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INFLUENCE OF ADDITIONAL VITAMINIZATION OF SCHOOLCHILDREN RATIONS IN THE ARCTIC ON VARIABILITY OF MORPHOFUNCTIONAL PARAMETERS OF THE IMMUNE SYSTEM

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The paper reports a representative study of the effect of vitaminization of children of the North on one of the most important indicators of health - immunity. **Objective** of the study: to identify the features of the variability of morphofunctional indicators of the immune system of schoolchildren after prolonged vitaminization in the Arctic.

Materials and methods. Practically healthy schoolchildren aged 10-11 years (60 people) living in the city of Norilsk was examined. Children from the same school, who regularly took a domestic multivitamin complex of 1 tablet once a day from September to March, made up the main group (n = 30). Children from another school who did not take multivitamins formed a comparison group (n = 30). The luminescent-histochemical method of H. Yokoo et al. (1982) modified by V.P. Novitskaya (2000), the content of catecholamines (CA) and serotonin (Ser.) in lymphocytes and the ratio of catecholamines: serotonin (CA / Ser.) were determined; hematological method was used to determine the blood composition indicators in percent: basophils, %, eosinophils, %, band neutrophils, %, neutrophils, %, lymphocytes, %, monocytes, %, and the Garkavi index : lymphocytes / neutrophils.

Results and discussion. It was established that after the inclusion of multivitamins in the diet of children, a decrease in the level of CA and an increase in the serotonin content in blood lymphocytes was observed. It was revealed that in boys of the main group the level of CA decreased by 2.6 times (p < 0.001), whereas in girls it was only 1.5 times (p < 0.01) relative to the children of the comparison group. Along with a change in the balance of neurotransmitters after taking multivitamins in girls and boys in the main group, an increase of 1.5-1.6 times (p < 0.05) was observed in the percentage of band neutrophils relative to children in the comparison group.

Conclusion. The results of the study showed the multivariate functioning of the immune system of schoolchildren in the conditions of the Far North after the inclusion of multivitamins in the diets. A change in the balance of regulatory indicators in schoolchildren's lymphocytes, which can change the functional activity of these cells, has been established. Carried out vitaminization, among schoolchildren of the Polar region significantly changes the balance of the cellular elements of peripheral blood in children in this region.

Keywords: North, schoolchildren, vitaminization, variability of blood parameters.

Introduction. The demand for scientific studies detailing the results of additional vitaminization of schoolchildren is related to the fact that the actual nutrition of children aged 7-14 years in the Arctic is characterized by significant shortcomings in the form of a deficiency of micro and macro nutrients, which increases the risk of developing many diseases [1, 5, 7, 12]. Especially important is the optimal supply of vitamins of children of primary school age, when intensive growth and formation of the organism.

The national program for the optimization of the provision of vitamins and minerals of children in Russia empha-

sized that one of the methods of choice that favorably differ from others is the vitaminization of children's food rations using multivitamin preparations [5]. This has been justified earlier in Russia [1, 5, 7] and abroad [9, 11, 12].

For reliable evidence of the effect of the use of vitamin complexes for prophylactic purpose the object of study should include the characteristics of homeostatic systems of indicators of the adaptive capabilities of the organism. These requirements are met by blood cells as components of the immune system involved in adaptive responses to preserve the changed homeostasis [3, 10].

It is well known the participation of blood cells in the mechanisms of the adaptation syndrome, including the conditions of the Far North [2, 4]. Monoaminergic systems exert their influence on immune responses through the hypothalamus-pituitary-adrenal system. The realization of these processes occurs through the action of mediators and hormones on the corresponding receptor structures of the cells of the immune system [3, 10].

It is known that hormones and neurotransmitters can affect the functional activity of these cells, causing either stimulation of the immune response with an increase in the proliferative abilities of the cells, or activate suppressor activity, re-

ducing the level of the immune response [2, 3, 10]. In the literature there is information that the complexes of vitamins and minerals exhibit immunomodulatory and antioxidant activity have an adaptogenic effect on the organism [1, 3, 7].

There are no studies on the variability of the immune system parameters in children of primary school age after prolonged vitaminization in the conditions of the Far North, which determines the relevance and scientific novelty of this work.

Aim of the study: to identify the features of the variability of morphofunctional indicators of the immune system of schoolchildren after prolonged vitaminization in the Arctic.

Material and methods of research. Schoolchildren - representatives of the alien population of the North aged 10-11 years living in the city of Norilsk (60 people) were under observation. The children of the same school, who regularly took a domestic multivitamin complex, 1 tablet once a day, during the school year from September to March, made up the main observation group (n = 30, 15 girls and 15 boys). Children from another school who did not take multivitamins constituted the comparison group (n = 30, 15 girls and 15 boys).

