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ARCTIC MEDICINE

K.O. Pashinskaya, A.V. Samodova, L.K. Dobrodeeva THE RELATIONSHIP OF THE CONTENT OF BLOOD TRANSPORT PROTEINS WITH THE STATE OF THE IMMUNE SYSTEM IN PRACTICALLY HEALTHY INHABITANTS OF THE SVALBARD ARCHIPELAGO DURING THE POLAR DAY

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The article presents data on the content of transport proteins of the blood system in relation to the state of the immune system in people living in extremely unfavorable conditions of the Svalbard archipelago. It has been established that the inhabitants of Spitsbergen have an activation of cell migration into tissues in case of insufficient oxygenation of tissues. A decrease in the level of lymphocytes in the circulation causes a violation of the regulation of immune reactions with the accumulation in the blood of extracellular forms of receptors, circulating immune complexes. People living in Svalbard have an increased need for transport components of the blood system: haptoglobin, transferrin and IgM.

Keywords: neutropenia, lymphopenia, free forms of cell receptors, immune complexes, haptoglobin, transferrin, immunoglobulins, Svalbard archipelago.

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Introduction. Physiological, biochemical and immunological reactions in the human body, as a rule, occur against the background of quantitative changes in the content of transport components of the blood system, including albumins, lipoproteins, haptoglobin, transferrin, a2-macroglobulin and immunoglobulins. The influence of the complex of unfavorable factors of the North and the Arctic is manifested in changes in the internal environment of the human body, including changes in the content of transport proteins and parameters of the blood system. Northern tissue hypoxia, low air temperature, lack of illumination, ionomagnetic disturbance voltage have an ambiguous effect on adaptive adjustments and can lead to depletion of the body's reserve capabilities [2,3,4]. The change in the content of components of blood transport systems is associated with the functional state of the human body and is aimed at maintaining homeostasis with participation in the regulation of the immune system.

Conducting research in the Svalbard

archipelago is difficult and few, which leads to insufficient data on the risks to human health.

Purpose of the work – to establish the state of the transport components of the blood system and the immune system in people living and working in extremely unfavorable conditions of the Svalbard archipelago.

Material and methods. The paper presents the results of studying the immunological parameters of 75 residents of the Barentsburg settlement of the Svalbard archipelago, 46 of them women and 29 men and 79 residents of the Arkhangelsk region 58 of them women and 21 men aged 20 to 60 years, practically healthy of the survey, at the during the polar day (July-August 2017). All research was conducted with the consenot of the volunteers and in accordance with the requirements of the World Medical Association's Declaration of Helsinki (2013). The work was approved and approved by the Commission on Biomedical Ethics at the N. Laverov Federal Center for Integrated Arctic Research of the



Ural Branch of the Russian Academy of Sciences (Protocol No. 5 of 11.02.2022).

The complex of immunological parameters included the study of hemogram, phagocytic activity of neutrophils in blood smears stained according to Romanovsky-Giemsa, isolation of mononuclear cells from peripheral blood by the method of A. Boymn [12]. The content of mature T-lymphocytes (CD3+), T-helpers (CD4+), cytotoxic T-lymphocytes (CD8+), precursors of B-lymphocytes (CD10+), B-lymphocytes (CD19+), T-lymphocytes with transferrin receptor (CD71+)), T-lymphocytes with the receptor for the Fc fragment of immunoglobulins (CD23+), lymphocytes prepared for apoptosis with the Fas-R receptor (CD95+) were studied by the method of indirect immunoperoxidase reaction using monoclonal antibodies (MedBioSpectrum, Sorbent, Moscow) in residents of the Svalbard archipelago in connection with research in difficult expeditionary and climatic and geographical conditions and flow cytometry using the Epics XL apparatus from Beckman Coulter (USA) with reagents from Immunotech a Beckman Coulter Company (France) in residents of Europe in the North of the Russian Federation. Regardless of the method of lymphocyte phenotyping, the obtained results were in fact completely consistent (when comparing two methods of lymphocyte phenotyping in residents of the European North).

