

A.I. Fedorova, D.K. Garmaeva, L.I. Arzhakova, D.S. Belolubskaya, O.G. Afanaseva, A.I. Egorova, T.I. Dmitrieva, I.P. Semyonov, A.P. Arzhakova

IMMUNE STRUCTURES – COLD – NATURAL ADAPTOGENES

ABSTRACT

The article presents an analysis of literature data on the effect of cold on human health, the structure of the immune system, and the properties and effects of natural adaptogens.

In general, the general cryogenic climatic parameters of the Far North create uncomfortable conditions for human existence and affect people's health. In extreme conditions, protective mechanisms and adaptive alteration of the body can lead to disruption – maladaptation. A whole series of pathological phenomena develops.

In modern conditions, the development of adaptogens from local raw materials for enhancing the body's resistance, prevention and treatment of immune response disorders in low temperature conditions of the Sakha (Yakutia) Republic is a priority area.

Keywords: cold, maladaptation, immune system, lymphoid tissue, lymph nodes, natural adaptogens, the Sakha (Yakutia) Republic.

The territory of the Sakha (Yakutia) Republic is located in the zone of extreme natural and climatic factors (permafrost with a large annual temperature range from +35°C in summer to -67°C in winter, anticyclonic regime and low oxygen partial pressure in winter, etc.) and is the coldest inhabited region in the northern hemisphere of the Earth, which is due to the considerable remoteness and isolation of mountain massifs affected by moist and warm air masses from the Atlantic and Pacific Oceans and proximity to the cold seas of the Arctic Ocean [11, 17, 42].

Despite the success of mankind in creating technical means of protection against unfavorable factors of the external environment, a person is still vulnerable to the harsh power of the Arctic. For Yakutia, the extra continental climate against the background of a constantly operating cooling screen from the surface of the earth is the main external factor that negatively affects the health of the northerner. The results of numerous studies have identified two important aspects of this problem: 1) the change in the structure of northern populations by constitutions, psychological makeup, adaptive types is the result of natural selection of people most effectively adapting to the North, i.e. having good prerequisites for adaptation in these conditions (preadaptation); 2) cost of adaptation is manifested in a decrease in functional reserves and efficiency at the organismic level and in life expectancy at the population level [21].

In general, these general cryogenic climatic parameters of the Far North create uncomfortable conditions for human existence and affect people's health [1, 9, 37]. In extreme conditions, protective mechanisms and adaptive

alteration of the body can lead to disruption – maladaptation. A whole series of pathological phenomena develops [7, 31].

It is known that the human body to the negative impact of various environmental factors corresponds to a violation of the immune system, especially local immunity. Damaged morphologically and functionally the organs of the immune system are not able to protect the human body from foreign influences, external or internal [32]. A consequence of the disturbance of the normal functioning of the immune system in the regions of the Far North is the widespread occurrence among residents of acute and chronic infectious and inflammatory diseases of the respiratory tract, allergic and autoimmune processes, and malignant neoplasms of certain localization [18]. The most common diseases characterized by sensitivity to climatic factors include respiratory diseases. The prevalence of respiratory diseases among children in the northern regions of the country is 1.5 to 2 times higher than the average for the Russian Federation [31].

A number of studies have shown that people arriving to the Far North from central regions of Russia and other countries (temperate latitudes) have a violation of adaptive mechanisms, characterized by a decrease in the adaptive capabilities of the body and the development of pathological conditions. In this regard, for the regions of the Far North, it remains relevant to study the mechanisms of adaptation, as well as the regulation of adaptive responses. [26]. In the studies of L.K. Dobrodeev, E.M. Dyuzhikova, L.V. Schegoleva et al. [36] showed that residents of the polar regions (Nenets Autonomous Okrug) have low rates of phagocytic activity. In

the inhabitants of the North, the switching of macrophages to other functions (the exchange of blood lipoproteins) reduces their role in the formation of an immune response. For example, in the North, this leads to a "breakthrough" of the antigens of the intestinal microflora in the body's lymphoid system, followed by an increase in the immune response.