Both schools were located in areas with the same environmental situation.

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The criterion for inclusion in the study was that the children were somatically healthy, did not take other medications and vitamin complexes, did not undergo vaccination during this period. The examination of children was carried out in consultation with the school administration, when parents signed an informed consent to conduct this observation and study.

The exclusion criterion from the study was deviations in the condition of the children and the disagreement of the children and the parents.

As a means for prophylactic vitaminization, a multivitamin complex containing basic vitamins was used, whose composition is close to the physiological daily needs of school-age children [4]. The composition of one multivitamin bean contains the following components: vitamins – A – 3300 IU (200% of daily need); B₁ – 0.002 g (133%); B₂ – 0.002 g (153%); B₆ – 0.003 g (143%); B₁₂ – 0.000002 g (6.7%); PP – 0.02 g (100%); P – 0.01 g (6.7%); E – 0.01 g (56%); C – 0.075 g (107%); folic acid – 0.00007 g (17.5%) and calcium pantothenate 0.03 g (60%).

After vitaminization, the children took blood from a finger. On blood smears using the fluorescent-histochemical method of H. Yokoo et al. (1982) modified by V.P. Novitskaya (2000), the content of monoamines, catecholamines (CA) and serotonin (Ser.) [6] was determined in lymphocytes. The level of catecholamines and serotonin was expressed in conventional units (cu) and the ratio of catecholamines: serotonin (CA / Ser.) was calculated.

The hematological method determined the composition of blood leukocytes in percent (leukocyte formula): eosinophils,%, basophils,%, band neutrophils,%, neutrophils,%, lymphocytes,%, monocytes,%. As an integration test, the adaptation index Garkavi was used, calculated the ratio of lymphocytes:neutrophils. Statistical processing was performed using the software package "Statistica v. 6.1". The data are presented as $X \pm x$, where X – is the arithmetic average, x – is the average error. The Mann – Whitney U-test was used to estimate the difference between the average in pairwise unrelated samples, the difference of values was considered significant at $p < 0.05$.

Results and discussion. Studies have shown that changes in the morphological and functional parameters of the cells of the immune system in the examined groups of children are characterized by significant differences (Table 1). First

of all, it was revealed that the level of catecholamines in lymphocytes of children living in conditions of the North (comparison group) is significantly higher, and the level of serotonin is significantly lower than in children living in middle latitudes [6]. This ratio is probably related to the initially large voltage of adrenergic systems, in extreme polar conditions, when the child's organism is to some extent protected from the effect of their excess, by accumulating catecholamines mainly in the blood cells.

The inclusion of a multivitamin complex in the diets of children of the Polar region, made it possible to identify the dependence of the variability of the morphofunctional parameters of the immune system on the sex of the child. After vitaminization in children of the main group of Norilsk, revealed a decrease in the content of CA and an increase in the level of serotonin in blood lymphocytes were found relative to the indicators of children in the comparison group (Table 1). So, when comparing the degree of decrease in the content in the lymphocytes of CA, it was found that in boys of the main group, the level of CA decreased by 2.6 times ($p < 0.001$), whereas in girls only 1.5 times ($p < 0.01$) relative to children comparison groups. Thus, after taking multivitamins in boys of the main group, the level of CA was

lower by 41.7% ($p < 0.001$) than in girls.

When comparing the degree of increase in the serotonin content in the lymphocytes of children, it was found that in girls of the main group the level of serotonin increased 2 times ($p < 0.01$) whereas in boys only 1.5 times ($p < 0.05$) compared to children of the comparison group. Accordingly, the ratio of CA / Ser. in boys of the main group, it was lower by 3.8 times ($p < 0.01$), and in girls it was only 2.5 times lower ($p < 0.01$) relative to the children of the comparison group. Thus, the ratio of CA / Ser. in boys 2 times lower ($p < 0.01$) than in girls of the main group (Table 1).

By themselves, these facts indicate a possible decrease in the rate of capture of CA by lymphocytes or a decrease in their synthesis by cells. On the other hand, the level of monoamines characterizes sexual dimorphism of the reactivity of immune cells in schoolchildren of the Far North.