The contents of haptoglobin, transferrin, immunoglobulins (IgM, IgG, IgA, IgE), cytokines (IL-1β, TNF-α, IL-6, IL-10), free forms of transferrin receptors (sCD71), intercellular adhesion molecules L-selectin (sCD62L) and receptors involved in apoptosis (sApo-1/Fas), Fas-ligands (sFasL) were studied by enzyme immunoassay on the Evolis automatic analyzer (Bio-RAD) using diagnostic kits. Serum was obtained by centrifugation of venous blood for 20 minutes at 1500 rpm. in plastic tubes with a coagulation activator after settling in a vertical position and stored at -70°C in Eppendorf tubes until analysis. The concentration of circulating immune complexes (CIC) was determined by precipitation using 3.5; 4.0; 7.5% PEG-6000.

The mathematical and statistical analysis of the research results was carried out using the software package "Microsoft Excel MX" and "SPSS Statistics 21.0".

Results and discussion. Residents of the Svalbard archipelago, compared with residents of the European North, have a higher frequency of registration of elevated hemoglobin concentrations (29.8 vs. 7.6%), erythrocytosis (57.6 vs. 31.6%), thrombocytosis (23.7 vs. 5.1%),

which indicates the presence of a risk of hypoxic state formation as a result of accelerated erythropoiesis in combination with an increase in fetal hemoglobin content in the conditions of the North and the Arctic [5].

The examined residents living in extremely uncomfortable conditions of the Svalbard archipelago are characterized by a high frequency of leukopenia (21.3 vs. 8.9%), neutropenia (32.4 vs. 10.1%), lymphopenia (18.7 vs. 16.4%), monocytopenia (29.3 vs. 1.27%), p < 0.01-0.001 (Fig. 1), this indicates increased migration of blood cells into tissues with the development of tissue hypoxia.

The increase in lymphocyte migration into tissues is confirmed by a higher frequency of registration of deficiency of mature T-lymphocytes (CD3+), T-helper cells (CD4+), lymphocytes with transferrin receptor (CD71+) and lymphocytes with apoptosis receptor (CD95+) in 92.1; 45.3; 88.1; 89.3%. Against the background of insufficient content of mature T-cells in the inhabitants of the Svalbard archipelago were found elevated levels of cytotoxic lymphocytes (CD8+), lymphocytes capable of proliferation (CD10+), B-lymphocytes (CD19+) in 10.7; 13.4; 16.0%, respectively (Fig. 2).

People living in extremely unfavorable conditions of the Arctic have a high frequency of increased concentrations of circulating immune complexes (CIC) in 56-100%. A high level of CIC is associated with the insufficiency of the complement system, phagocytic protection [3]. However, for the examined persons living in the Svalbard archipelago, 30.9% were characterized by an increased level of phagocytic activity of neutrophils 91.0 \pm 1.38% with phagocytosis intensity of 17.9 \pm 1.75 pcs., the deficiency of active phagocytes was established at 13.3%.

It is known that activation of phagocytosis occurs during the polar day. During the polar day, residents of the Svalbard archipelago have higher phagocytic activity compared to residents of the European North (69.25 \pm 1.19 vs. 46.05 \pm 0.69%, p <0.001), which confirms the data on the increase in the level of phagocytic activity as the severity of the climatic and geographical conditions of the territory increases [2]. Unfavorable environmental



Fig. 1. Frequency of registration of elevated and decreased levels of blood system parameters in persons living in the Svalbard archipelago. Note: the significance of the difference compared to the inhabitants of the European North ** - p < 0.01; *** - p < 0.001



Fig. 2. The frequency of registration of elevated and decreased levels of lymphocytes of the main phenotypes in the inhabitants of the Svalbard archipelago. Note: the significance of the difference compared to the inhabitants of the European North ** - p < 0.01; *** - p < 0.001

factors in the early stages increase the activity of phagocytes, but in the future, depletion of reserve capabilities may manifest itself by a decrease in the activity of phagocytosis and its intensity [1].

In the extremely unfavorable conditions of the Arctic, compared with the inhabitants of the European North, there is a higher registration of the extracellular pool of receptors for transferrin sCD71 (70.6 vs. 40.5%), the intercellular adhesion molecule sCD62L (53.3 vs. 27.8%), the free pool of receptors involved in the formation of apoptosis of sAPO-1/Fas immunocompetent cells (28.1 vs. 16.5%) and sFasL (13.6 vs. 7.6%) p < 0.05-0.001. The accumulation of an extracellular pool of receptors indicates the shedding of receptors in the absence of the need or ability of cells to respond to a biologically active substance or signal [3].

