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BIOMARKERS OF SYSTEMIC INFLAMMATION AS EVALUATION CRITERIA FOR THE BODY'S ADAPTIVE CAPABILITIES UNDER WHOLE-BODY COLD EXPOSURE

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Introduction. The complex of unfavorable natural and climatic factors in the North, creating a stressful living environment, induces a pronounced tension in the immune responses that maintain homeostasis. Determining the type of adaptation reaction and the level of reactivity makes it possible to diagnose the functional state of the body and predict its response patterns to environmental factors.
Objective. Determination of systemic inflammation biomarker levels, calculated based on complete blood count data, for assessing the stress and failure of the adaptation process.
Materials and methods. The study examined 178 practically healthy volunteers (136 women and 42 men; mean age 31.17 ± 0.85 years). The assessment of the body's adaptation state was carried out by analyzing leukograms. The types of non-specific adaptation reactions, levels of body reactivity, and adaptation state were determined according to Garkavi's method. According to this method, all subjects were divided into the following groups: "physiological norm" (group 1) — 68 women and 23 men, mean age 31.59 ± 1.29 years; "adaptation stress" (group 2) — 50 women and 10 men, mean age 31.21 ± 1.15 years; "adaptation failure" (group 3) — 18 women and 9 men, mean age 28.17 ± 2.51 years. General short-term cold exposure was modeled once in a climatic chamber (USHZ-25N, Russia), in which the subjects, dressed in cotton clothing, remained under continuous video observation for 5 min at an ambient air temperature of –25 °C. Hematological studies were performed using an XS-500i analyzer. The content of catecholamines, cortisol, PPARγC1α, HIF-1α, SIRT3, and BPI was determined by ELISA. Lymphocyte apoptosis and necrosis were assessed by double staining with Annexin V and propidium iodide (AnV/PI). The quantitative content of ATP was determined using the luciferin-luciferase method. The following systemic inflammation indices were calculated: systemic immune-inflammation index (SII), systemic inflammation response index (SIRI), and aggregate index of systemic inflammation (AISI). The results were processed using StatTech v.4.9.2 and Statistica 6.0 software.
Results. In the "physiological norm" group, an increase in leukocyte counts, enhanced cell migration activity, and improved mitochondrial energy supply for their functional activity indicated high non-specific resistance and the absence of a stress effect from this type of cold exposure. Under "adaptation stress", the fastest cardiovascular responses aimed at maintaining temperature homeostasis were recorded, accompanied by increased catecholamine levels, enhanced leukocyte recirculation and migration, allowing the body to respond rapidly to short-term stress factors. In the "adaptation failure" group, the baseline tension in the activity of regulatory systems, even after a single short-term cold exposure, did not lead to the activation of effective thermoregulation mechanisms; leukocyte migration activity was slowed, significantly increasing the risk of maladaptive and pro-inflammatory reactions. It was established that SIRI, SII, and AISI are significant risk criteria for adaptation strain at SIRI ≥ 0.97, SII ≥ 447.43, AISI ≥ 216.24, and for adaptation failure at index values of ≥1.23, ≥449.76, and ≥239.58, respectively.
Conclusions. "Adaptation stress" and "adaptation failure" are characterized by changes in cellular and humoral parameters of peripheral blood even before the clinical manifestation of the disease, and these changes may be exacerbated by additional exposure to negative factors, even if their impact is short-term. Baseline systemic inflammation indices (SIRI, SII, AISI) are significant predictors for assessing both "adaptation stress" and "adaptation failure". The use of these indices, calculated from complete blood count results, will make it possible to assess the presence of an initial imbalance in the body's adaptation mechanisms, which may subsequently be aggravated by exposure to stress factors.

Keywords: stress; adaptation; non-specific resistance; reactivity; whole-body cold exposure; biomarkers; systemic inflammation response index, SIRI; systemic immune-inflammation index, SII; aggregate index of systemic inflammation, AISI

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БИОМАРКЕРЫ СИСТЕМНОГО ВОСПАЛЕНИЯ КАК КРИТЕРИИ ОЦЕНКИ АДАПТАЦИОННЫХ ВОЗМОЖНОСТЕЙ ОРГАНИЗМА ПРИ ОБЩЕМ ХОЛОДОВОМ ВОЗДЕЙСТВИИ

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Введение. Комплекс неблагоприятных природно-климатических факторов на Севере, создавая дискомфортную среду обитания, формирует выраженное напряжение иммунных реакций, обеспечивающих гомеостаз. Определение типа адаптационной реакции и уровня реактивности позволяет диагностировать функциональное состояние организма и прогнозировать варианты реагирования на факторы окружающей среды.

Цель. Определение уровней биомаркеров общего воспаления, рассчитываемых на основе данных общего анализа крови, для оценки напряжения и срыва процесса адаптации.

Материалы и методы. Обследовано 178 практически здоровых добровольцев (136 женщин и 42 мужчины; средний возраст 31,17 ± 0,85 года). Оценка состояния адаптации организма проведена при анализе лейкограмм. Типы неспецифических адаптационных реакций организма, уровни реактивности организма, состояние адаптации определяли по методике Л.Х. Гаркави. В соответствии с ней все испытуемые были разделены на группы: «физиологическая норма» (группа 1) — 68 женщин и 23 мужчины, средний возраст 31,59 ± 1,29 года; «напряжение механизмов адаптации» (группа 2) — 50 женщин и 10 мужчин, средний возраст 31,21 ± 1,15 года; «срыв процесса адаптации» (группа 3) — 18 женщин и 9 мужчин, средний возраст 28,17 ± 2,51 года. Моделирование общего кратковременного охлаждения проведено однократно в климатической камере (УШЗ-25Н, Россия), в которой испытуемые находились в хлопковой одежде под постоянным видеонаблюдением в течение 5 мин при температуре атмосферного воздуха –25 °С. Гематологические исследования выполнены на анализаторе XS-500i. Методом ИФА определено содержание катехоламинов, кортизола, PPARγC1α, HIF-1α, SIRT3, BPI. Апоптоз и некроз лимфоцитов определяли методом двойного окрашивания AnV/PI. Количественное содержание АТФ определяли при помощи люциферин-люциферазного метода. Рассчитаны индексы системного воспаления: SIRI, SII, AISI. Результаты исследования обработаны с использованием StatTech v.4.9.2, Statistica 6.0.

Результаты. В группе «физиологическая норма» повышение числа лейкоцитов, усиление миграционной активности клеток и митохондриального энергообеспечения их функциональной активности свидетельствовало о высокой неспецифической резистентности и отсутствии стрессового влияния данного варианта холодового воздействия. При «напряжении механизмов адаптации» регистрировали наиболее быстрые реакции со стороны сердечно-сосудистой системы, направленные на сохранение температурного гомеостаза, с повышением уровней катехоламинов, усилением рециркуляции и миграции лейкоцитов, что позволяло организму быстро реагировать на кратковременное влияние стрессовых факторов. При «срыве процесса адаптации» фоновое напряжение активности регуляторных систем даже при однократном кратковременном охлаждении не приводило к включению механизмов эффективной терморегуляции, при этом миграционная активность лейкоцитов была замедлена, что значительно повышало риск дезадаптационных и провоспалительных реакций. Установлено, что SIRI, SII, AISI являются значимыми критериями риска напряжения адаптации при уровне SIRI ≥ 0,97, SII ≥ 447,43, AISI ≥ 216,24 и ее срыва при значениях индексов ≥ 1,23, ≥ 449,76, ≥ 239,58 соответственно.

