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The authors declare no conflict of interest in the submitted article.

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THE EFFECT OF ELEVATED AND PHYSIOLOGICAL CONCENTRATIONS OF CATECHOLAMINES ON THE FORMATION OF IMMUNOGLOBULINS IN HEALTHYINDIVIDUALS IN THE NORTHERN TERRITORIES OF THE RUSSIAN FEDERATION

An immunological assessment of the health status of 75 Arkhangelsk residents who had no history of acute or chronic diseases at the time of the study was carried out. The aim of the study was to study the effect of elevated and physiological concentrations of catecholamines on the formation of immune responses in residents of the northern territories of the Russian Federation. During a comprehensive immunological examination, a morphological analysis of the blood was performed, including a study of its cellular composition (hemogram). Thus, it has been established for the first time that practically healthy residents of the European North of the Russian Federation experience changes in the content of catecholamines and immunological parameters. An increase in the average dopamine content and a slight increase in the average IdM content was found, which amounted to 33.7±3.56 and 1.83±0.04, respectively. Studies have shown that patients have a tendency to increase the content of IgE immunoglobulin (74.3±8.16). In addition, abnormally high concentrations of IdM (36.84±3.18%) and elevated concentrations of IgG (25.0±2.49%) were detected. There was also a slight increase in the concentrations of cells capable of proliferation (CD10+), which amounted to 1.7±0.22%. Elevated concentrations of catecholamines in practically healthy people have not been established. Concentrations of dopamine were 7.81±0.43%, norepinephrine 4.76±0.08% and adrenaline 3.08±0.27%.The remaining immunological parameters did not exceed the values considered physiologically normal. These changes correlate with the impact of negative climatic factors. Such factors include violation of the light regime and low temperatures, which provoke a chronic state of stress in the body and, as a result, increased stress on the immune system. This phenomenon leads to a malfunction of the immune system and accelerated physiological wear of the body, which can become a predisposing factor for the development of various diseases.

Keywords: catecholamines, dopamine, norepinephrine, adrenaline, immune reactions, northern territories of the Russian Federation, lymphocytes. CD10+, CD95+, immunoglobulins.

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Introduction. The immune system of residents of the northern regions shows increased basic activity in a number of indicators. According to traditional views, the health of the population of the northern territories is subject to the complex effects of a number of adverse factors. These include natural and climatic conditions, including extreme weather conditions, geomagnetic activity, sudden changes in illumination, geochemical features of the area and the unpredictability of atmospheric phenomena. In addition, it is typical to observe sharp fluctuations in temperature, atmospheric pressure, and daylight hours throughout the year. Prolonged exposure to low temperatures combined with strong winds can lead to negative health consequences. Such a meteorological situation contributes to the development of oxygen starvation and an increase in the basic metabolism in the body. High levels of humidity also have a negative impact on health, disrupting cerebral circulation. The interaction of these factors has a complex effect on the functioning of all human body systems. In the context of the topic under discussion, it is also necessary to note the level of social protection of citizens in the field of healthcare, which is carried out at an insufficient level. The influence of extreme conditions on the human body, characteristic of the northern regions, may exceed its ability to adapt [2]. The issue of the scientific justification for setting standards for regional physiological parameters remains important and requires further study.

The state of health of residents of the northern territories of the Russian Federation is the most important indicator of the quality of life and reflects the ability to withstand adverse factors. The formation and functioning of the immune system in the inhabitants of the northern regions has its own characteristics [1]. Undoubtedly, climatic and anthropogenic health risk factors in the subjective assessments of residents of northern cities have a significant impact on the functioning of the immune system [8].

The level of immunity and adaptation to difficult environmental conditions play a key role in maintaining the health of northerners, and the level of resistance to diseases among residents of the northern regions is significantly lower than in other regions. There is a decreased resistance to diseases in the population of the northern regions, in comparison with other regions, as a result, there is a decrease in the immune response [14]. The total effect of exposure to the adverse factors of the North significantly increases the negative impact on the human body in the form of severe stress conditions [15].

In the difficult environment of the North, where living conditions are subject to frequent changes, the process of human adaptation is particularly difficult [3]. It requires significant energy expenditure and uses redundant, and sometimes ineffective, mechanisms to maintain the stability of the human body's homeostasis. The immune system, functioning as the body's defense mechanism, plays a key role in maintaining its stability. Thus, the state of the immune system and its reactivity are important indicators of the overall functional state of the human body and its ability to adapt to adverse conditions. The study of the immune system of representatives of northern populations is an urgent task due to the fact that specific climatic conditions and unfavorable ecology contribute to the modification of its functioning.