The extreme stage of the effect of cold on the human body is frostbite, which is aggravated by factors such as: alcohol, exhaustion, inactivity. In Russia, more than 1.5 thousand people die from frostbites annually. They are mostly men over 20, which is clearly associated with the consumption of alcohol [31].

The immune system is one of the most complex systems of the body, about the work of which scientists still do not have a comprehensive understanding.

It is a unique, natural defense mechanism. Thanks to the coherence of the entire functional system of immunity, the body is able to withstand many factors that have a negative impact. The uniqueness of the immune system lies in the fact that it contains such regulatory functions that allow, in the presence of each specific antigen being the starting point, to bring a huge machine called the immune system into action and react with a specific immune response in accordance with its individual characteristics [29]. Only two types of biological systems – nervous and immune – have the capacity for "intelligent" information processing, including memory, learning, recognition and decision-making in previously unknown situations. A new interdisciplinary approach to the study of the immune system will require additional information describing the interaction of its components, which should be presented in quantitative terms. In this form it will

be available not only to immunologists, but also to specialists from other fields of science - mathematicians, physicists, engineers and other researchers [4]. The computational capabilities of the immune system have only recently been evaluated as a new promising direction, called immunocomputing (IC) [43]. In this case, each cell of the body is subject to control of its own immune system (IMC) – an information security system that for each cell solves the problems of integrity, confidentiality and accessibility of information [4].

In recent years, interest in the immune system, its structure and functions has increased significantly. The cellular and subcellular levels of studying the organs of the immune system, in particular lymphoid tissue, are of particular importance in the development of the problems of immunomorphology. Structures of the immune system are present in virtually all organs and tissues. Some structures are located on the pathways of possible introduction into the body of foreign substances, others on the way of following them in the body. Located at the surface of the respiratory tract, lymphoid tissue serves as the first specific barrier to the penetration of foreign antigens. They are the first “target” on the way of penetration of cold air into the respiratory system [19, 31]. In connection with this, the resistance of the organism to the action of low temperatures, the formation of adaptive processes in it, depends on the functional activity of immune structures [12, 31].

Lymphoid tissue, being the main polygon of development of specific immunological reactions, contains the basic cellular populations (lymphocytes, macrophages, plasmatic, fat, reticular cells) involved in ensuring genetic consistency of the internal environment of the body. Carrying out a lifelong monitoring of the maintenance of antigen homeostasis, the immune system is in strict interaction with other functional systems (nervous, endocrine, etc.) involved in the processes of adaptation of the organism to the changing factors of the external and internal environment. The immune system protects the body from the effects of various damaging factors of exogenous and endogenous origin, provides protection against pathogens, viruses and fungi, performs antitumor protection, and participates in processes of elimination of tissue structures that have become due to mutation or alienation processes. The adequacy of the body's response to genetically alien agents and the likelihood of developing allergic, infectious, autoimmune and

oncological diseases depend on the state of the immune system, its adaptive capabilities [32, 34, 38].

Lymph nodes are the most numerous peripheral organs of the immune system that serve as biological filters. Lymph nodes are located on the path of lymph flow (tissue fluid) from organs and tissues. Alien substances enter the sinuses of the lymph node, where they are recognized by lymphocytes and destroyed with the help of macrophages. Through the lymph nodes, which together with the lymphatic capillaries, vessels and trunks form the lymphatic system, the tissue fluid is filtered and again returns to the bloodstream from all regions of the body. Therefore, the importance of lymph nodes and lymphatic system in general in the performance of protective functions in the body is great. The lymphatic system is considered as the most important component of the immune system [3, 6, 23, 28, 41].

As a result of exposure to the human body of various unfavorable factors of the external environment, the body's defenses are weakened. Damaged morphologically and functionally the organs of the immune system are not able to protect the human body from foreign influences, external or internal. Depending on the degree of damage, disruption of the structure and function of the immune system, a person is more often and heavier sick [32].

