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AGE-RELATED FEATURES OF THE ACTIVITY OF LYMPHOCYTE ENZYMES AND THEIR INTERCONNECTION IN CHILDREN OF THE FAR NORTH

DOI 10.25789/YMJ.2020.72.23

The research was conducted to study activity indicators of lymphocyte enzymes in 99 healthy children aged 3 to 15 years living in town Tynda in the summer season. The increase of enzymes activity in children's lymphocytes was noted as they mature. Differences in indicators of enzyme activity were manifested in a lower level of dehydrogenases in the group of 3-year-old children, higher acid phosphatase, and lower glycerol-3-phosphate dehydrogenase in all age groups. Some features of age-related dynamics of the correlation relationships of the studied indicators are noted and periods of greatest adaptive tension in children are determined.

Keywords: North, children, lymphocytes, enzymes, correlation

Introduction. The regions of the Far North and equivalent areas cover more than 64% of the territory of Russia [11]. Issues of human full life activity and protection of his health in extreme climatic conditions of the North are far from being resolved. The health of the population, especially children's is under the constant influence of changeable parameters of the climate system, which often leads to the formation of various pathologies.

The city Tynda, in which the studies were conducted, is located in the most northern city of the Amur Region and, according to a number of climatic and geographical features, is assigned to areas equated to the North.

For assessing a degree of impact of

the extreme environment per person, the characteristics of homeostatic systems reflecting the adaptive capabilities of the organism should be included. Blood cells are considered as components of the immune system involved in adaptive reactions [4].

Lymphocytes are the main morphological substrate of the immune system. And the regulation of the immune response is determined by functional capabilities of these cells, which are based on intracellular metabolic reactions. The latter ones, to a large extent, are provided by a certain level of intracellular enzymes activity [2,16].

The level of functioning of these cells is supported by the mechanisms of neuroendocrine regulation, in the complex interaction of intracellular relationships, wherein the variability of the level of these connections is the most important reserve of target results effects on the organism [3].

The urgency of the problem lies in the fact that children's organism is labile to the effects of the environment and its climatic features. Children of preschool and school age are characterized, on the one

hand, by intensive growth and development rates, and, on the other hand, by insufficiently high resistance to adverse factors during this period of ontogenesis.

We have chosen the metabolic parameters of blood lymphocytes and the correlation between them as integral indicators of the degree of environmental impact on the organism. A change in the correlations between the physiological parameters of the organism under the influence of various systems of adverse environmental factors has been repeatedly proven in adult populations [3, 5, 10].

Studies dedicated to the study on the characteristics of the activity of enzymes of lymphocytes, taking into account their relationships in children in the North, are few and poor in content.

Aim of the study: to reveal the features of age-related dynamics of the activity of lymphocyte enzymes and their relationships in children of the alien population of the North.

Material and methods of research. 99 children aged from 3 to 15 were examined years living in the city of Tynda, Amur Region. All children were divided into groups: 3, 5, 7, 10 and 15 years. The

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studies were conducted in the summer season (June). It is the most stable on fluctuations in weather conditions a period of time.

The criterion for inclusion in the study was that the children were of the 1st and 2nd health groups and did not get sick in the previous two months, and also were not vaccinated during this period. All children attended kindergartens or schools. The examination of children was carried out in agreement with the administration of kindergartens and schools, when parents signed informed consent to conduct this study. The research protocol of healthy individuals was in line with ethical standards, developed in accordance with the Helsinki Declaration of the World Medical Association and was approved by the Biomedical Ethics Committee of the NIIMPS SB RAS.

The criteria for exclusion from the study were deviations in the children's health status and disagreement of children and parents at each stage of the study.

Cytochemical method was determined in lymphocytes peripheral blood activity enzymes markers metabolic pathways: Krebs cycle – succinate dehydrogenase, (SDG); glycerophosphate shunt connecting glycolysis with the Krebs cycle – mitochondrial glycerol-3-phosphate dehydrogenase (G3PDG); glycolysis – lactate dehydrogenase (LDG) and its aerobic isoenzyme – (H-LDG); pentose phosphate pathway – NADPH₂-diaphorase (NADPH₂-D). catabolism – non-specific acidphosphatase, (ACP), according to [9]; catabolism of monoamines – monoamine oxidase (MAO) according to [7]. The activity of dehydrogenases and MAO was expressed by the number of formazan granules in 1 cell (gr./ cell), and ACP in Kaplow units.