The decrease in this ratio in children of the North after vitaminization indicates a change in the balance of neurotransmitters, which play a huge role in the process of human adaptation to the conditions of the North. The study showed that the use of multivitamins selectively modulates the activity of peripheral monoaminergic structures,

Analysis of hematological parameters obtained by us (Table 2) in children of

Table 1

the content of monoamines in the blood lymphocytes of children of two schools in Norilsk after vitaminization ($X \pm x$)

Indicator	Main group		Comparison group	
	Girls n=15	Boys n=15	Girls n=15	Boys n=15
Catecholamines (cu)	42.0± 3.57**	24.5± 1.9***	62.2± 3.99	63.93± 3.23
Serotonin (cu)	130.8± 21.34**	127.7± 12*	65.86± 6.14	85.2± 5.11
CA / Ser.	0.42± 0.09***	0.21± 0.02**	1.05± 0.11	0.8± 0.07

Note. In the Tables 1 and 2 statistically significant differences between the groups of children taking vitamins (main group) and the comparison group: * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

Table 2

Leukocyte blood counts in children from two schools in the city of Norilsk after vitaminization ($X \pm x$)

Показатель	Группа основная		Группа сравнения	
	девочки n=15	мальчики n=15	девочки n=15	мальчики n=15
Eosinophils, %	5.3± 1.31	4.47± 0.82	4.2± 0.93	5.53± 0.65
Basophils, %	0.3± 0.16*	0.31± 0.11	1.13± 0.28**	0.26± 0.12
Band neutrophils, %	4.7± 0.12*	4.15± 0.11*	3.13± 0.15	2.53± 0.12
Neutrophils, %	40.9± 1.74	39.73± 2.02	41.93± 1.79	43.4± 1.68
Lymphocytes, %	46.5± 1.69	50± 1.92	48.13± 1.49	47.06± 1.87
Monocytes, %	2.3± 0.38**	1.26± 0.2	1.46± 0.28	1.2± 0.2
Lymphocytes : Neutrophils	1.16± 0.08	1.34± 0.1	1.19± 0.01	1.12± 0.08

the alien population of the Polar region (comparison group) showed that the characteristic of the cellular composition of peripheral blood is mainly subject to patterns, studied in detail and well known in the literature. In these groups, high values of the Garkavi adaptation index are recorded, which correspond to the reaction of increased activation of the organism.

The shift in the level of neurotransmitters we noted after prophylactic vitaminization is also reflected in the composition of the leukocyte formula. (Table 2). The initial structure of the blood composition indicators (the comparison group) by gender did not significantly differ among schoolchildren in the Polar region. We can only note that in the comparison group girls, the level of basophils is 80% ($p < 0.01$) higher than in boys. Such a structure of blood parameters, apparently, can be regarded as one of the variants of regional specificity.

We found that after vitaminization there are differences in the leukocyte formula between girls and boys. Thus, in the girls of the main group, a decrease in the basophil content by 3.76 times ($p < 0.05$) relative to the girls of the comparison group was revealed. It is known that there is a close functional relationship between peripheral blood basophils and tissue basophils. It is noticed that with a decrease in cells of one type, the number of cells of another type increases [3]. Activation of tissue basophils is usually accompanied by the release of biologically active components, such as serotonin [3]. Confirmation of this, we see that after vitaminization in the lymphocytes of children in the main group of Norilsk, the level of serotonin was higher than in children of the comparison group.

Along with a change in the balance of neurotransmitters after taking multivitamins in children of the main group, a change in the percentage of band neutrophils was revealed. In both girls and boys of the main group, an increase of 1.5–1.6 times ($p < 0.05$) was observed in the percentage of band neutrophils relative to the children in the comparison group. The increased level of band neutrophils in the blood indicates the activation of bone marrow cells to enhance proliferation and mitotic activity, probably due to multivitamins.

The results described clarify the idea that an increase in band neutrophils

usually occurs during acute or moderate chronic stress. The development of neutrophilic leukocytosis is mainly associated with an increased intake of bone marrow or vascular neutrophils from the cellular reserve into the circulation, which are recruited by glucocorticoid and monoamines. According to modern concepts, central adrenergic, dopaminergic and serotonergic structures play a coordinating role in the implementation of the response of the blood system to the effects of extreme irritants of various etiologies [2].

In addition, in the main group of girls, an increase of 45.2% ($p < 0.01$) in the percentage of monocytes relative to the main group of boys was established (Table 2).

After vitaminization in the main groups of schoolchildren, high values of the Garkavi adaptation index were also observed, which correspond to the reaction of increased activation of the organism.

Conclusion. The research results showed the complexity and multivariability of the functioning of the immune system of schoolchildren in the conditions of the Far North after the inclusion of multivitamins in the diets. A change in the balance of regulatory indicators in schoolchildren's lymphocytes, which can change the functional activity of these cells, has been established. The decrease in the level of CA and the increase in the serotonin content are associated not only with the effect of the vitamin complex on biochemical mechanisms, the synthesis and decomposition of monoamines, but also with the state of the metabolic and regulatory systems of the inhabitants of the North.

