children with a significant deviation in the level of autoantibodies to the membrane components of the cells of the adrenal cortex (AdrM/D/c-0) was significantly higher in group 1, both relative to group 2 and control; a similar situation was observed in the number of children with abnormal levels of autoantibodies to TSH receptors (TSH-R), autoantibodies to membrane and cytoplasmic components of the kidney tissue (KiM-0.5 + KiS-0.7), autoantibodies to anionic proteins of vascular endothelium (ANCA), as well as autoantibodies to beta-adrenergic receptors and tissue of the large intestine. As we indicated above, the level of these autoantibodies was significantly higher in low birth weight infants born at 32–34 weeks of gestation relative to children born at term and at 35–37 weeks of gestation. These results indicate an increased susceptibility to damage along with the CNS, intestines and platelets, as well as the vascular endothelium, kidneys, heart, adrenal glands and thyroid gland in low birth weight newborns weighing 1500.0-1999.0 g. Involvement of the adrenal glands and thyroid gland can also lead to a violation of the adaptation of these newborns, which must be taken into account in the rehabilitation program.

We have studied the content of hormones TSH, T3 total, cortisol and ACTH to assess the adaptive reserve in these newborns. It was found that the level of ACTH in low birth weight newborns exceeded the control values by 3.1 and 2.6 times in children of

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groups 1 and 2, respectively, and the differences between groups 1 and 2 were statistically significant at $p<0.05$, and the level of cortisol in low birth weight infants newborns was significantly reduced, which indicates an insufficient overall adaptive reserve of the body and tension in the hypothalamic-pituitary-adrenal system(Table 4)

Table 4

The content of hormones in the blood of small newborns

	Reference interval	Control group	group 1 (n=26), p1	group 2 (n=38), p2
TSH, mIU/l	1-39	1,84±0,58	4,1±0,2*	3,6±0,2*,**
T3 total, nmol/l	1,5-11,4	1,66±0,06	1,26±0,03*	1,32±0,02*,**
ACTH, pmol/l	2,2-41,0	22,8±2,8	64,0±2,8*	53,0±1,5*,**
Cortisol, nmol/l	55-304	77,8±6,1	46,8±3,0*	52,9±1,5*

Note: *- differences are statistically significant from the control group at $p<0.05$;
**- differences are statistically significant between groups 1 and 2 at $p<0.05$

Thyroid axis status: Studies of thyroid hormones have shown some increase in TSH with a decrease in total T3 in low birth weight infants. The presence of these shifts against the background of an increase in autoantibodies to TSH receptors (TSH-R) and autoantibodies to the membrane components of the cells of the adrenal cortex (AdrM/D/c-0k) proves the contribution of autoimmunization to these tissues in the implementation of violations of their functions. From these results, it can be concluded that low-birth-weight newborns with abnormal levels of autoantibodies to endocrine tissues need close attention and monitoring, as well as an individual rehabilitation program.

An analysis of the results showed that mothers of low birth weight newborns were significantly more likely to have diseases of the thyroid gland, liver, kidneys, reproductive system, while the number of children with pathological levels of autoantibodies to TSH receptors (TSH-R), autoantibodies to membrane and cytoplasmic components of kidney tissue (KiM-0.5+KiS-0.7) was also significantly higher among low birth weight infants. This suggests the contribution of maternal autoantibodies in these children. The level of organotropic autoantibodies in this situation partly reflects the immunological pattern of the mother, which can potentially be realized in the child. There are 2 conflicting views on the origin of autoantibodies in the fetus. The first is that autoantibodies are high-affinity immunoglobulins of classes M and G, which have clustering and ontogenetic dynamics, are synthesized by the fetus, and also penetrate transplacentally from the mother. [5]. The reason for this was the detection in the cord blood of a different palette of autoantibodies, different from the maternal one, which is supplemented by the transplacental transfer of maternal autoantibodies; in ontogenesis, the spectrum of autoantibodies is supplemented and diversified; at the same time, the production of autoantibodies in fetuses has an internal cause, and not only external cross-reacting antigenic stimuli [23]. The second view of autoantibodies is that they are synthesized by the fetus, are immunoglobulins M of low affinity and broad specificity, which recognize both their own and microbial epitopes, are produced by B1a and B1b

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lymphocytes (1-5% of the total population); it is a self-sustaining population of B cells (CD20, CD27, CD43, CD5+, CD70), which are produced in the liver and bone marrow of the fetus in early ontogenesis, primarily dominate in the serous cavities and are able to disperse, including into the lamina propria of the gastrointestinal mucosa and inflammation foci , these lymphocytes have suppressor functions [7].