The connectivity of the studied indicators was assessed by correlation analysis. The intensity of adaptive reactions in children studied by method correlation adaptometry using the G-criterion. The weight of the correlation graph – G, was calculated by the formula – $G = \sum |r_{ij}|$, $|r_{ij}| \in [0,5]$, где r_{ij} are the pairwise correlation coefficients between the i-th and j-th parameters, and Σ – is the sum of the moduli of these coefficients [5,10]. The work analyzed only statistically significant correlation coefficients (r), $p < 0.05$ and higher, where p – is the achieved level of statistical significance. Statistical processing was performed using the software package "Statistica v. 6.1". The data are presented in the form $X \pm x$, where X – is the arithmetic mean, x – is the error of the mean. To assess the difference in means

in pairwise unrelated samples, the Mann – Whitney U-test was used, the difference in values was considered significant at $p < 0.05$.

Results and discussion When assessing the age-related features of the enzymatic metabolism of lymphocytes, it was found that the lowest activity of enzymes in the group of children 3 years old, while in older age groups, the level of enzymes increased (table 1). The low activity of energy and plastic metabolism enzymes in preschool children indicates a decrease in the functional capabilities of cells and their low immunoreactivity, which gives reason to regard this period as critical.

A feature of the metabolic system of lymphocytes in children of 5 years is a sharp jump in the level of activity of SDG and LDG by 1,5 times ($p < 0,01$) relative to the level of enzymes in children of 3 years, whereas in the middle-latitude zone a shift of the ontogenetic curve is observed at an older age [6,9].

At the studied stage of ontogenesis the activity of enzymes constantly increased, and in children 5, 7, 10, and 15 years old it was significantly different from the group of children 3 years old.

However, with increasing age the higher level of enzyme activity of the Krebs cycle and glycolysis in lymphocytes of children of Tynda was combined with inhibition of the glycerophosphate shunt. The activity of mitochondrial G3FDG was significantly lower than the enzyme indices of children living in middle latitudes [1,6,9].

The weakening of the catalytic function of the shuttle system G3FDG in mitochondria of lymphocytes in all age groups also violated the physiological ratio of G3PDG/SDG, which is normal – 0.59-

0.65 [6,9], and in children of Tynda it was less than 1.5-2 times, which allows us to judge the decrease in the energy potential of mitochondria. The low G3PDG activity of the lymphocytes of the children of the North is probably due; on the one hand, to the substrate outflow of glycerophosphate to the regenerative synthesis of membrane lipids. On the other hand, it is possible competition between SDG and MAO for the cofactor, given their localization in mitochondria.

In the age dynamics of the children of Tynda, an increase in LDG activity in lymphocytes was probably due to the growth of anaerobic forms of the enzyme. The proportion of the aerobic component of H-LDG decreased with age from 56% in children 3 years old to 39% in children 7-15 years old. Such a decrease in the content of the H-LDG isoenzyme indicates an increase in the intensity of anaerobic glycolysis with a decrease in the level of aerobic, which is the leading form of energy supply for lymphocytes [2]. Exactly with the activation of glycolysis with age is associated with a decrease in the aerobic fraction of LDG, because an increased concentration of pyruvate inhibits this isoenzyme [12].

In all the examined children in Tynda have a high activity of NADPH₂-D, which reaches maximum values in adolescents, exceeding the value of the indicator of the lymphocyte children 3-year in 2,5 times ($p < 0,01$). Such activation of the enzyme is apparently determined by an increased substrate flow through the pentose phosphate shunt and the corresponding synthesis of NADPH. Moreover, it is known that in the lymphocytes in the North the content of total lipids is increased, the synthesis of which depends on NADPH [1].

