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The immune status of Subarctic residents with different professional backgrounds

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Abstract. The complex effect on human body of climatic, geophysical, and ecological factors of the North lead to an extra load on adaptation potential in humans, causing diseases, premature ageing, and lower life expectancy. To employees under rotation schemes, the vast, poorly explored, and difficult-to-access area of the Arctic basin is challenging, as is to undergraduate students of the North who have to meet the demands the northern environment places on their health, physiology and psyche. Students constitute a special social group of the population not only in terms of age or work-life regime, but also in terms of the high, prolonged psychoemotional pressure they are exposed to. In individuals working or residing in extreme conditions (nomadic populations, combat situations, etc.), the intensity of changes in the immune status and hormonal background depends on the severity of occupational milieu. Reindeer herding represents a way of existence in adverse climatic conditions of the Far North.

1. Introduction

Any inadequacy in the performance of the immune system in northern residents, which is related to severe exposure to bioclimatic factors and occupational conditions, is likely to lead to latent deficiencies in immunological regulation, creating additional pressure on adaptation process and a tendency for acute inflammatory processes to become chronic. In populations residing in adverse climatic conditions, the ability to form an adequate immune response is preconditioned by the initial state of their immune system. As known, the immune responsiveness in northerners is characterized by the increased immunosuppression level that, in turn, indicates the activation of cellular and, ultimately, humoral mechanisms of immunity. Given the high immunosuppression level, circulating immune complexes emerge, as well as some of immunoglobulins and autoantibodies. In conditions of the expressed immunodeficiency of T-cells, the specified processes fully materialize the effect on human body of cell-mediated cytotoxicity. The annual series of preventive examinations show that the number of healthy undergraduate students tends to decrease from year to year. In the North, the process of adaptation to a higher education institution is complex and multifaceted, while the educational process itself places great demands on health, physiology and plasticity of mentality in youth [1, 10, 11, 12, 13]. Students constitute a special social group of the population not only in terms of age or work-life regime, but also in terms of the high, prolonged psychoemotional pressure they are exposed to. The factors students become exposed to include nonspecific (climatic and ecological) and specific (age, physiological and psychological features, emotional overload, sedentary lifestyle) that affect their health levels and



immune responsiveness [5, 6, 9]. Having to adapt to a variety new factors specific to higher school is associated with considerable tension in students of compensatory and adaptive systems, including the immune one. The prolonged intellectual and psychoemotional tension, as well as the disturbances in work-rest regime and nutrition, often cause adaptation to fail and diseases as serious as autoimmune develop.

It is known that in individuals working or residing in extreme conditions (nomadic populations, combat situations, etc.), the intensity of changes in the immune status and hormonal background depends on the severity of occupational milieu – increased levels of cortisol against the background of decreased testosterone concentrations; abnormally high concentrations of circulating immune complexes; inhibited monocyte and lymphocyte proliferation; decreased levels of CD7⁺, HLA-DR⁺, CD22⁺ cells; prevalence of proliferative responses over immunocompetent cells apoptosis [2, 3, 4, 8].

In the adverse climatic conditions of the Far North, reindeer herding represents a way of existence. The unfriendly climate and the social conditions that in many respects concede to those being enjoyed by residents of central and southern regions of the country largely reduce the resistance levels in northerners as their children show inhibited development of the immune system and adults the reduced immune responsiveness [7].

2. Materials and methods

Our immunological examinations covered 275 males aged 18 to 23 who were practically healthy at the time of the examination – 110 students of M.V. Lomonosov Northern (Arctic) Federal University; 92 nomadic reindeer herders (Nenets Autonomous Area); and 83 employees of Arkhangelsk-based Hydrographic Service. The series of immunological examinations targeted to identify the phenotypes of lymphocytes (CD4⁺, CD8⁺, CD3⁺, CD5⁺, CD16⁺, CD10⁺, CD71⁺, CD25⁺, HLA-DR⁺, CD22⁺, CD95⁺) in peripheral dark blood; immune serum globulins (IgA, IgM, IgG, IgE); and interleukins IL-1 β , IL-4, IL-6. The percentage of subpopulations of T-lymphocytes was determined using the method of indirect immunoperoxidase with the use of monoclonal antibodies (MedBioSpektr, Moscow) on ‘dry drop’ samples of lymphocytes, with use of peroxidase conjugate and colored chromogen solution for immersion microscopy (Nikon Eclipse 50i microscope). The amount of immune serum globulins (IgA, IgM, IgG, IgE) was quantified (JSC VECTOR-BEST, Russia) by method of the immunofermental analysis (IFA) on tablet immunofermental analyzer "Stat Fax 2100". CEA was performed using Can Ag (Switzerland); TNF- α –Cytimmune science (USA). The results were processed statistically with determination of average values and are presented as average arithmetic $\pm$ mean error ($M \pm m$); the reliability of difference was estimated by means of Student's t-criterion. The statistical reliability was assigned at $p < 0.05$. The correlations (r) between indicators were determined with the use of Spearman rank-order correlation coefficient, followed by reliability verification. Statistica 6.0 software was made use of.