Currently, the study of various organs of animals and humans subjected to cold exposure draws the attention of researchers. Influence of low natural temperatures in Sakha (Yakutia) Republic causes depletion of diffuse lymphoid tissue of the laryngeal mucosa, which is expressed by a decrease in the number of cells of the lymphoid series, in particular T-lymphocytes, B-lymphocytes, plasma cells, and a significant increase in the number of destructively altered cells, and as a consequence, macrophages [5]. Changes in diffuse lymphoid tissue in the mucous membrane of the larynx under the influence of low natural temperatures are characterized by a significant decrease in lymphopoietic processes, which is expressed in a decrease in the percentage of lymphoblastic cells and cells in mitosis [5, 8].

Complex morphological changes in the trachea of rats with cooling according to O.N. Lee et al. [25] showed changes characteristic for the stage of adaptive stress, at which destructive changes of ciliate cells, goblet cells, and expressed migration of mast cells occur. Under the action of low temperatures in the lungs of experimental animals, foci of fibrosis

and edema, dilatation of blood vessels, increased migration of mast cells and eosinophils to the bronchial epithelium appear [13]. The results of the studies N.P. Krasavin, V.A. Dorovskikh, S.S. Celuyko [20] showed that unfavorable factors of the air environment quite often have a negative effect on the airways, especially when the body stays in a low temperature for a long time. When the cold factor influences the organism, protective and compensatory processes at the subcellular and cellular levels are first mobilized [35].

According to the results of research L.A. Obukhova [27], O.V. Matkina [24], structural transformations in the thymus, revealed during experimental cooling, can be characterized as a pronounced accidental involution of the thymus in the stage of hypotrophy, the main manifestations of which are a decrease in the mass and volume of the organ, a decrease in the size of the cortical substance; oppression of the lymphopoietic function and an increase in the death of lymphocytes by the type of apoptosis, leading ultimately to a decrease in the number of lymphoid populations in the thymus. From the side of the lymph nodes during extreme cooling, changes characterized by activation of B-dependent zones with the formation of new ones and stimulation of pre-existing germinal centers, hypertrophy of the brain strands, development of plasmacytic, eosinophilic and mast cell responses were noted.

O.T. Devonayev [15] studied lymphoid structures of the urinary organs of rats susceptible to cold stress and high altitude conditions. With the action of cold for 7 days, the author observed a decrease in the length, width and area of lymphoid nodules, the number of lymphoid cells in the ureter and bladder, and the size of the glands of the bladder. The decrease in the amount of lymphoid tissue, the increase in degenerative processes in it, and the decrease in lymphocytopoiesis were maximal on day 14 of the experiment, after which gradual quantitative and qualitative normalization were observed.

Hypothermia has a depressing effect on the severity of the cellular and humoral immune response [10, 14, 16, 39]. The research of V.M. Nikolaev showed a change in the phagocytic activity of leukocytes when exposed to low temperatures. Reduction of the number of absorbed particles by leukocytes testifies to the suppression of nonspecific cellular immunity in hypothermia [26].

At the same time, structural changes in various organs and systems of the

organism in the extreme conditions of the North have not yet been studied. In this regard, in modern conditions, increasing unfavorable environmental and professional impacts, morphological studies of the immune system organs remain adaptable and promising, and maladaptation of the organism to the action of extreme factors. The data obtained will provide the basis for establishing the state of protective, adaptive capabilities of organs, taking into account the temperature regime of Yakutia.

The tasks of today are to find ways to preserve the health of workers in the Arctic region by modern means of medical and biological science. The search for solutions is seen in the prevention of psychoemotional stress, sleep and desynchronization disorders, physical stress (cold, hypoxia, etc.) [21]. One of the most effective ways of healing is the use of natural stimulants for the functions of organs and systems of the human body [40]. In these conditions, the task of restoring the working capacity of the human body systems responsible for adaptation to unfavorable environmental factors is urgent. One of the ways of healing is the use of natural stimulants of the functions and systems of the human body. There are two approaches to solving the problem of adaptation (adaptation) of a person to a new environment. The first is strict environmental protection and at least the preservation of its condition. The second is to increase the stability of the human body itself to harmful environmental factors. In connection with the second approach, substances that stimulate the body's resistance are of great interest, capable of mobilizing its unused reserve mechanisms under normal conditions. These compounds include stimulants and adaptogens (from the Latin "adaptation" – adaptation), differing in the mechanism of their impact. When adaptogens are used, all human protective forces are harmoniously mobilized, because these substances directly affect tissue metabolism, increase mental and physical performance, and also prevent disorders caused by emotional stress and other extreme effects [2].