Vitaminization among schoolchildren of the Polar region significantly changes the balance of the cellular elements of peripheral blood in children in this region.

References

1. Васильев А.В., Каспаров Э.В., Прахин Е.И. Перспективные задачи оптимизации питания на основе современных методов оценки пищевого статуса и энерготрат. Вопросы детской диетологии. 2010; 8(3): 44–46. [Vasilyev AV, Kasparov EV, Prakhin EI. Perspective tasks of optimizing nutrition based on modern methods of assessing food status and energy expenditure. *Voprosy detskoy dietologii*. 2010; 8(3): 44–46 (In Russ)].
2. Дыгай А.М., Скурихин Е.Г. Моноаминергическая регуляция кроветворения при экстремальных воздействиях. Бюллетень экспериментальной биологии и медицины. 2011; 151(2): 132–139. [Dygai AM, Skurikhin EG.

Monoaminergic regulation of blood formation under extreme conditions. *Byulleten' eksperimental'noy biologii i mediciny*. 2011; 151(2): 132–139. (In Russ)].

3. Практические аспекты диагностики и лечения иммунных нарушений: руководство для врачей. Козлов В.А., Борисов А.Г., Смирнова С.В. [и др.]. Новосибирск: Наука, 2009: 274. [Practical aspects of the diagnosis and treatment of immune disorders: a guide for physicians. Kozlov VA., Borisov AG., Smirnova SV. [et al.]. *Novosibirsk: Nauka* 2009: 274. (In Russ)].

4. Методические рекомендации. Нормы физиологических потребностей в энергии и пищевых веществах для различных групп населения РФ. МР 2.3.1. 24-32-08 от 18 декабря 2008. Вопросы детской диетологии. 2011; 9(6): 62–76. [Guidelines. Norms of physiological needs for energy and nutrients for various groups of the population of the Russian Federation. MR 2.3.1. 24-32-08 dated December 18, 2008. *Voprosy detskoy dietologii* 2011; 9(6): 62–76. (In Russ)].

5. Национальная программа по оптимизации обеспеченности витаминами и минеральными веществами детей России: (и использованию витаминных и витаминно-минеральных комплексов и обогащенных продуктов в педиатрической практике) / Союз педиатров России [и др.]. М.: ПедиатрЪ. 2017: 152. [National Program on Optimization of the Provision of Vitamins and Minerals of Russian Children: (and the use of vitamin and vitamin-mineral complexes and fortified products in pediatric practice) Union of Pediatricians of Russia [et al.]. M.: *Pediatr*. 2017: 152. (In Russ)].

6. Новицкая В.П. Модификация метода определения моноаминов в лейкоцитах на мазках периферической крови. Клиническая лабораторная диагностика. 2000; 1: 24, 33. [Novitskaya VP. Modification of the method for the determination of monoamines in leukocytes on peripheral blood smears. *Klinicheskaya laboratornaya diagnostika*. 2000; 1: 24, 33. (In Russ)].

7. Шевченко И. Ю. Научное обоснование коррекции питания и пищевого статуса детей школьного возраста Красноярского края: автореф. дисс. ... д-ра мед. наук Кемерово, 2009: 33. [Shevchenko IYu. Scientific rationale for the correction of nutrition and nutritional status of school-age children in the Krasnoyarsk Territory: author. diss. ... Dr. med Sciences. *Kemerovo*. 2009: 33.

8. Chavan SS, Tracey KJ. Essential Neuroscience in Immunology. *J. Immunol*. 2017; 198 (9): 3389 – 3397. DOI: 10.4049/jimmunol.1601613

9. Suboptimal micronutrient intake among children in Europe. Kaganov B, Caroli M, Mazur A, Singhal A, Vania A. *Nutrients*. 2015; 7(5): 3524 – 3535. DOI: 10.3390/nu7053524

10. Nicholson LB. The immune system. *Essays Biochem*. 2016; 60 (3): 275 – 301. DOI: 10.1042/EBEC20160017

11. Sichert-Hellert W, Kersting M. Vitamin and mineral supplements use in German children and adolescents between 1986–2003: results of the DONALD study. *Ann.Nut.Metab*. 2004; 48 (6): 414– 419. DOI: 10.1159/000083574

12. Use of multiple micronutrient powders for point-of-use fortification of foods consumed by infants and young children aged 6–23 months and children aged 2–12 years. WHO. 2016: 60. Licence: CC BY-NC-SA 3.0 IGO.