Table1

Indicators of enzyme activity in blood lymphocytes of children of different age groups of the alien population of the North (Tynda city, $X \pm x$)

Indicator	Age (years)				
	3 (1 group)	5 (2 group)	7 (3 group)	10 (4 group)	15 (5 group)
	n=15	n=25	n=15	n=15	n=29
SDG, gr./cl.	7.93±	11.75±	13.29±	17.20±	16.25±
G3FDG, gr./cl	3.40±	3.38±	4.61±	6.35±	6.07±
LDG, gr./cl.	5.98±	8.73±	10.15±	10.53±	12.21±
H-LDG, gr./cl.	3.37±	4.59±	5.19±	4.14±	5.20±
NADPH ₂ -D gr./cl.	4.19±	5.07±	5.81±	5.30±	10.25±
MAO, gr./cl.	1.82±	2.15±	1.66±	3.69±	–
				$p1.2.3 < 0.05$	
ACP, units Kaplow	162.0±	179.26.51	201.1±	167.69±	–

The age-related dynamics of the MAO activity level of lymphocytes in children of the city of Tynda was oscillatory in nature with a maximum enzyme activity in children of 10 years old, which reflects the peculiarity of the regulation of lymphocyte metabolism by biogenic amines in this region [15].

The activity of ACP in the lymphocytes of children of the city of Tynda is in 1,5-2 times higher than the indicators of age norms for children living in temperate latitudes [1,6,9]. Such high enzyme activity in lymphocytes indicates their accelerated maturation and entry into the bloodstream of young immunocompetent cells, and is also usually observed with inflammation and allergies [13,14].

The enzymatic systems of lymphocytes in children of Tynda are functioning with agreed coordination of the individual components, which is expressed in the presence of numerous relationships between them. Correlation analysis data showed that in all age groups of children of Tynda there are no indicators that are constantly interconnected with each other (table 2). So, in 3-year-old children, statistically significant correlations are not determined in lymphocytes. Such a decline correlation is most likely associated with a violation of intracellular regulation [8].

In the age group of children of 5 years, negative MAO-ACP relationship is revealed in lymphocytes, which indicates inhibition of catabolic reactions with an increase in the level of monoamines, as well as an increase in the interaction between energy and plastic metabolism - LDG-NADPH2-D, an increase in the intensity of aerobic glycolysis - a positive relationship LDG-H-LDG.

In the blood lymphocytes of children of 7 years old, close negative correlations of MAO and H-LDG with NADPH2-D are revealed, which indicate inhibition of biological synthesis reactions with an increase in the level of monoamines and with the intensification of aerobic glycolysis, closely associated with the work of shuttle systems (G3PDG- H-LDG).

In lymphocytes of children of 10 years of age there are more correlations than in other groups. The closest of them are noted between enzymes of energy metabolism. More weak ties in this age period are negative correlations - MAO-NADPH2-D and MAO-H-LDG, which reflect the inhibition of monoamine reactions of biological synthesis and glycolysis, and the connection H-LDG-NADPH2-D testifies to the conjugacy of these processes.

In adolescence, the number of correlation relationships between enzymes

Correlation dependence of enzyme activity indicators in blood lymphocytes in children of different age groups of the alien population of the North (Tynda)

Age, years	Enzymes	r	G
3		—	—
5	MAO - ACP LDG - NADPH2-D LDG - H-LDG	-0.55* 0.52* 0.54*	1.61
7	MAO - NADPH2-D H-LDG - NADPH2-D G3FDG - H-LDG	-0.63* -0.61* 0.60*	1.84
10	SDG - G3FDG SDG - LDG MAO - H-LDG MAO - NADPH2-D H-LDG - NADPH2-D LDG - H-LDG	0.63* 0.69** -0.53* -0.51* 0.55* 0.68**	3.59
15	SDG - G3FDG	0.52*	0.52

Note: r – the correlation coefficient; statistical significance of correlations: * – $p < 0.05$; ** – $p < 0.01$; G – correlation graph weight

decreases by 6 times, relative to children of 10 years, which reflects an increase in the number of possible options for the operation of intracellular systems and an increase in the metabolism capacity of immunocompetent cells. In lymphocytes adolescent is determined, only one positive correlation of SDG-G3PDH between enzymes of energy metabolism. Usually, such a connection arises when the level of cellular energetics changes. Probably, toward teenage age are formed new neuro-humoral regulatory impacts on lymphocyte metabolism when happens intensification of most types of metabolism [1].