Adaptogens have a specific immunostimulating and anabolic effect on the condition of the central nervous system, hemopoietic organs and hormones, causing a humoral response by sensitizing B-lymphocytes (immunoglobulin synthesis) and T-lymphocytes (thymus-dependent cells), the result of which is the cellular response [3, 22]. In conditions of general

body cooling, timely and targeted correction can help reduce the effect of cytotoxic factors. Addition to the main treatment application of adaptogen will prevent the development of chronic inflammation and optimize the quality of therapy for patients with respiratory diseases [13]. In the climatic conditions of the Far North, chronic lung diseases are characterized by a protracted course, and often accompanied by exacerbations, in connection with which the need for individualization of treatment and the selection of means of prevention becomes apparent. Therefore, one of the leading places is the use of drugs of natural origin, allowing to reduce the level of negative influence of low temperatures on the body [8, 29, 30].

Immunotropic or immunomodulating drugs are used to correct immunity. In the work of L.A. Obukhova [27] it was shown that when polyphenol compounds were introduced from the overground part of the cuff ordinary under conditions of physiological norm, tendencies were revealed in the structural transformations of lymphoid organs, indicating an increase in their functional activity and an increase in structural reserves. In the thymus – increased proliferation of lymphoid and epithelial cells, accompanied by an increase in the number of lymphocytes in the organ and the formation of additional endocrine structures (glandular formations); the formation of additional elements of the microcirculatory bed; activation of the mast cell population carrying out local regulatory functions; Enrichment of epithelial cells with subcellular structures responsible for protein synthesis and energy supply. In lymph nodes – an increase in the size of B-dependent zones and increased proliferation of cells of different specializations. Prophylactic and early pathogenetic correction by polyphenolic compounds from the overground part of the cuff of the ordinary leads to a decrease in the loss of body weight and lethality of animals during the period of extreme cooling, a decrease in the manifestation of involutive changes in the thymus, a decrease in the reactivity of the lymph nodes, not associated with the development of destructive processes in them, and full restoration lymphoid organs during the period of readaptation.

According to domestic and foreign studies, currently up to 30% of patients suffering from various diseases need the appointment of immunomodulatory therapy. The syndrome of secondary immune deficiency, accompanied, as a rule, by reversible disturbances in the functioning of the immune system,

its adaptive mechanisms and other functions, significantly complicates the course of any diseases. Violation of the normal functioning of the immune system not only determines the more severe, prolonged course of any illnesses, but also contributes to the generalization of inflammatory processes, the development of complications, to a decrease or lack of clinical effect from basic therapy, to an increase in lethality [33].

Thus, in modern conditions, the development of adaptogens from local raw materials for enhancing the body's resistance, prevention and treatment of immune response disorders in low temperature conditions of Sakha (Yakutia) Republic is a priority area.

References:

1. Agadzhanian H.A., Petrova P. G. Chelovek v usloviyah Severa [Man in the North] Moscow: - "KRUK" Publishing, 1996, 206 p.
2. Studencov E. P., Ramsh S.M., Kazurova N.G., Neporozhneva O.V., Garabadzhiu F.V., Kochina N.A., Voronkov N.G., Kuznetsov V.A., Krivorotov D.V. Adaptogeny i rodstvennye gruppy lekarstvennykh preparatov - 50 let poiskov [Adaptogens and Related Drug Groups – 50 Years of Research] Obzory po klinicheskoy farmakologii i lekarstvennoy terapii [Reviews of Clinical Pharmacology and Drug Therapy]. 2013, Vol. 11, No. 4, pp. 3-43.
3. Alekhin E.K., Lazareva D.N., Sibiryak S.V. Immunotropnye svoystva lekarstvennykh preparatov [Immunotropic Properties of Drugs]. Ufa: BGMI Publishing, 1993, 208 p.
4. Blyum V.S., Zabolotskiy V.P. Immunnaya sistema i immunokompyuting [Immune system and Immunocomputing] Matematicheskaya morfologiya: Ehlektronnyy matematicheskij i medikobiologicheskij zhurnal [Mathematical Morphology: Electronic Mathematical and Medico-Biological Journal]. 2007, Vol. 6, issue 4, available at: <http://www.sgma.alpha-design.ru>
5. Buzinaeva M.T. Immunomorfologicheskaya harakteristika limfoidnoj tkani gortani pri vozdejstvii nizkih prirodnykh temperature: avtoref. dis. kand. med. nauk. [Immunomorphological characteristics of the laryngeal tissue of the larynx under the influence of low natural temperatures: Abstract of Ph.D. dissertation, pathological anatomy]. Ulyanovsk, 2013, 26 p.
6. Buyanov V.M. Limfologiya endotoksikoza [Lymphology of endotoxemia]. Moscow, Medicine, 1990, 272 p.
7. Varlamova N.G. Dinamika

urovnya zdorovya u trudyashchihsya na Severe [Dynamics of Workers' Health in the North] Adaptatsiya i rezistentnost organizma na Severe [Adaptation and Resistance of Organism in the North]. Svytyvkar, 1990, pp. 64-73.

8. Selujko S.S., Gorbunov M.M., Namakonova V.S., Krasavina N.P. Vliyanie prirodnykh antioksidantov na regeneratsiyu ehpiteliya slizistoy obolochki trahei pri obshchem ohlazhdenii organizma [Effect of Natural Antioxidants on Regeneration of the Mucous Membrane Trachea's Epithelium with Overall Cooling of the Body] Dalnevostochnyj medicinskij zhurnal [Far Eastern Medical Journal]. 2014, No. 1, pp. 95-99.

9. Shapovalenko N.S., Dorovskikh V.A., Korshunova N.V., Shtarberg M.A., Slastin S.S., Nevmyako E.E. Vliyanie holodovogo stressa na intensivnost perekisnogo okisleniya lipidov i antioksidantnyu sistemu tkanej ehkspirementalnykh zhivotnykh [Effect of Cold stress on the Intensity of Lipid Peroxidation and the Antioxidant System of Experimental Animals] Byulleten' fiziologii i patologii dyhaniya [Physiology and Breathing Pathology Bulletin]. 2011, Vol. 39, pp. 22-25.

10. Volovich V.G. Chelovek v ehkstreimalnykh usloviyakh prirodnoy sredy [Man in Extreme Environmental Conditions]. Moscow: Thought, 1983, 196 p.

11. Gavrilo M.K. Klimaty holodnykh regionov Zemli: ucheb. posobie [Climate of Cold Regions of the Earth: study guide]. Yakutsk: RAS SB Publishing, 2003, 208 p.

12. Garmayeva D.K., Osinskaya A.A., Sapin M.R. Limfoidnye struktury dyhatel'nykh putej pri vozdeystvii almaznoy pyli v usloviyakh granil'nogo proizvodstva Respubliki Saha (Jakutija) v jeksperimente [Lymphoid structures of the airways under exposure of diamond dust in a lapidary industry of the Republic of Sakha (Yakutia) in the experiment]. Yakutsk, NEFU Publ., 2010, 278 p.

13. Li O.N., Dorovskikh V.A., Selujko S.S., Shtarberg M.A., Chzhou S.D., Li Ts Gistofiziologiya legkih kryys pri holodovom vozdeystvii na fone vvedeniya arabinogalakšana [Histophysiology of Rat Lungs with Cold Exposure Given Administration of Arabinogalactan] Byulleten' fiziologii i patologii dyhaniya [Physiology and Breathing Pathology Bulletin]. 2011, No. 39, pp. 40-42.