Выводы. «Напряжение механизмов адаптации» и «срыв процесса адаптации» характеризуются изменением клеточных и гуморальных показателей периферической крови еще до клинического проявления заболевания и могут усиливаться при дополнительном воздействии негативных факторов, даже если их влияние кратковременно. Фоновые индексы общего воспаления SII, SIRI, AISI являются значимыми предикторами при оценке «напряжения механизмов адаптации» и «срыва процесса адаптации». Использование данных индексов, рассчитываемых по результатам общего анализа крови, позволит оценивать наличие исходного дисбаланса в механизмах адаптации организма, которые могут в дальнейшем усилиться при воздействии стрессовых факторов.

Ключевые слова: напряжение; адаптация; неспецифическая резистентность; реактивность; общее охлаждение; биомаркеры; индекс системного воспалительного ответа; индекс системного воспаления; совокупный индекс системного воспаления

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INTRODUCTION

The complex of unfavorable natural and climatic factors in the North, by creating a stressful living environment, induces a pronounced tension in the immune responses that maintain homeostasis. In the Far North, the strain of adaptation mechanisms (adaptation stress) begins to manifest as early as childhood and is characterized by prolonged activation of the humoral component, including activation of the reaginic defense mechanism with elevated IgE levels [1].

The combination of anthropogenic load and the discomfort of climatic living conditions contribute to an exacerbation of the imbalance in immune mechanisms, leading to the formation of specific variations of secondary immunodeficiencies. Stress is a general adaptation syndrome and represents a set of non-specific reactions of the body during which energy and plastic resources are mobilized for the specific reconfiguration of various adaptive systems. In response to an exogenous or endogenous stress factor, anti-stress reactions involving immune and endocrine adaptation pathways are triggered in the body.

According to the theory of non-specific adaptation reactions by Garkavi, one can distinguish calm activation reactions, heightened activation reactions, training reactions, and stress reactions, each characterized by a specific ratio of leukocytes in the peripheral blood [2]. Non-specific adaptation reactions can have different levels of reactivity (high, medium, low, and very low) corresponding to the degree of adaptation tension, which is determined by the maximum and minimum ranges of deviation in the cellular components of the leukocyte formula. Determining the type of reaction and the level of reactivity makes it possible to diagnose the functional state of the body and predict its response patterns to environmental factors. This approach to assessing non-specific resistance is simple and informative, enabling its use in studying the health structure of populations, evaluating stress levels and the recovery process, as well as the effectiveness of treatment during rehabilitation [3–6].

In assessing the state of health, in addition to "a state of complete physical, mental, and social well-being," one of the important aspects is the ability to adapt to changing environmental conditions and to maintain the functional activity of regulatory systems for a long time without disrupting compensatory-adaptive reactions or developing disease and pathological conditions.

The body's adaptive capacity can be regarded as an integral indicator of health. Changes in the cellular composition of the blood in response to both external and internal factors are not visually apparent, but their deviation from the norm leads to the formation of maladaptive reactions. When assessing the intensity of inflammation in patients with various diseases, as well as for predicting treatment outcomes and disease progression, inflammation indices calculated from complete blood count data are used: the systemic inflammation response index (SIRI), the systemic immune-inflammation index (SII), and the aggregate index of systemic inflammation (AISI). These are easy-to-determine, cost-effective clinical markers that provide valuable prognostic and diagnostic information, offering a holistic view of inflammatory processes throughout the body.

Elevated levels of systemic inflammation markers are associated with the risk of complications from COVID-19, atherosclerosis, hypertension, type 2 diabetes mellitus, and other diseases [7–15]. It is of interest to study the baseline levels of systemic inflammation markers in practically healthy individuals permanently residing in northern territories, which could serve as reliable predictors of the development of adaptation stress and adaptation failure, including during short-term single exposure to a stress factor.

Aim — to determine the levels of systemic inflammation biomarkers calculated from complete blood count data for the assessment of adaptation stress and adaptation failure.

MATERIALS AND METHODS

A total of 178 practically healthy volunteers were examined, including 42 men and 136 women; mean age 31.17 ± 0.85 years. All subjects were born and permanently resided in the North of the European part of Russia. Throughout the study, the participants had no acute diseases or exacerbations of chronic diseases, and had not previously engaged in nor were currently undergoing cold hardening procedures. The study was conducted in the morning from 8:00 to 10:00, strictly on an empty stomach.

Short-term whole-body cold exposure was simulated once in a climatic chamber (USHZ-25N, Russia), in which the subjects, dressed in cotton clothing, remained under continuous video observation for 5 min at an ambient air temperature of -25 °C.

Before and immediately after general cooling, three-fold measurements of forehead skin temperature were taken (GP-300 non-contact infrared medical thermometer, China). Changes in systemic hemodynamics were assessed using blood pressure (systolic blood pressure — SBP; diastolic blood pressure — DBP) and heart rate measurements (Omron M3 Expert tonometer, China).

Blood collection was performed by qualified personnel from the cubital vein into Vacuette vacuum tubes with EDTA to obtain plasma and for hematological studies, and into tubes with a clotting activator to obtain serum. Serum and plasma were separated by centrifugation. The samples were frozen once at -20 °C.

To determine the type of adaptation reaction (stress, training, calm activation, heightened activation, overactivation) and the degree of adaptation tension (grades 0, I, II, III, IV) according to Garkavi's method and in accordance with the "Screening methods for assessing body adaptation in outpatient practice", a leukogram analysis of the subjects was performed[1]. First, based on the relative lymphocyte count, the type of non-specific adaptation reaction was determined: "stress" — lymphocyte count <20%; "training reaction" (TR) — 20–27.5%; "calm activation" (CAR) — 28–34%; "heightened activation" (HAR) — 34.5–44%; "overactivation" — >40–44%.

[1] Khursa RV, Eryomina NM, Korzun NN. Screening methods for assessing body adaptation in outpatient practice: educational and methodological manual. Minsk: BSMU; 2018.

Based on the calculated proportions of monocytes, eosinophils, basophils, band neutrophils, and the total leukocyte count, taking into account deviations of the parameters within the lower or upper half of the reference range, the levels of body reactivity (high, medium, low, and very low) were determined. When assessing the adaptation state, the following categories were distinguished: "physiological norm", "adaptation stress", and "adaptation failure". For this purpose, for each type of adaptation reaction, the number of individuals with different body reactivity levels was determined. For the CAR and HAR types with high or medium reactivity, as well as for the TR type with high reactivity, the adaptation state was assessed as "physiological norm". For the HAR and CAR types with low reactivity, the TR type with medium reactivity, and the stress type with high reactivity, the adaptation state was assessed as "adaptation stress". For the stress type with medium or low reactivity, the overactivation type with low reactivity, and all reactions with very low reactivity, the adaptation state was assessed as "adaptation failure".

According to the type of adaptation reaction and the degree of adaptation tension, the subjects were divided into the following groups: "physiological norm" (group 1) — 68 (74.73%) women and 23 (25.27%) men, mean age 31.59 ± 1.29 years; "adaptation stress" (group 2) — 50 (83.33%) women and 10 (16.67%) men, mean age 31.21 ± 1.15 years; "adaptation failure" (group 3) — 18 (66.66%) women and 9 (33.33%) men, mean age 28.17 ± 2.51 years.