When assessing the intensity of adaptive reactions in children using the G-criterion, it was found that in the group of children 3 years old $G = 0$, and in children 5,7,10 years old there is an increase in the weight of the correlation graph (table 2). The maximum G (and, therefore, adaptive tension) is determined in the group of children of 10 years old – $G = 3.59$.

In the group of adolescents, the weight of the correlation graph is 6,9 times lower relative to children of 10 years, which testifies a decrease in the level of adaptive tension.

Thus, the weight of the correlation graph serves as a rather sensitive criterion for adaptive tension, revealing the features of the process of adaptation of children to the conditions of the North at each stage of ontogenesis.

Conclusion. The research has shown the features of the formation of age-related dynamics of enzyme activity in the lymphocytes of children living in the Far North. In children of 3 years old the low-

est enzyme activity is revealed, which indicates reduced functional activity of these cells.

With the age of children, the increase in the enzyme activity of energy, plastic metabolism and the decrease in the proportion of aerobic glycolysis (H-LDG) were identified at higher level of acid phosphatase, which characterizes the peculiarities of the functioning of metabolic pathways in children in the North. The enzyme activity and their correlations determine the variants of the metabolic response of the cells of the immune system at each stage of ontogenesis. By the weight of the correlation graph, the periods of the greatest adaptation tension were identified the maximum of which was noted in children of 10 years old.

The parameters of lymphocyte metabolism in children from Tynda presented in this work as well as the nature of their interconnection, reflect the regional features of the immune status of children living in the Far North.

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DOI 10.25789/YMJ.2020.72.24

R.A. Yaskevich, E.V. Kasparov, N.G. Gogolashvili FEATURES OF THE DAILY PROFILE OF ARTERIAL BLOOD PRESSURE AT MIGRANTS OF FAR NORTH DEPENDING ON ACCOMMODATION TERMS IN NEW KLIMATOGEORGAPHIC CONDITIONS

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The aim of the study was to study features of the daily blood pressure profile of migrants in the Far North, depending on the period of residence in the new climatic and geographical conditions. Materials and methods: 267 patients of both sexes with hypertension, who arrived from the regions of the Far North for permanent residence in Central Siberia, the average age of 64.0 years, were examined. Indicators of the daily blood pressure profile were studied by the method of daily blood pressure monitoring using the BPLab MnSDP-2 device for 24 hours. Results: high frequency of the daily non-dipper profile was noted in both migrants and permanent residents of Krasnoyarsk. The non-dipper profile was more common among migrants who lived for six or more years after moving, which may indicate a more severe course of arterial hypertension during this period. Discussion: the prevalence of persons with non-dipper and night-piker profiles among migrants in the Far North indicates a more pronounced lesion of target organs and a more severe course of hypertension. Conclusions: Among migrants with longer periods of residence after moving (more than 10 years), there was an increase of indicators of the daily blood pressure profile, but the largest number of persons with the changed daily profile was found in migrants in the first 5 years after moving from the Far North. This may be due to increased adaptation processes (readaptation) to new living conditions, due to a high level of neuroticism and stress during this period.

Keywords: migrants, Far North, arterial hypertension, daily blood pressure profile.

Introduction. Arterial hypertension (AH) remains one of the most pressing modern problems, due to the high population frequency of AH, its negative impact on the state of health, working capacity and life expectancy of the population [5, 8]. The study of the characteristics of AH among the population living in harsh conditions of the North and Siberia is [3, 4, 6, 9, 10]. In harsh climatic conditions, the cardiovascular system (as highly reactive) is one of great importance the first

to be included in adaptive reactions [3, 11]. This cause certainly affects productivity and ability to work [2, 11]. In regions with extreme climatic conditions, this can cause a negative migration flow and destabilization of the population, in particular in the regions of the Far North [10]. Climatic conditions can also play a role in the re-adaptation of the human body in the new living conditions [10].

Currently, 24-h ambulatory BP monitoring (ABPM) is a valuable diagnostic