14. Golderova A.C., Zaharova F.A., Alekseev S.N. Osobennosti nespecificheskoy adaptivnoy reakcii u bolnykh s ostroy holodovoy travmoj [Features of Nonspecific Adaptive Response in Patients with Acute Cold

Trauma] Jakutskij medicinskij zhurnal [Yakut medical journal]. 2009, No. 1 (25), pp. 7-9.

15. Devonaev O.T. Strukturno-funktsionalnye harakteristiki i osobennosti morfogeneza limfoidnogo apparata mochevyvodyashchih putej v norme i pri vozdeystvii holodovogo stressa i vysokogorya: avtoref. dis.... dokt. med. nauk. [Structural and Functional Characteristics and Features of Morphogenesis of the Lymphoid Apparatus of the Urinary Tract in Normal Conditions and under the Influence of Cold Stress and High Altitude, Abstract of D. Sc. dissertation, Anatomy of Human]. Novosibirsk, 2007, 33 p.

16. Desyatov V. P. Smert ot pereohlazhdeniya organizma [Death by Hypothermia]. Tomsk, 1977, 128 p.

17. Ivanova R. N. Rekordno nizkie temperatury vozduha v Evrazii [Record Low Air Temperatures in Eurasia]. YSU Herald. 2006, Vol. 3, No.1, pp. 13-19.

18. Kaznacheev V.P. Sovremennyye aspekty adaptatsii [Contemporary Aspects of Adaptation]. Novosibirsk: Science, 1980, 190 p.

19. Kalinyuk I.G. Morfolicheskie izmeneniya v limfoidnykh strukturakh zheludka v dinamike postnatalnom ontogeneza v norme i pri antigennoy stimulatsii (ehkspirementalnoe issledovanie): dis ...kand. med. nauk [Morphological Changes in Lymphoid Structures of the Stomach in the Dynamics of Postnatal Ontogenesis in Normal Conditions and with Antigen Stimulation (experimental research)], Ph.D. Thesis, Anatomy of Human]. Uzhgorod, 2006, 178 p.

20. Krasavina N.P., Dorovskikh V.A., Celujko S. S. Morfofunktsionalnaya harakteristika soedinitel'noy tkani organov dyhaniya pri obshchem ohlazhdenii organizma na fone medikamentoznoy korrektsii [Morphofunctional Characteristics of the Connective Tissue of the Respiratory Organs with General Cooling of the Body Against the Background of Drug Correction] Dalnevostochnyj medicinskij zhurnal [Far Eastern Medical Journal]. 2002, No.1, p. 8.

21. Krivoshchekov S.G. Trud i zdorove cheloveka v Arktike [Work and Human Health in the Arctic] Zhurnal mediko-biologicheskikh issledovaniy [Journal of Biomedical Research]. 2016, No. 4, pp. 84-89.

22. Lazareva D.N., Alekhin E.K. Stimulyatory immuniteta [Stimulants of Immunoresponse]. Moscow: Medicine, 1985, 256 p.

23. Garmayeva D.K., Fedorova A.I., Afanas'eva O.G., Sokolova R.G.

Limfateskij uzel v jeksperimente: vospalenie, toksikoz, opuhol' [The lymph node in the experiment: inflammation, toxicosis, tumor]. Novosibirsk, Manuscript Publ., 2005, 160 p.

24. Matkina O.V. Patogeneticheskie izmeneniya v timuse i selezenke neinbrednykh belykh kryys pri ostrom stresse [Pathogenetic Changes in the Thymus and Spleen of Noninbred White Rats under Acute Stress] Permskij medicinskij zhurnal [Perm Medical Journal]. 2014, Vol. 31, No.1, pp. 121-128.

25. Li O.N., Dorovskikh V.A., Selujko S.S., Shtarberg M.A., Chzhou S.D., Li Ts Morfofunktsionalnaya ochenka trahei kryys v modeli obshchego ohlazhdeniya organizma pri ispolzovanii arabinogalakšana [Morphofunctional Evaluation of Rat Trachea in the Model of General Body Cooling Using Arabinogalactan] Byulleten' fiziologii i patologii dyhaniya [Physiology and Breathing Pathology Bulletin]. 2011, No. 39, pp. 26 - 28.

