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FEATURES OF CELLULAR AND HUMORAL IMMUNE REACTIONS IN THE INHABITANTS OF THE EUROPEAN NORTH AND THE ARCTIC

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The features of cellular and humoral immune responses in the inhabitants of the European North and the Arctic have been studied. It has been established that a parallel increase in the frequency of registration of erythrocytosis, thrombocytosis, elevated hemoglobin, hematocrit and thrombocrit in residents of the Murmansk region is a mechanism for adaptation to an increased need for O2 in the Arctic. The examined individuals showed a high frequency of registration of leukocytosis, lymphocytosis, neutrophilia, monocytosis, eosinophilia and basophilia against the background of a significant level of deficiency of active phagocytes. A feature of the immunological reactivity of the inhabitants of the polar village is the predominance of reactions of cell-mediated and antibody-dependent cytotoxicity against the background of an increase in pro-inflammatory cytokines IL-6, IFN-γ, reagins, intercellular adhesion molecules sCD54 and sCD62L.

Keywords: erythrocytes, platelets, hematocrit, thrombocrit, phagocytosis, NK cells, cytokines, IgE, intercellular adhesion molecules, Arctic.

Introduction. The complex of natural and climatic factors typical for the Arctic poses a significant risk to the health of residents exposed to them [4; 15]. The cumulative effect of all unfavorable climatic and ecological conditions of these territories enhances their negative impact on the human body, causing a more intense reaction of adaptation to constantly changing living conditions, with increased energy consumption and the use of not always economical options for regulating and maintaining homeostasis [2; 6]. In people living in the northern climate, there is a decrease in immune protection [5; 6].

According to the integrated map of the impact of natural conditions on the territory of the Russian Federation on the living conditions of the population, the Arkhangelsk region belongs to a relatively unfavorable natural zone. The settlements of the Murmansk region belong to the regions of the Far North of the Russian Federation, are located beyond the Arctic Circle and are located in the area of residence with a pronounced effect of uncomfortable conditions on people, causing stress on the body's adaptation systems [1; 3; 11].

The aim of our study was to identify the characteristics of cellular and humoral immune responses in residents of the European North and the Arctic.

Material and methods. 315 currently practically healthy residents of the village were examined. Revda, Murmansk region, 237 women and 78 men, aged 21 to 50 years. The comparison group consisted of 181 practically healthy people of the Arkhangelsk region of the same age range, 138 women and 43 men.

All studies were carried out with the consent of the volunteers and in accordance with the requirements of the document "Declaration of Helsinki of the World Medical Association. Ethical principles for conducting medical research involving a person as a subject" (1964, as amended and supplemented in 2013), and also approved and approved Commission on Biomedical Ethics at the IFPA FGBUN FITSKIA Ural Branch of the Russian Academy of Sciences (protocol No. 5 dated February 11, 2022).

The complex of immunological examination included the study of hemogram, phagocytic activity of neutrophilic leukocytes in peripheral blood. The number and ratio of hemogram cells were counted in blood smears stained by the Romanovsky–Giemsa method. The phagocytic activity of neutrophilic granulocytes was determined using the Reacomplex test kit (Russia). On the hematological analyzer XS-500i (Sysmex, Japan), in the peripheral venous blood of the examined, WBC (total leukocyte count), RBC (total erythrocyte count), HGB (hemoglobin concentration), HCT (hematocrit - the proportion of blood volume occupied by erythrocytes), PLT (total platelet count), PCT (thrombocrit - the proportion of platelets in the total blood volume.).Lymphocyte phenotypes (CD3+, CD4+, CD8+, CD10+, CD16+, CD71+, CD25+, HLADRII, CD23+, CD95+, CD19+, CD54+, CD56+) were studied by indirect immunoperoxidase reaction using monoclonal antibodies (Sorbent, Moscow) and flow cytometry using an Epics XL apparatus from Beckman Coulter (USA) with reagents from Immunotech a Beckman Coulter Company (France). The content of pro-inflammatory cytokines IL-6, IFNγ, anti-inflammatory cytokine IL-10 immunoglobulin E, free intercellular adhesion molecules sCD54 and sCD62L with reagents from Bender Medsystems (Austria) in blood serum was studied by enzyme immunoassay on an automatic enzyme immunoassay analyzer Evolis manufactured by Bio-RAD "(Germany).

The obtained data were statistically processed using the Statistica 21.0 software package (StatSoft, USA). The results are presented as the arithmetic

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mean and error of the mean (M±m). An independent sample t-test was used for comparison between groups. For bivariate normal distribution data, the Pearson correlation coefficient was calculated. The critical significance level (p) in the work was taken equal to 0.05.