Our data are more consistent with the first hypothesis, according to which the autoantibody fraction is mixed - maternal and fetal.

We have identified autoantibodies to the components of the nervous tissue, platelets, and intestines in all low birth weight newborns, regardless of the pathology of these systems in mothers, which indicates the synthesis of these autoantibodies in the fetuses themselves. The fact that disturbances in the production of ACTH, TSH, T3 and cortisol were associated with abnormal levels of autoantibodies to these tissues in newborns indicates a direct damaging effect of autoantibodies.

According to the literature, initially, the increase in autoantibodies is aimed at increasing the efficiency of the clearance of damaged tissue and activation of regeneration processes. Identification of persistent anomalies in the content of marker autoATs of certain specificity makes it possible to analyze the nature of the changes occurring in the patient's body (including at the stages of pre-illness), more reasonably approach the prescription of therapy and evaluate the effectiveness and sufficiency of the treatment. [12,17]. To do this, it is necessary to identify a risk group from among low birth weight newborns. Taking into account that the physiological autoimmune reactions observed in most cases are induced in response to tissue damage and reflect the compensatory activation of the immune system aimed at restoring disturbed body homeostasis [19], the detection of an increase in the level of tissue-specific autoantibodies makes it possible to predict somatic pathology in a low birth weight newborn. Thus, the detection of a pathological level of autoantibodies in low birth weight newborns is necessary to predict the reserve of their adaptive capabilities and the development of somatic pathology both in the early neonatal period and in childhood. Also, the detection of autoantibodies to tissues will allow the choice of therapeutic and rehabilitation tactics.

Conclusions.

1. Total immunoreactivity, assessed by the level of autoantibodies, in newborns after 32 weeks of gestation is reduced, regardless of gestational age and birth weight.

2. A statistically significant increase in autoantibodies to components of the nervous tissue: MBP, protein S100, GFAP indicates damage to the nervous tissue in low birth weight newborns against the background of a decrease in the elimination of products of incomplete catabolism and apoptosis of brain cells, more pronounced in children born weighing 1500.0-1999 0 g at 32-34 weeks of gestation.

3.The most pronounced pathological changes in the content of autoantibodies in low birth weight newborns were found for autoantibodies to the brain, liver mitochondria, platelets, double stranded DNA, which indicates a greater vulnerability of these tissues to damage in the neonatal period.

4. Pathological shifts in the level of autoantibodies to the membrane components of the cells of the adrenal cortex (AdrM/D/c-0), TSH receptors (TSH-R), to the membrane and cytoplasmic components of the kidney tissue (KiM-0.5+KiS-0.7) , anionic proteins of the vascular endothelium (ANCA), to beta-adrenergic receptors, tissue of the large intestine (ScM), liver mitochondria (HMMP) are significantly more common in low-weight children born at 32-34 weeks of gestation relative to children born at term and at 35- 37 weeks of gestation, which indicates an increased risk of damage to these tissues in low birth weight newborns weighing 1500.0-1999.0 g.

5. Pathological changes in the level of autoantibodies to TSH receptors (TSH-R) and autoantibodies to the membrane components of the cells of the adrenal cortex (AdrM/D/c-0k) were combined with an increase in ACTH and TSH against the background of a decrease in cortisol and T3, which proves the contribution of autoimmunization to these tissues in violation of their functions.

6. The presence of somatic pathology in mothers (pathology of the respiratory, circulatory, reproductive system) was combined with the presence of pathological abnormalities in the level of the corresponding organotropic autoantibodies in newborns, which proves the influence of the mother's health status on the level of autoantibodies in newborns.

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