Hematological studies were performed on an XS-500i hematology analyzer (Sysmex, Japan). In blood smears stained according to Romanowsky–Giemsa, a lymphocytogram was examined under a Vision Hema microscope (West Medica, Austria) at immersion magnification ×40 using the Kassirsky method. [16], determining the content of large (>12 μm), medium (8–12 μm), and small (<8 μm) lymphocytes.

The following parameters were determined by enzyme-linked immunosorbent assay: adrenaline (IBL, Germany), noradrenaline (IBL, Germany), cortisol (DBC, Canada), and bactericidal/permeability-increasing protein (BPI) (Hycult Biotech, Netherlands). In lymphocyte lysates, the concentrations of hypoxia-inducible factor 1-alpha (HIF-1α) (Cloud-Clone Corp., USA), sirtuin 3 (SIRT3) (RayBiotech, USA), and peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PPARγC1α) (Cloud-Clone Corp., USA) were determined. Results were evaluated using a Multiscan FC plate reader (Thermo Scientific, USA).

The quantitative ATP content was determined in 100 μl of a lymphocyte suspension at a concentration of 10^6 cells per μmol using the luciferin-luciferase method. The reaction results were assessed using a LUM-1 luminometer (Lumtek, Russia) with standard Lumtek reagent kits.

The phagocytic activity of neutrophils was determined using a 1% suspension of latex particles 1.5 μm in size (Diaem, Russia). For this purpose, 100 μl of a latex suspension for phagocytosis was added to 100 μl of peripheral blood, and the mixture was incubated in a thermostat at 37 °C for 30 min. Blood smears were fixed according to May–Grünwald and stained according to Romanowsky–Giemsa. Phagocytic activity was assessed under a microscope at ×1000 magnification (per 100 cells). The percentage of neutrophils that had phagocytosed particles and the average number of phagocytosed latex particles per cell were counted.

The level of lymphocyte apoptosis and necrosis was determined using an Epics XL flow cytofluorimeter (Beckman Coulter, USA) by double staining with annexin V (AnV) and propidium iodide (PI), analyzing at least 5,000 cells. The results were evaluated based on cell staining patterns: live cells — AnV^-/PI^-; early apoptosis — AnV^+/PI^-; late apoptosis — AnV^+/PI^+; and necrosis — AnV^-/PI^+.

The following systemic inflammation indices were calculated [17–19]:

- systemic inflammation index (SII) = neutrophil count × platelet count / lymphocyte count;
- systemic inflammation response index (SIRI) = neutrophil count × monocyte count / lymphocyte count;
- aggregate inflammation systemic index (AISI) = neutrophil count × monocyte count × platelet count / lymphocyte count.

The study results were processed using the StatTech v. 4.9.2 software package (Stattech, Russia) and Statistica 6.0 (StatSoft, USA). Quantitative parameters were assessed for normality of distribution using the Shapiro–Wilk test. Mean values (M) and standard deviations (SD) were determined. For distributions close to normal, the Student's t-test was used to compare results, with differences considered significant at $p < 0.05$. In the absence of a normal distribution, quantitative data were described using the median (M_e) and the lower and upper quartiles [Q_1; Q_3]. The statistical significance of differences was determined using the non-parametric Mann–Whitney U-test. Rates of increase and decrease were calculated to assess the dynamics of changes in parameter levels. ROC curve analysis was used to evaluate the discriminatory ability of quantitative features for predicting adaptation stress or adaptation failure. The cut-off value was determined by the maximum Youden index. Differences were considered statistically significant at $p < 0.05$.

RESULTS AND DISCUSSION

Initially, we determined the types of adaptation reaction and the degree of adaptation tension. Analysis of leukograms showed that 51.41% of the examined subjects corresponded to the "physiological norm" adaptation level, "adaptation stress" was identified in 33.80% of participants, and "adaptation failure" in 15.25%.

When studying the cardiovascular system's response to general cold exposure, a compensatory

vasoconstrictor reaction aimed at maintaining temperature homeostasis was observed, characterized by a statistically significant increase in blood pressure in two groups: in the "physiological norm" group — DBP from 76.35 ± 0.83 to 77.96 ± 0.97 mmHg and SBP from 122.68 ± 1.41 to 125.59 ± 1.37 mmHg; in the "adaptation stress" group — DBP from 76.05 ± 1.07 to 77.35 ± 1.24 mmHg and SBP from 122.27 ± 1.35 to 125.26 ± 1.45 mmHg. In the third group, "adaptation failure", no significant changes in blood pressure parameters were found.

A decrease in body temperature was observed in subjects across all study groups. Calculation of the rate of temperature decrease showed that the fastest change occurred in the "adaptation stress" group — 10.16%, while the smallest change was in the "adaptation failure" group — 5.74%. In the "physiological norm" group, the rate of temperature decrease was borderline, at 7.54%.

Thus, for the "physiological norm" group, this type of cold load was not stressful, and the range of adaptive reactions was small. In the "adaptation stress" group, the responses were more pronounced, while in the "adaptation failure" group, they were delayed.

The mean cortisol concentration in the peripheral blood of subjects in group 3 ("adaptation failure") was significantly higher and at the upper limit of the physiological norm — 526.75 ± 25.48 nmol/L (Fig. 1). In the "physiological norm" adaptation reaction (group 1) and "adaptation stress" (group 2), cortisol levels did not differ significantly and were significantly lower: 317.60 ± 35.39 and 314.26 ± 30.70 nmol/L, respectively.

Catecholamine levels in the study groups were within the physiological norm; however, in the "adaptation stress" group (subjects in group 2), the concentrations of adrenaline and noradrenaline were statistically significantly lower, which may indicate depletion of the neurotransmitter component under conditions of chronic stress (Fig. 2).

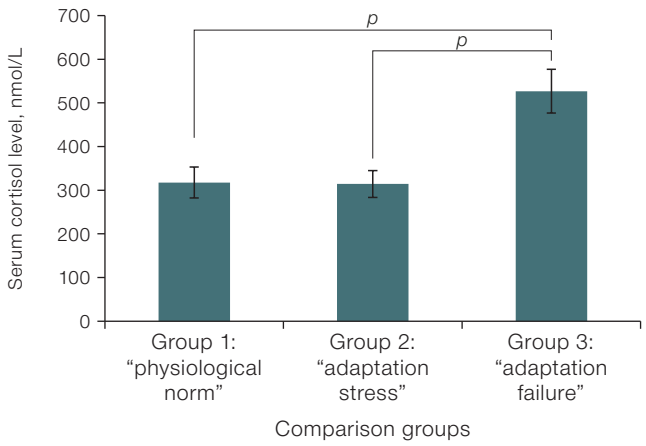

Figure prepared by the authors based on their own data

Fig. 1. Baseline serum cortisol level in the subjects before cold exposure

After short-term whole-body cold exposure, the ratio of cortisol levels in the study groups did not change significantly; however, in the "adaptation failure" group (subjects in group 3), the highest cortisol level was maintained — 415.93 ± 15.87 nmol/L; in group 2 with "adaptation stress" — 302.53 ± 28.53 nmol/L ($p < 0.001$); in participants from group 1 with the "physiological norm" adaptation type — 330.82 ± 35.78 nmol/L ($p < 0.001$).

During the study, changes in catecholamine levels in response to cold exposure were observed. In subjects with "adaptation stress" (group 2) and "adaptation failure" (group 3), the catecholamine response was characterized by increased levels of adrenaline (up to 45.70 ± 3.37 and 61.22 ± 10.25 pg/mL, respectively) and noradrenaline (up to 104.77 ± 9.05 and 152.48 ± 7.67 pg/mL, respectively). This may have contributed to the mobilization of adaptive systems and changes in hemodynamics aimed at maintaining homeostasis in response to external stimuli.