26. Nikolaev V.M. Izmeneniya prooksidantno-antioksidantnogo ravnovesiya v otvetnykh ehkologo-biohimicheskikh reaktsiyakh organizma zhivotnykh i cheloveka na deystvie holoda: diss..... kand. biol. nauk [Changes in Prooxidant-Antioxidant Equilibrium in Response Ecologo-Biochemical Reactions of the Animal and Human Organisms to Cold Action, Ph.D. Thesis, Ecology]. Yakutsk, 2007, 112 p.

27. Obuhova L.A. Strukturnye preobrazovaniya v sisteme limfoidnykh organov pri deystvii na organizm ehkstreimalno nizkikh temperatur i v usloviyakh korrektsii adaptivnoy reaktsii polifenolnymi soedineniyami rastitelnogo proiskhozhdeniya: avtoref. dis. dokt. med. nauk. [Structural Transformations in the System of Lymphoid Organs with the Action on the Organism of Extremely Low Temperatures and in Conditions of Correction of Adaptive Reaction by Polyphenolic Compounds of Plant Origin, Abstract of D. Sc. dissertation, Anatomy of Human]. Novosibirsk, 1998, 43 p.

28. Borodin Yu. I. Obshchaya anatomiya limfateskoy sistemy [General Anatomy of the Lymphatic System]. Novosibirsk: Science, 1990, 137 p.

29. Petrov R.V. Immunologiya [Immunology]. Moscow: Medicine, 1982, 636 p.

30. Borodin Yu. I., Zykov A.A., Golovnyov V.A., Gorchakov V.N. Prirodnye bioflavonoidy kak sredstva dlya ehndoeekologicheskoy sanatsii [Natural Bioflavonoids as Means for Endoecological Sanitation] Chelovek i lekarstvo: tez. dokl. V Rossijskogo

nacionalnogo kongressa [Man and Medicine: theses of V Russian National Congress]. Moscow, 1998, p. 30.

31. Revich B.A. Izmenenie zdorovya naseleniya Rossii v usloviyah menyayushchegosya klimata [Changes in the Health of the Russian Population in Changing Climate] Problemy prognozirovaniya [Problems of Forecasting]. 2010, No. 3. – pp. 140- 150.

32. Sapin M.R., Nikitjuk D.B. Immunnaya sistema, stress i immunodeficit [The immune system, stress and immunodeficiency]. Moscow, Dzhanger Publ., 2000, 184 p.

33. Semyonova I.B. Zakonomernosti korrektsii vtorichnyh immunodeficitov immunomodulyatorami (na primere anatoksina stafilokokkovogo ochishchennogo i likopida): dis... dokt. med. nauk. [Patterns of Correction of Secondary Immunodeficiencies by Immunomodulators (on the Example of Purified Staphylococcus Anatoxin and Lycopene), D. Sc. Thesis, Allergology and Immunology]. Moscow, 2004, 262 p.

34. Sepiashvili R.I. Funktsionalnaya sistema immunnogo gomeostaza [Functional System of Immune Homeostasis] Allergologiya i immunologiya [Allergology and Immunology]. 2015, Vol. 16. - No.1. - pp. 91-100.

35. Celujko S. S., Krasavina N.P., Semenov D.A., Gorbunov M.M., Chzhou S.D., Li Ts Sovremennye vzglyady na voprosy proliferatsii i differentsirovki stvolovykh kletok organov dyhaniya v norme i pri holodovykh vozdeystviyakh [Modern Views on the Proliferation and Differentiation of Stem Cells of the Respiratory System in Norm and under Cold Influences] Byulleten' fiziologii i patologii dyhaniya [Physiology and Breathing Pathology Bulletin]. 2012, No. 45, pp. 98 -103.

36. Dobrodeeva L.K., Dyuzhikova E.M., Shegoleva L.V. Sostoyanie immunnogo sistema u detej prozhivayushchih na severe v zonah razlichnoy stepeni diskomfortnosti [State of the Immune System in Children

Living in the North in Zones of Varying Degrees of Discomfort] Immunologiya [Immunology]. 2004, No. 4, pp. 238 -242.