Results and discussions. It was found that the residents of the village Revda has a higher content of erythrocytes, hemoglobin, platelets (table 1), which is confirmed by an increase in the frequency of registration of erythrocytosis by 1.6 times (51.43±0.23 versus 31.49±0.31%, respectively), an increased content of hemoglobin by 3, 2 times (54.92±0.23 and 17.13±0.23%) and thrombocytosis by 2.5 times (21.90±0.15 and 8.84±0.16%).

In parallel with the increase in the content of erythrocytes and platelets, the levels of hematocrit (43.42±0.40 and 40.23±0.39%, p<0.001) and thrombocrit (0.27±0.012 and 0.23±0.007%, p= 0.028). Low air temperatures have a significant impact on the function of oxygen transport in the body, exposing it to the development of pathological processes. [7]. It is known that the inhabitants of the North have a low life expectancy of erythrocytes, the average content of hemoglobin in them. Changes in the shape of red blood cells and thickening of their cell wall reduce the activity of providing oxygen to tissues [8; 10]. A decrease in blood flow velocity and an increase in the content of erythrocytes and platelets contributes to the activation of the process of erythrocyte aggregation in microvessels, causing hypoxia. Previously, we have shown that the activity of aggregation of erythrocytes, platelets and leukocytes of peripheral venous blood in residents of the Arctic is 1.5–2.5 times higher than that in people living in the European North of the Russian Federation [20]. The mechanism for compensating for impaired oxygen supply to tissues is the increased formation of hemoglobin.Most likely, a parallel increase in the content of erythrocytes, platelets, hematocrit and thrombocrit levels, hemoglobin concentration can be considered as a mechanism for adaptation to an increased need for O_2 in the Arctic. An increase in hematocrit leads to a slowdown in blood flow velocity, creating favorable conditions for aggregation of erythrocytes in microvessels and adhesion of leukocytes on vessel walls [9]. It has been shown that during short-term general cooling at t-25°C for 5 minutes, an increase in hematocrit is associated with an increase in the concentration of endothelin-1 and irisin, which indicates the activation of vasoconstriction and heat production [12].

In the surveyed residents of the Murmansk region, the total content of leukocytes in the blood is higher due to lymphocytes, neutrophils, incl. stab and segmented forms, respectively, monocytes, eosinophils and basophils (table 2).

It is noteworthy that the residents of the polar village, compared with the comparison group, have a 7 times higher frequency of registration of leukocytosis, 9 times higher - lymphocytosis, 5.5 times - neutrophilosis, 4 times - monocytosis, 13 times - eosinophilia and 8 times - basophilia (Fig. 1.).

In the examined persons of the Murmansk region, an increase in the content of stab neutrophils was recorded in the blood, which indicates a shift in the leukocyte formula to the left. Along with increased concentrations of blood cells in the examined individuals, almost the same level of leukopenia was recorded, but the frequency of registration of lymphopenia in residents of the Arkhangelsk region was 3 times higher, neutropenia - 2 times and monocytopenia - 3 times (Fig. 2.).

Phagocytosis activates the body's immune defense reactions, ensuring the duration and activity of the immune response. The phagocytic activity of neutrophils is on average lower in residents of the Murmansk region (51.46±0.92 and 65.42±1.10, p<0.001) without changing the phagocytic number (5.46±0.10 and 5.52±0,25 pcs.) with a 4-fold higher frequency of active phagocyte deficiency (47.62% versus 12.71%). The lack of phagocytic protection may be associated with the predominance of immature neutrophils.

An increase in the total content of lymphocytes in residents of the village. Revda occurs mainly due to cytotoxic lymphocytes CD8+, natural killers CD16+ and CD56+ (Fig. 3.), which is confirmed by the high frequency of registration of these cells (respectively in 34.92%, 52.7% and 16.51% of cases) and indicates activation of cell-mediated and antibody-dependent cytotoxicity.

It is known that the mechanism of the cytotoxic action of natural killers and cytotoxic T-lymphocytes is associated with the content of perforin and granzyme granules, which have lytic activity with subsequent DNA degradation and programmed cell death [21].