The study was performed within the framework of state-funded project No. AAAA-A15-115122810184-6 “Physiological significance of immune homeostasis and immunocompetent cells’ functional and receptor activity in individuals exposed to extreme environmental conditions”.

3. Results

In populations residing in adverse climatic conditions, the ability to form an adequate immune response is preconditioned by the initial state of their immune system.

As known, the immune responsiveness in northerners is characterized by the increased immunosuppression level that, in turn, indicates the activation of cellular and, ultimately, humoral mechanisms of immunity. Given the high immunosuppression level, circulating immune complexes emerge, as well as some of immunoglobulins and autoantibodies. In conditions of the expressed immunodeficiency of T-cells, the specified processes fully materialize the effect on human body of cell-mediated cytotoxicity.

The annual series of preventive examinations show that the number of healthy undergraduate students tends to decrease from year to year. The comprehensive immunological examination of students

of northern higher education institutions have shown increased levels of tension of the immune mechanisms against the background of high CD10⁺ lymphocyte concentrations and cell-mediated cytotoxicity, caused by CD25⁺, HLA-DR⁺, CD71⁺ activated in conditions of CD5⁺ T-cell deficit and low level of T-cell differentiation. Moreover, the identified occurrence of active lymphoproliferative reactions evidences the activated status of cellular immunity in first-year students during the period of intense adaptation to studies, depending on the type of indicator (5%-80%), the common forms being abnormal helper-suppressor ratios, blast-cell transformations, and phagocytal defence.

The active status of T-cellular immunity is further evidenced by rather high levels of CD25⁺ and wide distribution range of the specified imbalance ($p < 0.001$) in 13.89% of students of younger age and in 17.65% of students of older age.

The increased levels of activated T-lymphocytes have been found in undergraduate students mainly due to CD25⁺ (17.65%), CD71⁺ (47.62%) and HLA-DR⁺ (17.65%) T-lymphocytes – in conditions of CD5⁺ T-cell deficit and low level of T-cell differentiation. Thus, the presented imbalances of the immune reactions in students – highly active background lymphoproliferation, apoptosis, cytokines; prevalent deficit of functionally differentiated active T-lymphocytes (CD3⁺), all T-cells (CD5⁺) and transferrin receptor carriers CD71⁺ – affect the efficiency of immune protection. Highly common among the immunity status imbalances revealed in students is IgA deficiency (19.74%).

Junior students are found to show strained humoral immunity (IgM, HLA-DR⁺; CD22⁺) – in 8% to 40% of students; and moderately activated cellular links (CD4⁺; CD16⁺; CD8⁺) – in 16% to 28% of students, depending on the level. Lymphoproliferative reactions with increasing CD10⁺ concentrations are found in 19.45% of junior students and 11.77% of senior students, whereas the deficit of differentiated immunocompetent cells (CD3⁺) is found in 44.45%-41.18% depending on the year of studies.

Senior students (aged 21-23) are found to show the increased differentiation of T-helpers (23.53%), natural killers (17.24%) and cytotoxic lymphocytes (44.12%). Most manifest is the increase in CD8⁺ concentrations, reflecting activated cell-mediated cytotoxicity. The increased proinflammatory cytokine contents (IL-1 β ; IL-4) in blood serum is found in 8%-12% of students. In senior students, the occurrence of high concentrations of CD71⁺ lymphocytes is 3.5-times higher than in junior ones (47.62% and 13.89%, respectively).