The aim is to establish the effect of elevated and physiological concentrations of catecholamines on the formation of immunoglobulins in healthy individuals in the northern territories of the Russian Federation.

Materials and methods. The data of the immunological examination of 75 practically healthy people living in Arkhangelsk, who at the time of the examination had no history of acute and chronic diseases, were studied and analyzed. The average age was 45.4 years. The study participants were in the age group from 18 to 65 years old. The examination was conducted at the Biolam medical company, Arkhangelsk. The study was conducted in accordance with the provisions of the Helsinki Declaration and approved by the Ethics Committee of the Federal State Budgetary Educational Institution FITSKIA Ural Branch of the Russian Academy of Sciences (Protocol No. 001-20/01 dated January 20, 2025). The survey was conducted with the written consent of the respondents.

Blood samples were taken for laboratory examination in the morning (from 8 to 10 o'clock), on an empty stomach. The blood serum was isolated by centrifugation, which made it possible to separate the liquid fraction from blood cells (erythrocytes) in order to prepare biological material for further analysis.

As part of the complex of immunological research, an analysis of the morphological composition of blood was carried out using the Romanovsky-Giemse staining method. The concentrations of catecholamines (dopamine, norepinephrine, epinephrine) in blood serum were studied by enzyme immunoassay on an automatic Evolis enzyme immunoassay analyzer (Bio-RAD, Germany) using diagnostic kits manufactured by IBL Hamburg, Germany. The level of cells capable of proliferation (CD10+) and cells labeled for death (CD95+) was assessed by indirect immunoperoxidase reaction using monoclonal antibodies (Sorbent, Moscow). The content of immunoglobulins A (IdA), M (IdM), G (IgG), and E (IgE) was studied using Biosourse test kits (USA). In the course of statistical analysis of the research data, software packages "Microsoft Excel 2010" and "Statistica 7.0" (StatSoft, USA) were used. The Shapiro-Wilk criterion was used to assess the compliance of the data distribution with the normal law. The results of the analysis showed the similarity of the distributions with the normal one. In this regard, the arithmetic mean (M) and the standard error of the mean (m) were calculated to describe the data. The boundaries of the normal distribution of the studied indicators are also determined. The relationship between the parameters was estimated using the Pearson correlation coefficient (r). The statistical significance of the differences was established at the significance level of the t-test $p < 0.05$.

Results and discussion. The increased content and physiological concentrations of catecholamines, as well as the peculiarities of immune reactions in people living in the North, have been established. According to the results of the study, an increase in the average content of dopamine in the peripheral venous blood was revealed. The reaction from other catecholamines was relatively low. A slight increase in the average IdM content was also found. Studies have shown that patients have a tendency to increase the content of IgE immunoglobulin. The level of other immunological parameters corresponded to the standard values (Table 1).

Dopamine is a monoamine neurotransmitter produced by the synapses of neurons in the brain, which functions

as a chemical mediator and transmits nerve signals between neurons, as well as between the brain and various organs. Dopamine synthesis is also carried out in the adrenal glands, kidneys and intestines. It has been established that approximately 90% of the dopamine circulating in the blood is produced in the intestine [18, 19]. In the context of the functioning of the gastrointestinal tract, dopamine acts as a vasodilator, contributing to the expansion of blood vessels and increased blood flow in the mesenteric region. At the same time, there is a decrease in peristaltic activity. This secretion helps to reduce intestinal motility, as well as modify absorption processes while increasing mucus production. These processes are usually accompanied by an increase in the concentration of specific proteins in the blood serum. Dopamine performs important functions in the body, acting as a hormone. Its effects include: cardiovascular, gastrointestinal and renal. Cardiovascular: increased blood pressure, increased heart rate and strength. Gastrointestinal: relaxation of the smooth muscles of the gastrointestinal tract. Renal: stimulation of fluid filtration in the kidneys, increased blood flow in them, accelerated excretion of sodium in the urine. The effect of dopamine is diverse and depends on its concentration and localization of effects on cells of specific tissues.

Research by scientists shows that residents of the northern regions have elevated levels of the neurotransmitter dopamine [6, 7]. This feature is presumably an adaptive reaction of the body to extreme living conditions at low temperatures. The study examined the effect of catecholamines on the immune status of practically healthy people living in the northern regions. The results showed a statistically significant increase in dopamine levels in a significant part of the examined group [12]. Researchers have established a relationship between the concentration of dopamine and the activity of the thyroid gland in residents of the northern regions. It was found that men have the highest concentration of dopamine. At the same time, women living in the European North are characterized by low levels of this neurotransmitter [13]. This fact deserves close attention and may become a starting point for an in-depth study of the role of dopamine in the functioning of other organs and systems in the inhabitants of the North. Researchers from the laboratories of the Institute of Physiology of Natural Adaptations have also shown that the level of dopamine in the peripheral venous blood of residents of the North is usually elevated. At the same time, there is a seasonal variation: dopamine concentration peaks during the polar day and decreases during the winter months [11].