In residents of the Murmansk region, the concentration of the pro-inflammatory cytokine IL-6 is significantly higher (13.79±0.80 pg/ml versus 3.05±0.28 pg/ml, p<0.001), however, it is within the physiological limits of the content. Ac-

Table 1

Erythrocyte and platelet parameters of venous blood in residents of the Arkhangelsk and Murmansk regions (M±m)

Indicator	Residents of the Arkhangelsk region (n=181)	Residents of the Murmansk region (n=315)
Erythrocytes. 10^9 cells/l	4.58±0.05	4.83±0.05***
Platelets. 10^9 cells/l	215±7.53	283.38±6.13***
Hemoglobin. g/l	215±7.53	283.38±6.13***

Note: *** p<0.001 - significance of differences when comparing results

Table 2

Indicators of the cellular composition of venous blood in residents of the Arkhangelsk and Murmansk regions (M±m)

Indicator, 10^9 cells/l	Residents of the Arkhangelsk region (n=181)	Residents of the Murmansk region (n=315)
Leukocytes	5.32±0.12	7.50±0.34***
Lymphocytes	2.10±0.06	2.70±0.08***
Stick-nuclear neutrophils	0.22±0.01	0.59±0.04***
Segmented neutrophils	2.50±0.08	2.88±0.12***
Neutrophils	2.73±0.08	3.79±0.21***
Monocytes	0.36±0.02	0.68±0.03***
Eosinophils	0.12±0.01	0.26±0.02***
Basophils	0.04±0.01	0.15±0.02***

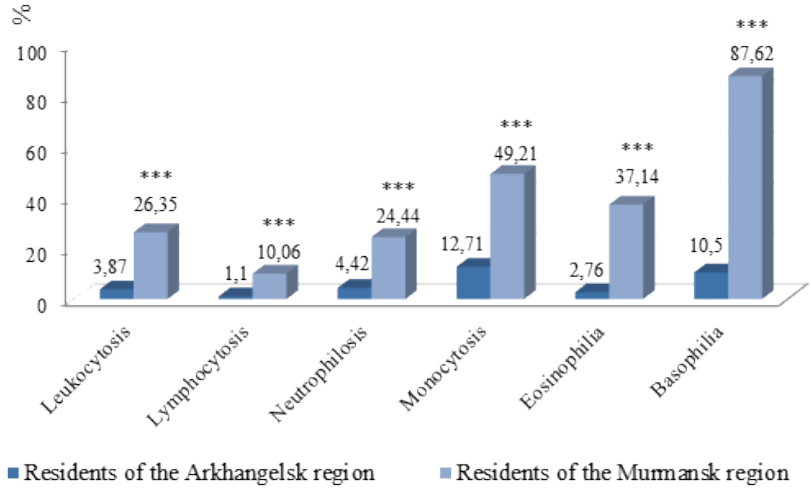

Fig. 1. The frequency of registration of elevated concentrations of blood cells in residents of the Arkhangelsk and Murmansk regions. Note: *** p<0.001 - significance of differences when comparing results.

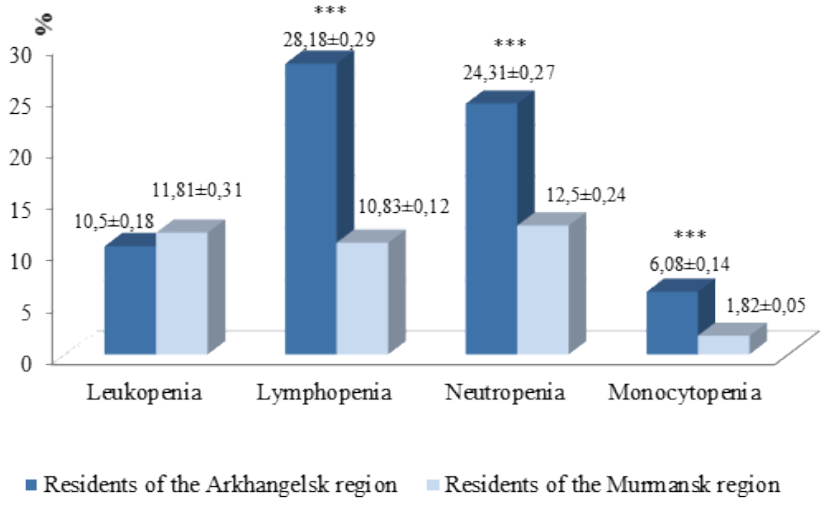

Fig. 2. The frequency of registration of low concentrations of blood cells in residents of the Arkhangelsk and Murmansk regions. Note: *** p<0.001 - significance of differences when comparing results.