It is known that in individuals working or residing in extreme conditions (nomadic populations, combat situations, etc.), the intensity of changes in the immune status and hormonal background depends on the severity of occupational milieu – increased levels of cortisol against the background of decreased testosterone concentrations; abnormally high concentrations of circulating immune complexes; inhibited monocyte and lymphocyte proliferation; decreased levels of CD7⁺, HLA-DR⁺, CD22⁺ cells; prevalence of proliferative responses over immunocompetent cells apoptosis. In the conditions of rotational work, the adverse occupational factors are complemented by change of climate and social milieu, physical and psychoemotional load on the main functional systems of the body, leading to fast exhaustion of reserve capacity and adaptive potential. Our research has found that men under short on/off rotation schemes in the Arctic tend to show lower CD5⁺, CD25⁺, CD71⁺, CD95⁺ T-cell concentrations, lower B-cellular (HLA-DR⁺) and phagocytic activity against the background of low levels of total and free testosterone.

Of interest to us was the ratio between testosterone and immunological parameters in immune homeostasis regulation in men working in the Subarctic region, based on occupational (long and short on-off schemes).

Our analysis has shown that individuals under varying on/off schemes have low occurrence of phagocytic imbalance – within 12% of deficit – against the background of the increased levels of monocytic and neutrophilous cells. Considering that mean phagocytic value varies between 6.82 ± 0.47 and 6.70 ± 0.29 microorganism/cell, and given the increased mean values for monocytes (0.44 ± 0.05 ; $0.40 \pm 0.03 \cdot 10^9$ cell/l) and neutrophils (3.32 ± 0.27 ; $3.64 \pm 0.21 \cdot 10^9$ cell/l), we tend to consider these increased levels to be a compensatory and adaptive reaction of the body to extreme occupational conditions.

In men under short on/off schemes, leukocytoses (14.29%) and lymphocytoses (19.05%) occur 3 times more often than in men under longer on/off schemes (4.66% and 7.69%, respectively).

Regardless of the duration of on/off periods, the average content of mature, functionally active, differentiated T-lymphocytes (CD3⁺) in all the individuals examined is extremely low: 0.54 ± 0.02 and $0.47 \pm 0.04 \cdot 10^9$ cell/l. The general population of all T-cells (CD5⁺) has extremely low average values in all the individuals examined: 0.49 ± 0.03 and $0.47 \pm 0.05 \cdot 10^9$ cell/l. The deficit of T-cells (CD5⁺) is twice higher than that of (CD3⁺). The obtained data is indicative of the reduction in the entire T-cells pool and in its differentiated, mature and functionally active population (CD3⁺).

The concentrations of helper-inductors (CD4⁺) equaled 0.53 ± 0.03 and $0.49 \pm 0.04 \cdot 10^9$ cell/l, respectively. The obtained data indicate that the concentration of helper-inductors (CD4⁺) approximates the lower limit of physiological norm in 58% and 50% of the individuals examined, being twice more common in men under short on/off rotation schemes (16% and 42.50%). The increased values of this indicator were found in 4.02% of men under short on/off rotation schemes and in 16.65% of men under long on/off rotation schemes. We tend to consider the increased concentrations of helper-inductors (CD4⁺) to be a compensatory reaction against the background of expressed T-cell deficit.

At the same time, helper-suppressor ratio equaled 0.96-1.01, indicating the expressed T-suppression in 80.00% of men under short on/off rotation schemes and in 60.50% of men under long on/off rotation schemes at beacons. We tend to consider the immune imbalances among CD3⁺, CD5⁺, CD4⁺ to be the adaptation-related immune responses. At the same time, the decrease in cytokine activity and total testosterone levels in men under short on/off rotation schemes (with total testosterone deficit 3-times more common in them) is an indirect evidence of reduced immunological homeostasis and, as a result, slower adaptation response to changes in ambient conditions. The multitude of weak correlative interrelations between the indicators under analysis in both the groups is seen as an indirect indication of the fact that changes in hormone concentrations do not depend on fluctuations in lymphoid populations, with exception of T-suppressors (CD8⁺, $p < 0.001$). The obtained data indicates that the decreased adaptive capacity and immunological homeostasis is more common in men (aged 40.0 ± 5.0) working in the North under short on/off rotation schemes, with compensatory reactions occurring in them 3 times more often than in men under long on/off rotation schemes. The content of T-suppressors (CD8⁺) exceeds the known physiological limits – 0.51 ± 0.03 and $0.50 \pm 0.04 \cdot 10^9$ cell/l, respectively. Lower contents of T-suppressors were found in neither of cases. Oppositely, they tend to be extremely high – 76% and 57.50%, respectively. Therefore, the reason why the helper-suppressor coefficient CD4⁺/CD8⁺ equals one and is extremely low are the excessively high concentrations of cytotoxic cells (CD8⁺).