37. Savinov D.D., Petrova P. G., Zaharova F.A. [i dr.] Sreda obitaniya i zdorove cheloveka na Severe [Habitat and Human Health in the North]. Novosibirsk: Science, 2005, 291p.

38. Trufakin V. A., Robinson M.V. Morfocitohimicheskie metody dlya ocenki immunokompetentnykh kletok i limfoidnykh organov metodicheskoe rekomendatsii [Morphocytochemical Methods for Evaluation of Immunocompetent Cells and Lymphoid Organs: guidelines]. Novosibirsk, 1990, pp. 13-15.

39. Tumasov S.A. Smert ot ohlazhdeniya na Kamchatke [Death by Hypothermia in Kamchatka]. TSU Publishing, 1977, 26 p.

40. Tutelyan V.A. Biologicheski aktivnye dobavki - neizbezhnyy ehlement pishchi XXI veka [Biologically Active Additives – the Inevitable Element of Food of the XXI Century] BAD- nutreceptiki i ih ispolzovanie s profilakticheskoy i lechennoy tsel'yu pri naibolee rasprostranennykh zabolevaniyakh: III mezhdunarodnyy simpozium [BAA – Nutraceuticals and their Use with Preventive and Curative Purpose for Most Common Diseases: III International Symposium]. Tumen University Publishing, 1997, pp. 7-8.

41. Chava S.V. Issledovanie perifericheskikh organov immunnogo sistema pri vvedenii v organizm immunomodulyatorov novogo pokoleniya (ehksperimentalno-morfologicheskoe issledovanie: dis... dokt. med. nauk. [Investigation of Peripheral Organs of the Immune System when New Immunomodulators are Introduced into the Body (Experimental Morphological Study), D. Sc. Thesis, Anatomy of Human]. Moscow, 2008, 524 p.

42. E. V. Kornienko Yakutiya: Istoriko-kulturnyy atlas [Yakutia: Historical and Cultural Atlas]. Moscow: Design Publishing. Information. Cartography, 2007, pp. 50-59.

43. Tarakanov A.O., Skormin V.A., Sokolova S.P. Immunocomputing:

Principles and Applications. New York.: Springer, 2003, p. 230.

Credits:

1. Fedorova Aida Ivanovna, Candidate of Medical Sciences, M.K. Ammosov NEFU Medical Institute Docent, +79241696871, e-mail fed.aida@rambler.ru

2. Garmaeva Darima Kyshektovna, Doctor of Medical Sciences, Professor, M.K. Ammosov NEFU Medical Institute Docent, +79142349680, e-mail dari66@mail.ru

3. Arzhakova Lena Ignatievna, Candidate of Medical Sciences, M.K. Ammosov NEFU Medical Institute Docent, +79644150606, e-mail lenaarzhakova@mail.ru

4. Belolyubskaya Dariya Stepanovna, Candidate of Medical Sciences, M.K. Ammosov NEFU Medical Institute Docent, +79142976118, e-mail b_d_st@mail.ru

5. Afanasyeva Oksana Gavrilovna, Candidate of Medical Sciences, доцент M.K. Ammosov NEFU Medical Institute Docent, +79142671992, e-mail kafanatomiya@mail.ru

6. Egorova Angelina Innokentievna, Candidate of Biological Sciences, Junior Research Associate, M.K. Ammosov NEFU Medical Institute Docent, +79148220249, e-mail egorovaanil@mail.ru

7. Dmitrieva Tuyara Ivanovna, Candidate, Federal State Budget Educational Institution "Yakut State Agricultural Academy", +79644298776, e-mail dark_dell@mail.ru

8. Semenov Ilya Petrovich, 2nd year student of "General Medicine" at M.K. Ammosov NEFU Medical Institute, +79246647537, e-mail llyamedik@icloud.com

9. Arzhakova Aleksandra Petrovna, Аржакова Александра Петровна, Candidate of Sociological Sciences., Senior Associate. RAS SB Institute of Biological Problems of Cryolithozone, e-mail sasha.a7.t9@mail.ru.