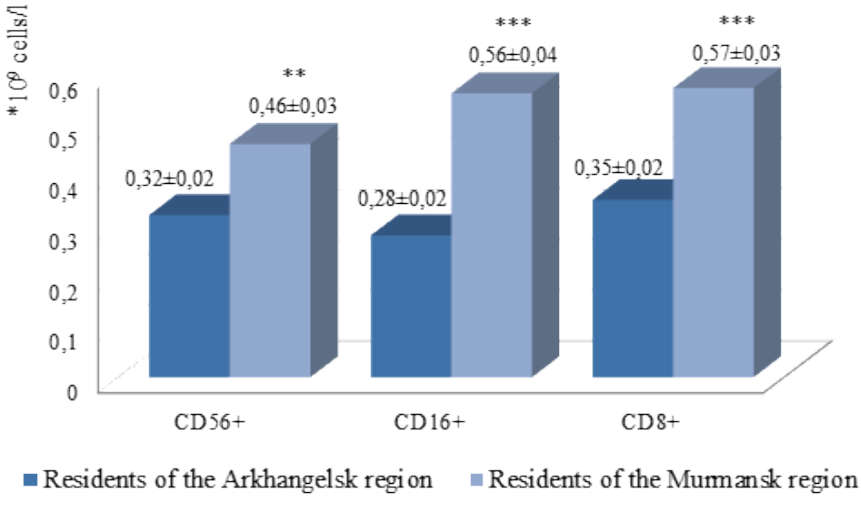

Fig. 3. The concentration of cytotoxic lymphocytes and natural killers in the blood of residents of the Arkhangelsk and Murmansk regions. Note: ** p<0.01, *** p<0.001 – significance of differences when comparing results.

cording to the available data, a sharp increase in the content of the pro-inflammatory cytokine IL-6 was found during hypoxia [14]. IL-6 is the main stimulator of acute phase reactions, accompanied by increased blood viscosity and an increase in the number of active platelets, promotes inflammation of vascular smooth muscle cells and activation of endothelial cells, inducing the expression of chemoattractant proteins and adhesion molecules [19].Indeed, the concentration of free intercellular adhesion molecules sCD54 (202.96±6.11 and 173.92±13.18 ng/ml, p<0.001) and sCD62L (8.44±0.76 and 4, 38±0.62 ng/ml, p<0.001), which are capable of forming the formation of cell conglomerates, autorosettes and clusters [13]. The concentration of pro-inflammatory IFN-γ is 6 times higher in residents of the Arctic (74.74±6.77 versus 12.14±0.22, pg/ml p<0.001) and is confirmed by an increased registration rate of 72.38±0.27% cases.

In 14.60% of the inhabitants of the village. Revda revealed increased concentrations of reagins (79.72±11.23 versus 55.32±10.16 IU/ml, p<0.01), which corresponds to a higher content of T-lymphocytes with the Fc IgE receptor (0.53± 0.04 versus 0.30±0.02X109 cells/l; p<0.001) in 32.06% of cases. IgE binds to lymphocytes, macrophages, monocytes, eosinophils, mast cells and basophils. The Fc receptor for CD23 reagins is involved in the regulation of the response involving immunoglobulins E [18]. The ability for antibody-dependent cytotoxicity of macrophages and eosinophils is carried out through IgE binding. The inhabitants of the village Revda, an increase in the concentration of IgE is interconnected with an increase in the concentration of eosinophils (r=0.87). Eosinophil peroxidase binds to mast cell granules without losing its activity [18]. On the surface of eosinophils, there are IgG, IgE, C3b, C4, CIs, C3a, C5a receptors, the combination of which with the antigen provides a cytotoxic effect, while the cytotoxic effect of eosinophils is sharply enhanced by mast cell secretion products [17].

Conclusion. So, in comparison with people living in more favorable conditions, residents of the Murmansk region have a higher frequency of registration of erythrocytosis, elevated hemoglobin, thrombocytosis, as well as hematocrit and thrombocrit. A parallel increase in the content of erythrocytes, platelets, hematocrit and thrombocrit levels, and hemoglobin concentrations can be considered as a mechanism for adaptation to an increased need for O2 in the Arctic. A high frequency of registration of leuko-

cytosis by 7 times, lymphocytosis by 9 times, neutrophilia by 5.5 times, monocytosis by 4 times, eosinophilia by 13 times and basophilia by 8 times was revealed against the background of a significant level of deficiency of active phagocytes (47.62% vs. 71%), which indicates an increased need for immunocompetent cells in tissues. A feature of the immunological reactivity of the inhabitants of the polar village is the predominance of reactions of cell-mediated and antibody-dependent cytotoxicity against the background of an increase in pro-inflammatory cytokines IL-6, IFN-γ, reagins, intercellular adhesion molecules sCD54 and sCD62L.

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