In the adverse climatic conditions of the Far North, reindeer herding represents a way of existence. The unfriendly climate and the social conditions that in many respects concede to those being enjoyed by residents of central and southern regions of the country largely reduce the resistance levels in northerners as their children show inhibited development of the immune system and adults the reduced immune responsiveness. The research has shown that the immune response in practically healthy reindeer herders are characterized by deficit of mature, functionally active T-cells (CD3⁺), which is responsible for activation and wide spread of cytotoxic lymphocytes (high concentrations of CD8⁺ and CD16⁺); increased immunosuppression and resulting apoptosis (CD95⁺); and increased generation of young cells (CD10⁺ lymphoproliferation). The obtained data enable a conclusion that in nomadic reindeer herders the immune response is defined by increased concentrations of cytotoxic lymphocytes, i.e. immunosuppression, which possibly compensates for the deficit of mature CD3⁺ cells by maintaining certain stages in the immune response at moderate (not prominent) levels (increased CD71⁺ levels were found only in 8% of the surveyed; 30% had increased HLA-DR⁺ levels). The analysis has shown increased concentrations of CD8⁺ and CD16⁺ cytotoxic lymphocytes ($0.71 \pm 0.14 \cdot 10^9$ and $0.64 \pm 0.08 \cdot 10^9$ cell/l) in 62.50% of nomadic reindeer herders, 45.34% of settled residents, of CD16⁺ - in 45.84% of nomadic reindeer herders and 40.00% of settled residents.

4. Conclusion

Senior undergraduate students (aged 21-23) are found to show the increased differentiation of T-helpers (23.53%), natural killers (17.24%) and cytotoxic lymphocytes (44.12%). Most manifest is the increase in CD8⁺ concentrations, reflecting activated cell-mediated cytotoxicity. The increased proinflammatory cytokine contents (IL-1 β ; IL-4) in blood serum is found in 8%-12% of students. In senior students, the occurrence of high concentrations of CD71⁺ lymphocytes is 3.5-times higher than in junior ones (47.62% and 13.89%, respectively).

The immune imbalances (deficit of CD3⁺, CD5⁺, CD71⁺, CD95⁺, HLA-DR⁺ T-cells and CD10⁺ lymphoproliferation receptor cells) against the background of low testosterone (total and free) are 3 times more common in men under short on/off rotation schemes (90.00%) than in men under long on/off rotation schemes (30.00%). By the end of a long working period (256 days), the activity of CD25⁺, CD71⁺, CD8⁺ and CD16⁺ cells approximates the upper limit of physiological norm. The activation of T- and B-cells with signs of a lymphoproliferation and cytotoxic activity is associated more with the duration of the shift. Decreased levels of activated T- and B-lymphocytes and concentrations of total testosterone occur less in men under short on/off schemes (16 days). The decrease in total testosterone concentration is associated with the decrease in phagocytic activity of neutrophils, with lower concentrations of activated CD4⁺, CD25⁺ cells and higher CD8⁺, CD16⁺ levels. Individuals with increased contents of total testosterone tend to have higher cytotoxic activity and wider variety of immune imbalances, regardless of length of service or duration of shift.

In nomadic population, the increased levels of CD8⁺, CD16⁺ lymphocyte phenotypes is linked with deficient phagocytic activity ($r=0.80$), deficit of mature, functionally active CD3⁺ cells ($r=0.78$) and increased levels of CD95⁺apoptosis-receptor cells ($r=0.80$) – in 27%-89% of the examined. The involvement of CD8⁺, CD16⁺ lymphocyte phenotypes in the mechanism for regulating the activity of cellular and humoral immunity relates to concentrations of B-cells (CD20⁺) and activator cells (CD71⁺, CD25⁺, HLA-DR⁺) – in 7%-30% of nomadic population and 9%-10% of settled residents ($r=0.72-0.80$).

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