In the examined inhabitants of the Svalbard archipelago, the levels of proinflammatory cytokines IL-1ß (11.86 \pm 3.22 pg/ml), IL-6 (5.40 \pm 0.29 pg/ml), TNF- α (14.05 \pm 0.70 pg/ml) are within physiological limits, elevated levels were not detected.

Thus, the state of the immune system in people living in extremely unfavorable conditions of the Arctic is characterized by the activation of migration processes in conditions of tissue hypoxia and a high level of CIC, free forms of receptors.

The inhabitants of the Svalbard archipelago, compared with the inhabitants of the European North, have a higher level of content and frequency of registration of elevated concentrations of haptoglobin, transferrin and IgM (Fig. 3.).

The average level of haptoglobin in the blood is higher in the inhabitants of the Svalbard archipelago compared to the inhabitants of the European North (1865.12±22.18 vs. 1194.86 ±32.25 mg/l; p < 0.001) with a frequency of increased concentrations of 17.3% versus 1.26%, respectively (Fig. 3.). The increase in haptoglobin content is explained by the need to bind hemoglobin, which is released during the lysis of erythrocytes in circulation with a decrease in their energy supply or violation of the integrity of the membrane [6,10]. In conditions of hypoxia, the increased breakdown of erythrocytes is compensated by intensive hematopoiesis [5,6].

Residents of the Svalbard archipelago have a higher average transferrin content (496.05 \pm 57.02 vs. 295.60 \pm 3.65 mg/dl; p <0.01) and the frequency of elevated concentrations (43.6% vs. 31.8%, respectively) (Fig. 3.). An increase in the transferrin content in the blood is associated with an increase in the concentra-



Fig. 3. Matrix of changes in the content of transport components of the blood system in the inhabitants of the Svalbard archipelago. Note: ** - p < 0.01; *** - p < 0.001 - the reliability of differences when comparing indicators with practically healthy residents of the European North of the Russian Federation.

Table 1

The content of lymphocyte phenotypes in the blood with an increase concentrations of transferrin in the residents of the of the Svalbard archipelago

Parameters	Normal serum content of transferrin	Elevated serum concentrations of transferrin	Reference limits of content
Transferrin level, mg/dl	222.0±4.72	558±8.96***	170-340
The content of lymphocytes, 10^9 cl/l	2.37±0.25	1.88±0.18**	1.5-4.0
CD3+, 10 ⁹ cl/l	0.79±0.14	0.56±0.08*	1.0-2.0
CD10+, 10 ⁹ cl/l	0.46 ± 0.05	0.41 ± 0.04	0.05-0.6
CD4+, 10 ⁹ cl/l	0.66 ± 0.06	$0.42 \pm 0.07*$	0.4–0.8
CD8+, 10 ⁹ cl/l	0.43 ± 0.09	0.33±0.04	0.2-0.6
CD19+, 10 ⁹ cl/l	0.72 ± 0.07	0.32±0.04**	0.1-0.7
CD71+, 10 ⁹ cl/l	$0.47{\pm}0.11$	0.28±0.05*	0.5-1.0
CD95+, 10 ⁹ cl/l	0.43±0.07	0.28±0.03*	0.5-1.12

Note: * - p<0.05; ** - p<0.01 – the reliability of differences in the content of lymphocyte phenotypes at elevated serum concentrations of transferrin in the residents of the Svalbard archipelago

Table 2

The content of lymphocyte phenotypes in the blood with an increase concentrations of IgM in the residents of the of the Svalbard archipelago