Class M immunoglobulins (IgM) play a key role in the primary immune response to the appearance of antigens. Their production starts immediately after the antigen enters the body and is identified by the immune system. In blood serum, IgMs have the ability to agglutinate bacteria, neutralize viruses, and activate the complement system. They also ensure the elimination of pathogens from the bloodstream and stimulate the phagocytic activity of cells of the immune system.

Immunoglobulin E (IgE), found in human blood serum, belongs to the class of gamma globulins and is produced by B lymphocytes. Immunoglobulin E (IgE) plays an important role not only in the presentation of antigens, but can also directly affect the maturation of dendritic cells and promote the activation of specific T-lymphocyte proliferation [17]. Their main purpose is to participate in immediate reactions (reagin reactions) and to protect the body from parasitic infections.

Abnormally high concentrations of IdM and elevated concentrations of IgG were detected. Residents of the northern territories demonstrate elevated levels of immunoglobulins [4]. There was also a slight increase in the concentrations of cells capable of proliferation (CD10+). Elevated concentrations of catecholamines in practically healthy people have not

Table 1

Average content of catecholamines and immunological parameters in peripheral venous blood of healthy individuals in the northern territories of the Russian Federation, (M±m)

Investigated parameters	The average content in practically healthy people, n=75, (M±m)	Physiological limits
Dopamine, pg/ml	33.7±3.56	>30 пг/мл
Norepinephrine, pg/ml	391.03±23.82	100-600
Adrenaline, pg/ml	58.94±2.56	<125
Cells capable of proliferation (CD10+), ×109 cells/l	0.47±0.11	0.2-1.5
Cells labeled for death (CD95+), ×109 cells/l	0.52±0.02	0.2-1.5
Immunoglobulin A (IdA), g/l	1.65±0.23	1.2-5.4
Immunoglobulin M (IdM), g/l	1.83±0.04	0.7-1.8
Immunoglobulin G (IgG), g/l	18.35±0.47	7-24
Immunoglobulin E (IgE), units/ml	74.3±8.16	<100

Table 2

Frequency of registration of elevated concentrations of catecholamines and immunological parameters in peripheral venous blood in healthy individuals in the northern territories of the Russian Federation, %

Investigated parameters	Frequency of registration of elevated concentrations in practically healthy people, n=75, %	Physiological limits
Dopamine, pg/ml	7.81±0.43	>30 пг/мл
Norepinephrine, pg/ml	4.76±0.08	100-600
Adrenaline, pg/ml	3.08±0.27	<125
Cells capable of proliferation (CD10+), ×109 cells/l	1.7±0.22	0.2-1.5
Cells labeled for death (CD95+), ×109 cells/l	-	0.2-1.5
Immunoglobulin A (IdA), g/l	2.94±0.5	1.2-5.4
Immunoglobulin M (IdM), g/l	36.84±3.18	0.7-1.8
Immunoglobulin G (IgG), g/l	25.0±2.49	7-24
Immunoglobulin E (IgE), units/ml	28.0±0.7	<100

been established. The remaining immunological parameters did not exceed the values considered physiologically normal (Table 2).

Cells capable of proliferation (CD10+) characterize a population of mature neutrophils capable of suppressing the T-cell immune response. In addition, CD10+ receptor expression is detected on the surface of immature B-lymphocytes during their differentiation. During blast transformation, these immature B lymphocytes are transformed into plasma cells, which are responsible for the synthesis of various immunoglobulins and support T-helper and macrophage activity in triggering and coordinating an adaptive immune response. The presence of an increased level of lymphocytes carrying the CD10+ marker indicates a possible activation of the immune response, characterized by pronounced lymphoproliferation.

The functioning of immunity in the population of the northern regions is influenced by numerous factors related to the category of climatic, ecological, and socio-economic conditions [5, 16]. In the harsh climatic conditions of the North, there is an increase in the production of antibodies, including autoantibodies. This phenomenon is associated with the effectiveness of the body's adaptation to adverse environmental conditions. In the harsh conditions of the northern climate, the range of antigenic structures of the body expands. Adverse weather conditions contribute to an increase in the concentration of metabolic products of tissues with autoantigenic properties. This, in turn, leads to increased production of autoantibodies. Living in the northern regions leads to significant changes in the functioning of humoral immunity, which, in turn, can contribute to an increase in the level of class M immunoglobulins (IgM) in the body. In the unfavorable conditions of the northern climate, there is an increase in the antigenic load on the body. This leads to a significant increase in the diversity of antigenic structures, including those that are difficult to identify [10]. An increase in the level of IgG immunoglobulin in the population of the northern territories may also be due to the influence of adverse meteorological factors. The increased level of immunoglobulin IgE in the population of the northern regions may be associated with the negative effects of climatic factors, including a cold climate characterized by low temperatures, a lack of sunlight and various diseases of allergic and non-allergic etiology. Cells capable of proliferation (CD10+) have a noticeable tendency to increase in the inhabitants of the northern territories. This correlation is due to the influence of unfavorable climatic and geographical factors, as well as a number of other circumstances that affect the characteristics of the body's immune responses. Disorders of the immune system in the population living in the northern regions may be associated with exposure to ionizing radiation. It can cause increased cell proliferation, which can negatively affect the functioning of the immune system [9].

Conclusion. In the course of a study devoted to the study of the immune system of healthy individuals in the European North of the Russian Federation, characteristic features were identified. Healthy Northerners are characterized by the activation of the humoral link of immunity, manifested by a high concentration of IgM, increased IgE, as well as signs of autosensitization with high levels of autoantibodies. An increase in the average dopamine content and a slight increase in the average IdM content was found, which amounted to 33.7±3.56 and 1.83±0.04, respectively. Studies have shown that healthy people tend to increase the average content of immunoglobulin IgE (74.3±8.16). In addition, abnormally high concentrations of IdM (36.84±3.18%) and elevated concentrations of IgG (25.0±2.49%) were detected. There was also a slight increase in the concentrations of cells capable of proliferation (CD10+), which amounted to 1.7±0.22%. Elevated concentrations of catecholamines in healthy Northerners have not been established. Concentrations of dopamine were 7.81±0.43%, norepinephrine 4.76±0.08% and adrenaline 3.08±0.27%. The remaining immunological parameters did not exceed the values considered physiologically normal. Thus, it was found that healthy individuals in the European North of the Russian Federation experience changes in the content of catecholamines and immunological parameters in peripheral venous blood. These changes correlate with the impact of negative climatic factors. Such factors include violation of the light regime and low temperatures, which provoke a chronic state of stress in the body and, as a result, increased stress on the immune system. This phenomenon leads to a malfunction of the immune system and accelerated physiological wear of the body, which can become a predisposing factor for the development of various diseases.

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SCIENTIFIC REVIEWS

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ANALYSIS OF RISK FACTORS FOR ANASTOMOTIC LEAKAGE IN PATIENTS AFTER SURGICAL TREATMENT OF COLORECTAL CANCER: A SYSTEMATIC LITERATURE REVIEW

This systematic literature review analyzes the risk factors for anastomotic leakage (AL) in the surgical treatment of colorectal cancer. Based on 42 studies, key risk predictors for AL were identified. The incidence of AL in the studies included in this review ranged from 2,8% to 24,7%. The introduction of the RALAR scale significantly improved the objective assessment of AL risk. A comprehensive approach to prevention, based on risk stratification and treatment personalization, can significantly improve the outcomes of surgical treatment for colorectal cancer.

Keywords: colorectal cancer, anastomotic leakage, risk factors, systematic review, PRISMA

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Introduction. Colorectal cancer (CRC) ranks among the leading oncological diseases in terms of both incidence and mortality [18, 36]. According to the World Health Organization, CRC is the third most common malignant neoplasm worldwide [95]. In 2022, more than 1.9 million new cases of CRC were reported, along with approximately 903,000 deaths related to the disease [36]. In the Russian Federation, CRC also holds a leading position in the structure of oncological morbidity, with a rising trend in the number of patients affected by this pathology, potentially reaching 2.2 million cases by 2030 [2, 3].

Surgical intervention remains the primary treatment for CRC, where anastomosis formation is a key stage determining functional outcomes and patients' quality of life [4, 84]. Anastomotic leakage (AL), occurring in 2–19% of cases, continues to be a serious complication [79, 96].

The International Study Group on Rectal Cancer defines AL as a defect in the integrity of the intestinal wall at the anastomotic site [24]. This complication is associated with high morbidity (20–30%), mortality (up to 22%), prolonged hospitalization, increased risk of recurrence, reduced survival rates, and diminished quality of life [59, 89, 90].

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