In the group of participants with the "physiological norm" adaptation type, a statistically significant increase in the total pool of circulating lymphocytes in the peripheral blood was observed in response to general cooling, from 1.78 [1.40; 2.09] to 1.82 [1.47; 2.23] × 10^9 cells/L ($p < 0.05$). Lymphocytes are characterized by high mitochondrial activity in terms of the intracellular concentration of PPARγC1α (peroxisome proliferator-activated receptor gamma coactivator 1-alpha), a key regulator controlling mitochondrial quantity and biogenesis, and the lowest HIF-1α/SIRT3 ratio. This manifested as an increase in intracellular ATP and a twofold increase in ATP levels after cooling, from 1.61 [0.57; 3.03] to 3.12 [1.48; 4.16] μmol/10^6 cells ($p < 0.01$) (Table 1). PPARγC1α is involved in antioxidant defense and regulates mitochondrial reactive oxygen species generation by increasing the expression of uncoupling proteins

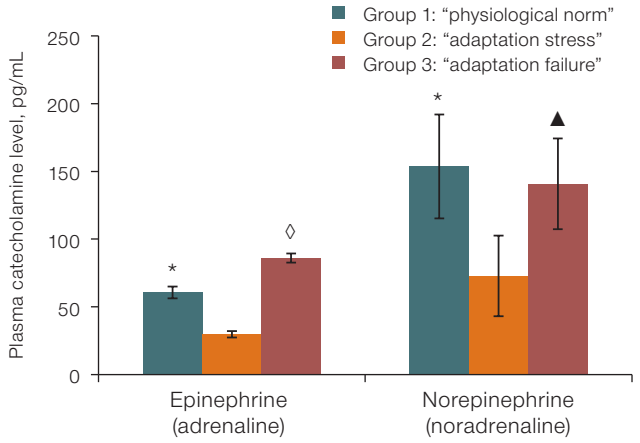

Figure prepared by the authors based on their own data

Fig. 2. Baseline plasma catecholamine level before whole-body cold exposure. * — $p < 0.01$ statistical significance of differences between groups 1 and 2; statistical significance of differences between groups 2 and 3; ▲ — $p < 0.01$; ◊ — $p < 0.001$

Table 1. Levels of intracellular markers associated with lymphocyte metabolic activity

Parameter	Comparison groups		
	Group 1: "physiological norm"	Group 2: "adaptation stress"	Group 3: "adaptation failure"
Peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PPARγC1α), 10^9 cells/L	1.08 ± 0.15	1.33 ± 0.41*	0.97 ± 0.13▪
Hypoxia-inducible factor 1-alpha (HIF-1α), 10^9 cells/L	1.86 ± 0.24	1.91 ± 0.10	1.18 ± 0.29◊
Sirtuin 3 (SIRT3), 10^9 cells/L	0.42 ± 0.07	0.31 ± 0.06	0.14 ± 0.02◊
Hif1α/SIRT3	4.42	6.16*	8.42◊

Table compiled by the authors based on their own data

Note. * — statistical significance of differences between groups 1 and 2 at the level of $p < 0.01$; ▪ — significance of differences between groups 1 and 3 at the level of $p < 0.05$, ◊ — $p < 0.01$; data are presented as mean value and standard deviation ($M \pm SD$).

UCP2 and UCP3, thereby participating in thermoregulation processes [20–22]. An increase in antioxidant defense is a necessary factor in the formation of stable adaptation of the body to low-temperature exposure, including the protection of cell membranes from the formation of protein-lipid cross-links that increase their microviscosity, which reduces migratory activity and increases the likelihood of hypoxic and chronic infectious conditions.

In the second group of subjects with "adaptation stress", no changes in the content of circulating lymphocytes were recorded; their levels were 1.62 [1.26; 2.28] and 1.57 [1.26; 2.03] × 10^9 cells/L, respectively. At the same time, the intracellular ATP content decreased statistically significantly from 1.26 [0.21; 2.07] to 1.04 [0.55; 1.49] mmol/10^6 cells. However, this group was characterized by the highest concentration of PPARγC1α, indicating a switch to predominantly mitochondrial energy supply for the cells. Under stress (adaptation failure group), mitochondrial activity of cells was lower, with a shift in metabolic activity toward glycolysis and activation of hypoxia-inducible factor, accompanied by a decrease in lymphocyte levels from 1.67 [1.26; 2.17] to 1.43 [1.14; 2.12] × 10^9 cells/L ($p < 0.05$). The ATP level in circulating lymphocytes increased from 0.96 [0.53; 3.23] to 1.80 [0.66; 2.15] mmol/10^6 cells.

It was shown that after general cooling, in subjects of group 1 ("physiological norm") and group 2 ("adaptation stress"), an increase in the number of small lymphocytes was recorded in the lymphocytogram structure, with their growth rates being 4.80% and 20.91%, respectively (Fig. 3). In the "adaptation failure" group (group 3), the content of small lymphocytes did not change significantly. An increase in the number of circulating small lymphocytes is a positive adaptive response for maintaining homeostasis under low-temperature exposure, by enhancing tissue sanitation and subsequent antigen-stimulated differentiation and proliferation of cells in the lymph nodes [23].

The level of lymphocyte necrosis did not change under this type of cold exposure in subjects from all study groups (Fig. 4). In the first group of subjects with the "physiological norm" adaptation type, cold exposure did not significantly affect the number of lymphocytes

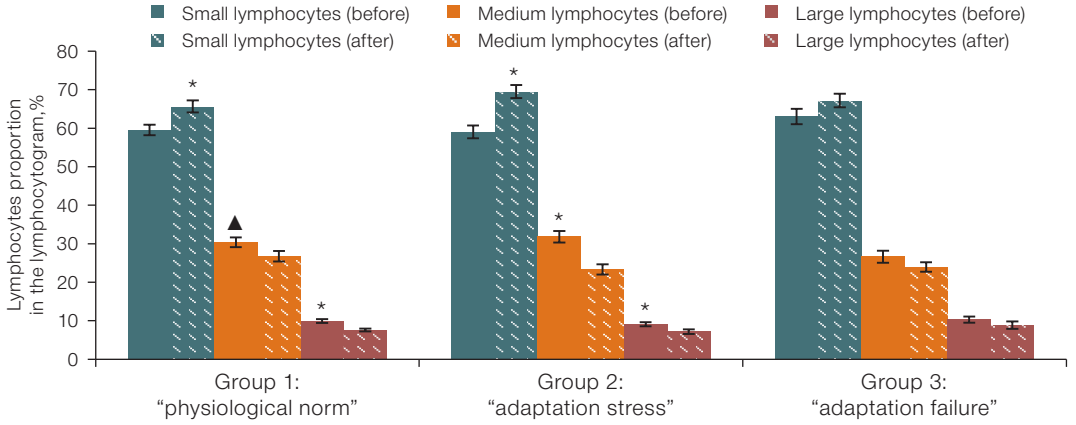

Figure prepared by the authors based on their own data

Fig. 3. Lymphocytogram structure: pre- and post-cold exposure in comparison groups. ▲ — significance of differences $p < 0.01$; * — significance of differences $p < 0.001$

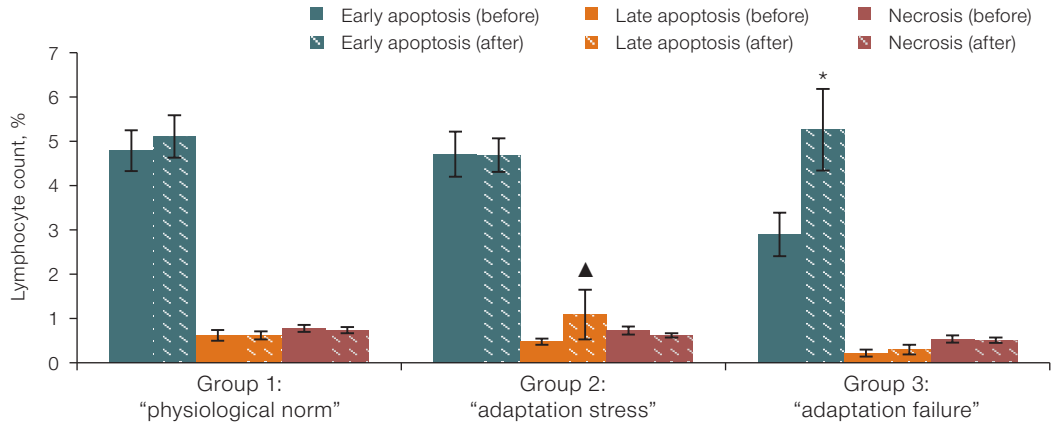

Figure prepared by the authors based on their own data

Fig. 4. Levels of lymphocyte necrosis and apoptosis in volunteers before and after whole-body cold exposure. ▲ — significance of differences $p < 0.01$; * — significance of differences $p < 0.001$

labeled for apoptosis, either early or late. In the "adaptation stress" group, the level of late apoptosis increased. In the "adaptation failure" group, the percentage of cells in early apoptosis significantly increased. Apoptosis, as a form of cell death, regulates cellular homeostasis and the processes of physiological cell regeneration; it can be initiated by both internal and external factors of the extracellular microenvironment, such as hypoxia, ischemia/reperfusion, exposure to physical and chemical agents, disruption of cell cycle signaling, and others [24]. Some studies have shown that apoptosis can be reversible, and cell survival or death depends on the balance of pro-apoptotic and anti-apoptotic stimuli [25–27]. The cancellation of apoptosis is associated with cell survival, differentiation, and proliferation, which, on the one hand, serves as a mechanism of recovery, but is also a risk factor for increased cell mutagenesis in response to external stimuli.

In subjects of group 1 with the "physiological norm" adaptation type, an increase in neutrophil release from the depot and an expansion of the circulating neutrophil pool, as well as migration into tissues with a more intensive rate of increase in the capillary blood count, were recorded in response to general cooling (Table 2). In all groups, no changes were observed in the activity of phagocytic reactions or in the level of BPI.

Table 2. Parameters of neutrophil phagocytic activity in subjects before and after whole-body cold exposure

Parameter	Comparison groups					
	Group 1: "physiological norm"		Group 2: "adaptation stress"		Group 3: "adaptation failure"	
	cold exposure		cold exposure		cold exposure	
	before	after	before	after	before	after
Percentage of active phagocytes, %	70.00 [60.00; 81.00]	69.50 [60.00; 83.00]	73.50 [59.00; 92.00]	74.00 [65.00; 87.00]	70.00 [60.00; 85.00]	73.00 [52.00; 86.00]
Phagocytic intensity, particles/cell	4.70 [3.47; 5.90]	4.55 [3.56; 6.90]	5.00 [3.64; 6.90]	4.90 [4.00; 6.87]	5.90 [4.50; 9.20]	6.09 [4.95; 9.40]
Bactericidal/permeability-increasing protein (BPI), pg/mL	0.46 [0.33; 0.55]	0.40 [0.36; 0.53]	0.38 [0.32; 0.51]	0.38 [0.34; 0.52]	0.32 [0.23; 0.48]	0.40 [0.36; 0.53]
Venous blood neutrophils, $\times 10^9$ cells/L	2.84 [2.32; 3.22]	3.06 [2.52; 3.67]*	2.58 [2.15; 3.67]	2.93 [2.15; 3.90]	4.66 [3.19; 6.39]	5.17 [3.58; 6.43]
Capillary blood neutrophils, $\times 10^9$ cells/L	2.82 [2.18; 3.22]	3.22 [2.60; 3.97]▲	3.10 [2.23; 3.87]	3.50 [2.40; 4.15]	3.62 [2.80; 5.47]	4.84 [3.65; 6.98]

Table compiled by the authors based on their own data

Note. Data are presented as the median and interquartile range M_e [Q_1; Q_3]; * — significance of differences $p < 0.05$; ▲ — significance of differences $p < 0.001$.

It was found that in subjects from all observation groups, monocyte levels were higher in capillary blood. After cold exposure in the "physiological norm" group, the number of monocytes increased in both venous and capillary blood, indicating stimulation of cell release from the depot and activation of their migration into tissues. In subjects with "adaptation stress," a significant increase in monocytes was recorded in capillary blood, increasing the likelihood of their further migration into tissues. In group 3 ("adaptation failure"), monocyte migration through small vessels was slowed, against the background of a significant increase in their level in peripheral blood, which may indicate increased activity of inflammatory reactions (Table 3).

The different baseline state of the body under a single short-term general cold exposure is characterized by the formation of distinct adaptive adjustments. In subjects with the "physiological norm" adaptation type (group 1), the increase in leukocyte count, enhanced cell migration activity, and improved mitochondrial energy supply for their functional activity indicated high non-specific resistance and the absence of a stress effect from this factor. In the "adaptation stress" group (group 2), the fastest responses were recorded from the cardiovascular system, aimed at maintaining temperature homeostasis, with increased catecholamine levels and enhanced leukocyte recirculation and migration. Thus, the baseline state of "adaptation stress" allows for rapid responses to short-term stress challenges. In the "adaptation failure" group (group 3), the baseline tension in the activity of regulatory systems, even under a single short-term cold exposure, did not lead to the activation of effective thermoregulation mechanisms, while leukocyte migration activity was slowed, significantly increasing the risk of maladaptive and pro-inflammatory reactions.

It is of interest to identify effective markers (systemic inflammation indices) for assessing the baseline state of the body evaluated as "adaptation stress" and "adaptation failure".

The mean values of the SIRI, SII, and AISI indices are presented in Table 4. It was found that their levels in "adaptation stress" and "adaptation failure" were statistically significantly higher than in the "physiological norm".

Table 3. Monocyte levels in peripheral venous and capillary blood of subjects before and after whole-body cold exposure

Parameter	Comparison groups					
	Group 1: "physiological norm"		Group 2: "adaptation stress"		Group 3: "adaptation failure"	
	cold exposure		cold exposure		cold exposure	
	before	after	before	after	before	after
Venous blood monocytes, 10^9 cells/L	0.41 [0.30; 0.53]	0.51 [0.41; 0.59]▲	0.48 [0.37; 0.63]	0.52 [0.41; 0.67]	0.46 [0.26; 0.80]	0.68 [0.59; 0.86]*
Capillary blood monocytes, 10^9 cells/L	0.46 [0.32; 0.59]	0.56 [0.45; 0.70]▲	0.51 [0.40; 0.60]	0.61 [0.49; 0.49]*	0.64 [0.46; 0.91]	0.71 [0.50; 0.93]

Table compiled by the authors based on their own data

Note. Data are presented as the median and interquartile range M_e [Q_1; Q_3]; * — significance of differences $p < 0.05$; ▲ — significance of differences $p < 0.001$.

Table 4. Systemic inflammation indices across the study groups

Index	Study groups		
	Group 1: "physiological norm"	Group 2: "adaptation stress"	Group 3: "adaptation failure"
SIRI	0.72 [0.58; 0.88]▲	0.94 [0.46; 1.15]	1.94 [1.35; 2.44]▪
SII	324.56 [272.68; 423.26]◊	477.83 [407.80; 558.26]	549.05 [491.36; 659.44]♦
AISI	156.14 [116.67; 207.99]*	198.74 [118.10; 305.62]	335.69 [288.63; 566.38]▪

Table compiled by the authors based on their own data

Note. Data are presented as median and interquartile range M_e [Q_1; Q_3]; significance of differences between groups 1 and 2 * — $p < 0.05$, ▲ — $p < 0.01$, ◊ — $p < 0.001$. Significance of differences between groups 2 and 3. ♦ — $p < 0.05$, ▪ — $p < 0.001$.

Table 5. ROC analysis results

Index	Cut-off value of the index for adaptation stress	AUC	95% CI (confidence interval)	Cut-off value of the index for adaptation failure	AUC	95% CI (confidence interval)
SIRI	0.966	0.6330	0.526–0.740*	1.231	0.930	0.830–1.000■
SII	447.427	0.816	0.718–0.915■	449.761	0.719	0.537–0.901*
AISI	216.240	0.826	0.680–0.913■	239.580	0.626	0.517–0.735*

Table compiled by the authors based on their own data

Note. SIRI — systemic inflammation response index; SII — systemic immune-inflammation index; AISI — aggregate index of systemic inflammation; AUC — area under the curve; significance of differences * — $p < 0.05$, ■ — $p < 0.001$.

To assess the discriminatory ability of the inflammation indices in predicting a specific outcome — either "adaptation stress" or "adaptation failure" — the ROC curve analysis method was applied, and the cut-off values of the studied parameters were calculated (Table 5).

It was found that the systemic inflammation indices are statistically significant predictors for forecasting adaptation stress. The cut-off values (corresponding to the highest Youden index) were: for SIRI — 0.966, for SII — 447.427, and for AISI — 216.24. Adaptation stress was predicted when the index values were equal to or above these thresholds (Fig. 5).

When assessing the discriminatory ability for the "adaptation failure" state using SIRI, SII, and AISI with ROC analysis, the curves shown in Figure 6 were obtained. It was found that the systemic inflammation indices are statistically significant predictors for forecasting adaptation failure. The cut-off values (corresponding to the maximum Youden index) were: for SIRI — 1.231, for SII — 449.761, and for AISI — 239.580. Adaptation failure was predicted when the index values were equal to or above these thresholds. The obtained data are consistent with the literature data on the assessment of these indices in various pathologies; in particular, it has been shown that cut-off values of SIRI > 1.05, AISI > 248, and SII ≥ 694.3 are associated with the risk of cardiovascular pathology, atherosclerosis, thrombosis, and acute coronary syndrome [28–30].

CONCLUSIONS

The formation of adaptive and maladaptive reactions in response to environmental factors depends on the baseline level of adaptation mediators and the energy supply of immunocompetent cells. The "physiological norm" group is characterized by a high level of non-specific resistance in response to the type of cold exposure studied in this work.

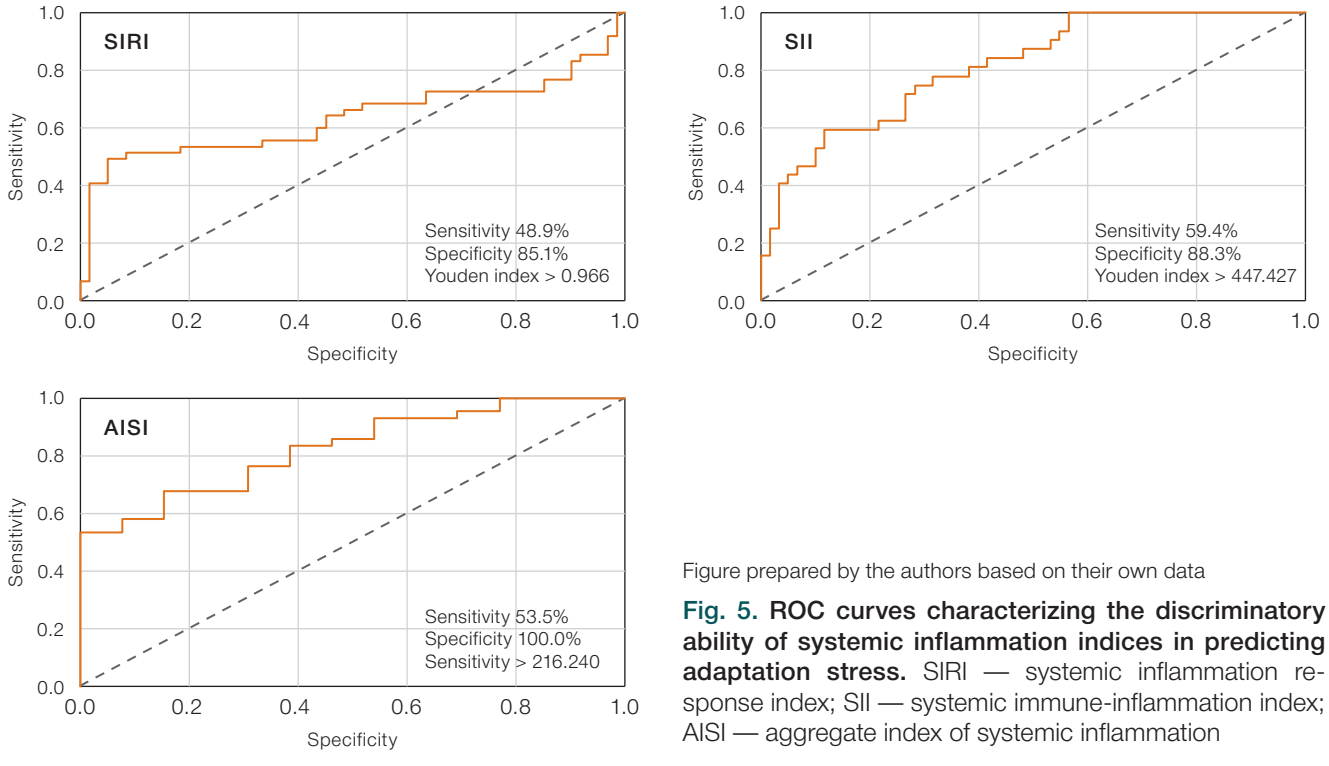

Figure prepared by the authors based on their own data

Fig. 5. ROC curves characterizing the discriminatory ability of systemic inflammation indices in predicting adaptation stress. SIRI — systemic inflammation response index; SII — systemic immune-inflammation index; AISI — aggregate index of systemic inflammation

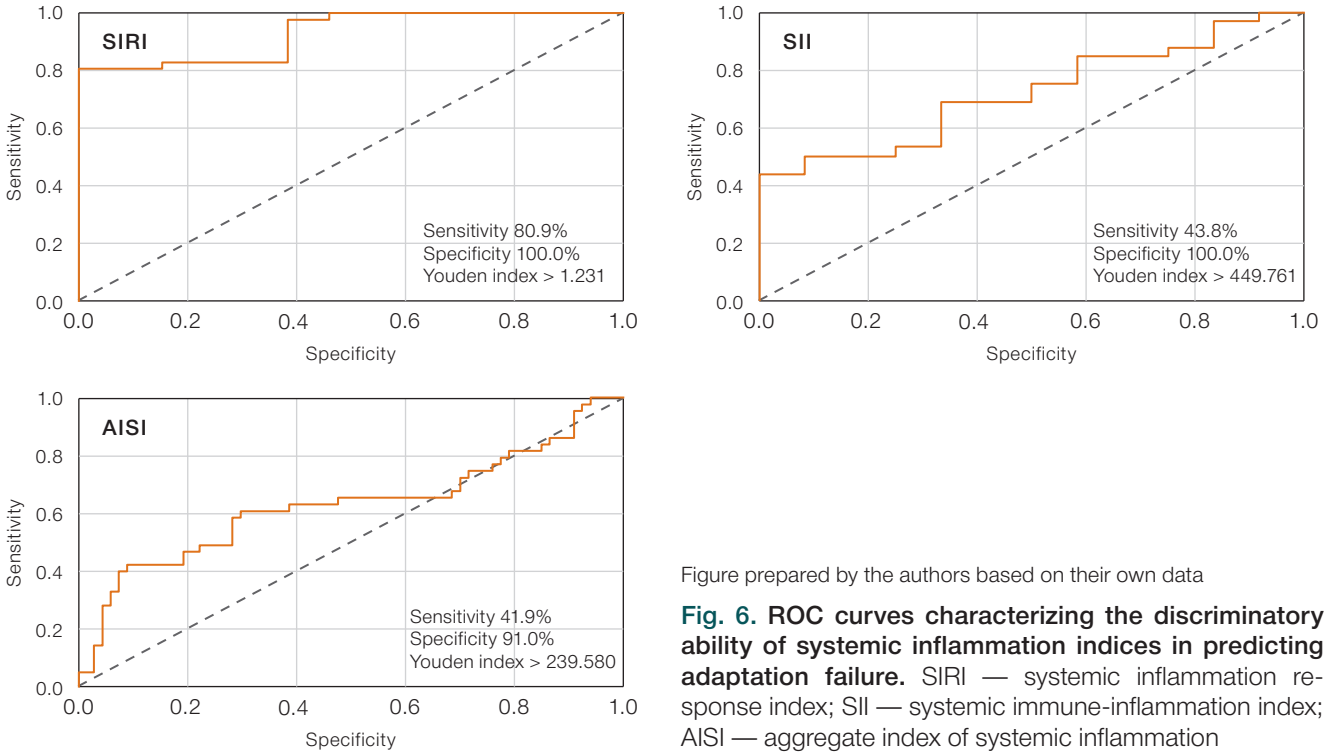

Figure prepared by the authors based on their own data

Fig. 6. ROC curves characterizing the discriminatory ability of systemic inflammation indices in predicting adaptation failure. SIRI — systemic inflammation response index; SII — systemic immune-inflammation index; AISI — aggregate index of systemic inflammation

In “adaptation stress”, the effect of chronic stress was characterized by depletion of the mediator component and, consequently, low baseline concentrations of catecholamines. After short-term cold exposure, their levels increased, which ensured the formation of rapid adaptive hemodynamic responses.

Lymphocytes are characterized by a high intracellular concentration of PPARγC1α, a key regulator controlling the number and biogenesis of mitochondria, indicating a shift toward predominantly mitochondrial energy supply for the cells. In response to cold exposure, leukocyte recirculation and migration increased, thereby improving tissue sanitation and subsequent antigen-stimulated differentiation and proliferation of lymphocytes. At the same time, a decrease in intracellular ATP levels occurred, reflecting an increase in the activity of energy-consuming reactions of phosphorylation and synthesis of intracellular components. In “adaptation failure,” the baseline tension in the activity of regulatory systems, even under a single short-term cold exposure, did not lead to the activation of effective thermoregulation mechanisms. This group is characterized by high baseline cortisol levels with a simultaneous increase in catecholamine concentrations after general cooling; the mitochondrial activity of cell energy supply is lower, with a shift in metabolic activity toward glycolysis and activation of HIF-1α, accompanied by a decrease in the total level of circulating lymphocytes and an increase in the proportion of cells in the early stage of apoptosis. This increases the risk of enhanced cell mutagenesis in response to external stimuli.

The body’s adaptive capacity determines the formation of an adequate response of regulatory systems to external and internal stimuli without failure and without the development of pathological conditions. “Adaptation stress” and “adaptation failure” are characterized by changes in cellular and humoral parameters of peripheral blood even before clinical manifestation of the disease, and these changes may be exacerbated by additional exposure to negative factors, even if their impact is short-term.

It was established that the baseline systemic inflammation indices (SII, SIRI, and AISI) are significant predictors for assessing both “adaptation stress” and “adaptation failure”. The use of these indices, calculated from complete blood count results, allows for the assessment of an initial imbalance in the adaptation mechanisms, which may subsequently be exacerbated by exposure to stress factors.

References

1. Dobrodeeva LK. *Immunological zoning*. Syktyvkar: KNC UrO RAN; 2001 (In Russ.).
2. Garkavi LH, Tolmachev GN, Mikhailov NYu, Esipov YuV, Benia FM, Zverintseva MM, et al. Adaptation reactions and levels of reactivity as effective diagnostic indices of prenosological states. *Science in South Russia*. 2007;3(1):61–6 (In Russ.). EDN: KVYTWD
3. Zhiemuratova GK, Mambetkarimov GA. Features of the adaptation status of children in the Aral region. *Children’s Medicine of the North-West*. 2021;9(1):148 (In Russ.). EDN: WHCDGU

4. Gordeeva RV, Filimonov SN, Kuzmenko OV, Kireeva LN, Martynova EA, Mitichkina TV. Adaptive therapy in early rehabilitation of the patients with industrial injuries as an indicator of the effectiveness of course programs. *Russian Journal of Occupational Health and Industrial Ecology*. 2020;60(6):409–14 (In Russ.). https://doi.org/10.31089/1026-9428-2020-60-6-409-414
5. Pustovoit VI, Nikonov RV, Samoylov AS, Klyuchnikov MS, Nazaryan SE, Petrova MS. Main cytological and biochemical parameters of blood in the development of a non-specific adaptive reaction with athletes participating in extreme sports. *Resort Medicine*. 2020;2:85–91 (In Russ.). https://doi.org/10.51871/2304-0343_2021_2_85
6. Petushkov MN, Papin MA. Comparative characteristics of the types of non-specific adaptive reactions of the organism in highly qualified athletes in different training periods. *Herald of Tver State University. Series: Biology and Ecology*. 2022; 4(68):7–14 (In Russ.). https://doi.org/10.26456/vtbio275
7. Xiu J, Lin X, Chen Q, Yu P, Lu J, Yang Y, et al. The aggregate index of systemic inflammation (AISI): a novel predictor for hypertension. *Frontiers in Cardiovascular Medicine*. 2023;10:1163900. https://doi.org/10.3389/fcvm.2023.1163900
8. Zinellu A, Paliogiannis P, Mangoni AA. Aggregate Index of Systemic Inflammation (AISI), Disease Severity, and Mortality in COVID-19: A Systematic Review and Meta-Analysis. *Journal of Clinical Medicine*. 2023;12(14):4584. https://doi.org/10.3390/jcm12144584
9. Su Z, Cao L, Chen H, Zhang P, Wu C, Lu J, et al. Obesity indicators mediate the association between the aggregate index of systemic inflammation (AISI) and type 2 diabetes mellitus (T2DM). *Lipids in Health and Disease*. 2025;24(1):176. https://doi.org/10.1186/s12944-025-02589-4
10. Tang J, Li TX, Deng L, Huang XC, He PY, Zhao H. Inflammatory indices AISI and SIRI in atherosclerosis risk stratification: validation across community and intensive care populations. *Annals of Medicine*. 2025;57(1):2530792. https://doi.org/10.1080/07853890.2025.2530792
11. Zhang K, Ma X, Zhou X, Qiu G, Zhang C. Machine learning based association between inflammation indicators (NLR, PLR, NPAR, SII, SIRI, and AISI) and all-cause mortality in arthritis patients with hypertension: NHANES 1999–2018. *Frontiers in Public Health*. 2025;13:1559603. https://doi.org/10.3389/fpubh.2025.1559603
12. Ghobadi H, Mohammadshahi J, Javaheri N, Fouladi N, Mirzazadeh Y, Aslani MR. Role of leukocytes and systemic inflammation indexes (NLR, PLR, MLP, dNLR, NLPR, AISI, SIR-I, and SII) on admission predicts in-hospital mortality in non-elderly and elderly COVID-19 patients. *Frontiers in Medicine*. 2022;9:2434. https://doi.org/10.3389/fmed.2022.916453
13. Zinellu A, Paliogiannis P, Mangoni AA. Aggregate index of systemic inflammation (AISI), disease severity, and mortality in COVID-19: a systematic review and meta-analysis. *Journal of Clinical Medicine*. 2023;12:4584. https://doi.org/10.3390/jcm12144584
14. Fois AG, Paliogiannis P, Scano V, Cau S, Babudieri S, Perra R, et al. The systemic inflammation index on admission predicts in-hospital mortality in COVID-19 patients. *Molecules*. 2020;25:5725. https://doi.org/10.3390/molecules25235725
15. Frantsiyants EM, Bandovkina VA, Dzhavadov DA, Kozel YuYu, Kovalenko VA, Shashkina LY, et al. The opportunities of the systemic immune inflammation index usage for the antitumor treatment in adolescents with Hodgkin's lymphoma effect assessment. *Modern Problems of Science and Education*. 2025;2:14 (In Russ.). https://doi.org/10.17513/spno.33981
16. Kassirskiy N A, Alekseyev GA. *Clinical Gematology*. Moscow: Meditsina; 1970 (In Russ.).
17. Qi Q, Zhuang L, Shen Y, Geng Y, Yu S, Chen H, et al. A novel systemic inflammation response index (SIRI) for predicting the survival of patients with pancreatic cancer after chemotherapy. *Cancer*. 2016;122(14):2158–67. https://doi.org/10.1002/cncr.30057
18. Hu B, Yang XR, Xu Y, Sun YF, Sun C, Guo W, et al. Systemic immune-inflammation index predicts prognosis of patients after curative resection for hepatocellular carcinoma. *Clinical Cancer Research*. 2014;20:6212–22. https://doi.org/10.1158/1078-0432.CCR-14-0442
19. Bai X, Cheng L, Wang H, Deng Y, Tong X, Wen W, et al. The aggregate index of systemic inflammation (AISI) and the risk of all-cause, cardiovascular, and cardio-cerebrovascular mortality in congestive heart failure patients: results from NHANES 1999–2018. *Scientific Reports*. 2025;15(1):18282. https://doi.org/10.1038/s41598-025-01196-8
20. Valle I, Alvarez-Barrientos A, Arza E, Lamas S, Monsalve M. PGC-1α regulates the mitochondrial antioxidant defense system in vascular endothelial cells. *Cardiovascular Research*. 2005;66(3):562–73. https://doi.org/10.1016/j.cardiores.2005.01.026
21. Goto T. A review of the studies on food-derived factors which regulate energy metabolism via the modulation of lipid-sensing nuclear receptors. *Bioscience, Biotechnology & Biochemistry*. 2019;83(4):579–88. https://doi.org/10.1080/09168451.2018.1559025
22. Jamwal S, Blackburn JK, Elsworth JD. PPARgamma/PGC1alpha signaling as a potential therapeutic target for mitochondrial biogenesis in neurodegenerative disorders. *Pharmacology & Therapy*. 2021;219:107705. https://doi.org/10.1016/j.pharmthera.2020.107705
23. Gowans JL. The lymphocyte — a disgraceful gap in medical knowledge. *Immunology Today*. 1996;17(6):288–91. https://doi.org/10.1016/0167-5699(96)80547-0
24. Galluzzi L, Vitale I, Aaronson SA, Abrams JM, Adam D, Agostiniset P, et al. Molecular mechanisms of cell death: recommendations of the Nomenclature Committee on Cell Death 2018. *Cell Death & Differentiation.* 2018;25(3):486–541. https://doi.org/10.1038/s41418-017-0012-4
25. Feng M, Zheng C, Li X, Chen B, Li W. Reversal of lipopolysaccharide-induced cardiomyocyte apoptosis via alpha7nAChR by dexmedetomidine. *Cellular and Molecular Biology*. 2024;70(5):127–31. https://doi.org/10.14715/cmb/2024.70.5.17
26. Xu Y, Surman DR, Diggs L, Xi S, Gao S, Gurusamyet D, et al. Bile acid-induced «Minority MOMP» promotes esophageal carcinogenesis while maintaining apoptotic resistance via Mcl-1. *Oncogene*. 2020;39(4):877–90. https://doi.org/10.1038/s41388-019-1029-6
27. Tang HM, Talbot CC, Fung MC, Tang HL. Transcriptomic study of anastasis for reversal of ethanol-induced apoptosis in mouse primary liver cells. *Scientific Data*. 2022;9(1):418. https://doi.org/10.1038/s41597-022-01470-8

28. Shvarts VA, Talibova SM, Sokolskaya MA, Ispiryan AYu, Shvarts EN, Petrosyan AD, et al. Association of novel biomarkers of systemic inflammation with atherosclerosis and its severity. *Russian Journal of Cardiology*. 2024;29(8):67–74 (In Russ.). https://doi.org/10.15829/1560-4071-2024-6025
29. Yang YL, Wu CH, Hsu PF, Chen SC, Huang SS, Chanet WL, et al. Systemic immune-inflammation index (SII) predicted clinical outcome in patients with coronary artery disease. *European Journal of Clinical Investigation*. 2020;50(5):e13230. https://doi.org/10.1111/eci.13230
30. Li Q, Ma X, Shao Q, Yang Z, Wang Y, Gao F, et al. Prognostic impact of Multiple lymphocyte-based inflammatory indices in acute coronary syndrome patients. *Frontiers in Cardiovascular Medicine*. 2022;9:811790. https://doi.org/10.3389/fcvm.2022.811790

Author's contribution. All authors confirm that their contributions meet the ICMJE criteria for authorship. The primary contributions are distributed as follows: Veronika P. Patrakeeva — supervision and oversight of the research planning and conduct, application of statistical and laboratory analytical methods, manuscript preparation, ensuring patient participation in the study, providing comments and corrections, scientific novelty analysis; Vyacheslav A. Shtaborov — data collection, laboratory analysis, data visualization.

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