Parameters	Normal serum content of IgM	Elevated serum concentrations of IgM	Reference limits of content
The content of IgM, g/l	$1.52{\pm}0.06$	2.84±0.12***	0.70-1.9
The content of lymphocytes, 10 ⁹ cl/l	2.09±0.07	2.31±0.09*	1.5-4.0
CD3+, 10 ⁹ cl/l	0.58±0.03	$0.74 \pm 0.07*$	1.0-2.0
CD10+, 10 ⁹ cl/l	0.41±0.02	$0.49{\pm}0.06$	0.05-0.6
CD4+, 10 ⁹ cl/l	$0.44{\pm}0.02$	$0.54{\pm}0.06$	0.4–0.8
CD8+, 10 ⁹ cl/l	0.34±0.02	$0.48 \pm 0.04*$	0.2–0.6
CD19+, 10 ⁹ cl/l	0.39±0.03	$0.54{\pm}0.05*$	0.1-0.7
CD71+, 10 ⁹ cl/l	0.27±0.02	0.41±0.04**	0.5-1.0
CD95+, 10 ⁹ cl/l	0.32±0.02	0.37±0.04	0.5-1.12

Note: * - p<0.05; ** - p<0.01 – the reliability of differences in the content of lymphocyte phenotypes at elevated serum concentrations of IgM in the residents of the Svalbard archipelago.

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tion of the serum transferrin receptors sCD71 (from 3770 ± 134 to 6960 ± 199 ng/ml; p <0.05), which indicates an increase in the transport of the necessary amount of iron to maintain erythropoiesis at high latitudes. The marked activation of iron redistribution with an increase in the serum transferrin receptors indicates a reduction in the reserve capabilities of activating the immune system in conditions of tissue hypoxia.

With an increase in transferrin content in the inhabitants of the Svalbard archipelago, a decrease in the total level of lymphocytes was found mainly due to mature T-lymphocytes CD3+, T-helper cells CD4+, B-lymphocytes CD19+, lymphocytes with transferrin receptor CD71+ and lymphocytes labeled with apoptosis CD95+ (Table 1). In 90.9% of the surveyed residents of the Svalbard archipelago, an increase in transferrin concentration was associated with a decrease in the content of lymphocytes with a membrane receptor for transferrin (CD71+), which reflects the processes of self-regulation by the type of feedback at the level of changes in the receptor sensitivity of cells or shedding into the intercellular medium.

Photoperiodicity and the intensity and intensity of the magnetic environment are specific factors of high latitudes, affecting the immune system. The Svalbard archipelago is located in the region of the Earth with the maximum intensity of the geomagnetic field [7]. It has been shown that under the influence of magnetic disturbances, the functional activity of cellular receptors is inhibited by changing the distance between ligands and receptors with a decrease in blood T-lymphocytes with CD3+, CD5+, CD71+, CD95+ receptors. It was found that on magnetically disturbed days, the content of CIC increases sharply with the absence of changes on the part of serum immunoglobulins [2,8].

In the inhabitants of the Svalbard archipelago, the concentrations of IaM (1.74±0.09 g/l), IgG (7.56±0.34 g/l), IgA (1.98±0.08 g/l) and IgE (63.60±10.47 IU/ ml) are within the physiological limits with a shift of the IgM to the upper limit of the norm and IgA, IgG to the lower limits of the content. Elevated concentrations of IgM and IgE were found in the 26.7% and 12.0%, respectively. Deficiency of IgA and IgG content is registered in 22.7 and 46.7% (Fig. 3.). An increase in IgM content against the background of IgG deficiency indicates an inhibition of switching the synthesis of Ig class M to G (Fig. 3.). Deterioration in the production of high-affinities IgG occurs when B-lymphocytes

are reprogrammed for glycolytic metabolism in hypoxia [9,13].

A decrease in the level of IgA in the blood serum is a negative shift in the inhabitants of the North and the Arctic under the influence of climatogeographic factors (Scheme 1). Insufficient oxygen density in the atmosphere, increased humidity correlates with a low level of IgA [2].

In the inhabitants of the Svalbard archipelago, an increase in IgM concentrations is associated with an increase in the level of lymphocytes mainly due to increase of mature T-lymphocytes CD3+, cytotoxic lymphocytes CD8+, B-lymphocytes CD19+ and lymphocytes with transferrin receptor CD71+ (Table 2).

Increased concentrations of immunoglobulins can lead to a damaging effect due to the activation of cytokine synthesis and antibody-dependent cytotoxicity with an increase in tissue and cell damage products. An increase in IgM concentration, coupled with an increase in the level of CIC against the background of an imbalance of serum immunoglobulins in the inhabitants of the Svalbard archipelago, reflects the risk of disruption of adaptive rearrangements. Increased concentrations of CIC in the blood are caused by a violation of their clearance efficiency, which leads to their deposition on membranes, vessel walls with impaired microcirculation [2,3].

Conclusion. In the extremely unfavorable conditions of the Arctic, in the body of the inhabitants of the Svalbard archipelago, cell migration into tissues is activated due to tissue hypoxia. The decrease in the content of circulating neutrophils and monocytes is compensated by an increase in the activity and intensity of phagocytosis. A decrease in the level of lymphocytes, mainly mature T-lymphocytes, T-helper cells, lymphocytes with a transferrin receptor and lymphocytes with a receptor for apoptosis causes the risk of developing an immunodeficiency condition.

In the body of the inhabitants of the Svalbard archipelago, there is a need to increase the transport proteins of the blood system. The increase in haptoglobin content is explained by insufficient tissue oxygenation with an increase in erythrocyte lysis. An increase in the transferrin content associated with an increase in the concentration of the serum transferrin receptor sCD71 indicates an increase in the transport of the necessary amount of iron to maintain erythropoiesis at high latitudes.

An increase in the IgM content reflects to a certain extent the activation of autoantibody formation. IgM belong to autoantibodies, performing regulatory functions to preserve homeostasis, but on the type of feedback inhibits antibody formation on other antigens [11]. The activity of autoantibody synthesis depends on the level of autoantigens [3]. An increase in autoantigens in the residents of the archipelago Svalbard may be caused by a violation of membrane permeability due to the damaging effect of increased concentrations of CIC [8]. An increase in IgM concentration associated with an increase in the level of CEC in the residents of the archipelago Svalbard displays the risk of disruption of adaptation restructuring.

In the inhabitants of the Svalbard archipelago, an increase extracellular forms of lymphocyte receptors in the blood indicate shedding of receptors in the absence of the ability to respond to a signal, including as a result of a change in the distance between ligands and receptors with a violation of their interaction. An increase in the extracellular pool of receptors against the background of a deficiency of active phagocytes indicates the risk of insufficient utilization of the products of adaptive reactions.

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DYNAMICS OF THE MAIN MEDICAL AND DEMOGRAPHIC INDICATORS OF MATERNAL AND CHILD HEALTH CARE IN THE ARCTIC REGIONS OF THE REPUBLIC OF SAKHA (YAKUTIA)

The analysis of the main medical and demographic indicators of maternal and child health care in 13 Arctic regions of the Republic of Sakha (Yakutia) is presented in the article. It is demonstrated that the studied period is marked by a decrease in population size, and despite this, there are high birth rates, as well as high rates of total mortality, a significant decrease in the infant mortality rate, and high rates of child morbidity.

Keywords: demography, birth rate, mortality, morbidity, Arctic, Yakutia.

Introduction. The industrial development of the Arctic territories of Russia is one of the priorities of the state development. In the current geopolitical conditions, it acquires special significance [3,4]. In this regard, the development of such an important area of medicine as Arctic medicine requires consolidation and cooperation [1,6]. It is possible to determine the initial situation of health care in the Arctic territories by analyzing the main medical and demographic indicators that are public health parameters [2,5,6]. The state of health of children and adolescents in the Arctic has always been a priority. In recent years, extensive federal programs for the protection of women's and children's health in the Russian Federation have been approved and implemented. All this has significantly affected the availability and quality of medical care in the regions of the Arctic zone of the Russian Federation. And this program should be continued. After

all, healthy children are the future of the Arctic.

Purpose of the study: to analyze the dynamics of the main medical and demographic indicators in the Arctic regions of the Republic of Sakha (Yakutia) in 2000-2022 in order to establish the main directions for improving the system of maternal and child health care.

Materials and Methods: The dynamics of the main medical and demographic indicators of maternal and child health protection in 13 Arctic regions of the Republic of Sakha (Yakutia) according to the data of the YARMIAC for the period of 2000-2022 was analyzed. Two time periods (2000 and 2022) were taken. The methodology of calculating the indicators of the dynamic series is used.

Results. Since 2000, the population in the Arctic regions of the Republic of Sakha (Yakutia) has decreased by 30%. Moreover, in 4 Arctic districts the population has decreased by more than 40%: