ORIGINAL RESEARCH

N. V. Zaitseva, M. A. Zemlyanova, Yu. V. Koldibekova, E.V. Peskova

STUDY OF NEGATIVE EFFECT INDICATORS IN CHILDREN UNDER THE INFLUENCE OF ADVERSE FACTORS OF THE SUBARCTIC CLIMATE

DOI 10.25789/YMJ.2021.75.01

UDC 613.1: 616.1: 616.2: 616.4: 616.8

Currently, considering the regional features of subarctic climatic conditions affecting the increased public morbidity is of importance. There it is necessary to carry out in-depth study devoted to changes in the indicator level reflecting the negative effects of target organs. This study aims at examining the biochemical and general clinical indicators of negative effects in children living under the adverse factors of the subarctic climate.

Materials and methods. The object of the study was the state of children's health. The exposure of adverse factors of the subarctic climate, the values of biochemical and general clinical indicators were assessed, information regards children's diseases was analyzed, statistical data processing was carried out using the Statistica 10 program and the dependence between the frequency of the disease and the impact of a complex of adverse climatic factors was parameterized.

Results and discussion. Under the influence of adverse factors of the subarctic climate, changes in the level of biochemical and general clinical indicators were found out in children 4-7 years old. This indicators prove the development of such negative effects as stress of thyroid function (an increase by 1.4 times in the level of TSH in blood serum), the formation of an inflammatory process (an increase of up to 1.7 times in the level of leukocytes and ESR in the blood), the risk of early vascular disorders (a decrease by 1.2 times in Apo A1 and an increase of up to 1.3 times in the level of Apo-B and Apo-B/ApoA1 in blood serum), deterioration of endogenous vasomotor activity in the myocardial tissues and neuro-endocrine regulation (a decrease by 1.2-2.5 times in the content of cortisol and serotonin, and, on the contrary, an increase in the level of adrenaline in the blood). 1.2-5.6-times increased frequency of functional disorders of the nervous, endocrine and circulatory systems proves the negative effects regards the target organs. This might happen due to the complex impact of adverse factors of the subarctic climate.

Conclusion. The found indicators of negative effects should be used to monitor the health state and improve the effectiveness of the development of medical and preventive measures for children living under the influence of adverse (extreme) factors of the subarctic climate.

Keywords: adverse factors of the subarctic climate, air temperature, air humidity, wind speed, target organs, negative effects, biochemical and general clinical indicators, child population.

Introduction. The climate is one of the priority environmental factors that determines the comfort of living conditions. Low temperature, high relative humidity and wind speed, huge atmospheric pressure swings typical for territories with a subarctic climate can have both direct and indirect long-term adverse effects on human health [3-5]. It is known that these adverse effects lead to the disorders in the regulatory homeostasis mechanisms, the development of maladaptive reactions, an increase in the rate of oxidation-reduction processes, stress on the mechanisms of immuno-hormonal regulation, blood circulation, and the bronchopulmonary system, and, as a result, an increased chronic morbidity in the population living under extreme exposure to adverse climatic factors [3-5, 9]. Considering the regional features of subarctic climatic conditions leading to an increased morbidity, in children in particular, as the most sensitive subpopulation to the effects of environmental factors, requires to perform in-depth study of changes in the indicator level showing negative effects of target organs.

In this regards, this study aims at examining the biochemical and general clinical indicators of negative effects in children living under the adverse factors of the subarctic climate. The found biomarkers of negative effects can be used to improve the monitoring system of the public health status and to develop effective measures for the prevention of non-communicable diseases associated with the impact of adverse (extreme) factors of the subarctic climate.

Materials and methods. The study object was the health state of children living under adverse factors of the subarctic climate. The comparison area is characterized by an extreme continental climate, which differs from the observation area by milder climatic conditions, namely, positive long-term temperatures, weak winds, and short warm summers. The observation and comparison areas have almost the same population endowment, socio-economic indicators, and minimal chemical pollution of atmospheric air.

General information in terms of climate factors (temperature and relative humidity, wind speed, atmospheric pressure) was obtained from meteorological observations from 01/01/2016 to 31/12/2018 provided by the Federal Service for Hydrometeorology and Environmental Monitoring of the studied areas and open sources of climate and geographical information. As a scenario for the exposure of climatic factors, their complex impact is taken for 11 months per year within 70 years. At that, annual leave outside the residential area was not considered. The most effective and informative indicator reflecting the complex impact of three climatic factors (air temperature and humidity, wind speed) is the normal equivalent-effective temperature (NEET). It was calculated using the formulas A. Missenard [16] and I. V. Buteva [1]. The values of NEET in the range from 12 to 24 °C are accepted as comfortable and sub-comfortable [2]. The atmospheric pressure exposure is calculated based on the value of daily atmospheric pressure differences in the ranges 0 – 3 hPa, 3.1 – 6 hPa, 6.1 – 17 hPa for the year season, which is the difference between the average atmospheric pressure

FBSI "Federal Scientific Center for Medical and Preventive Health Risk Management Technologies", Perm: **ZAITSEVA Nina Vladimirovna** – Member of Russian Academy of Sciences, Doctor of Medicine, Professor, Research advisor, tel.: (342) 237-25-34, znv@fcrisk.ru, http://orcid.org/0000-0003-2356-1145; **ZEMLYANOVA Marina Aleksandrovna** – Doctor of Medicine, Chief Researcher, Head of the Department, tel: (342) 236-39-30, zem@fcrisk.ru, http://orcid.org/0000-0002-8013-9613; **KOLDIBEKOVA Yuliya Vyacheslavovna** – Candidate of Biological Sciences, Senior Researcher, Head of the Laboratory, tel: (342) 237-18-15, koldibekova@fcrisk.ru, http://orcid.org/0000-0002-3924-4526; **PESKOVA Ekaterina Vladimirovna** – Junior researcher, tel: (342) 237-18-15, peskova@fcrisk.ru, https://orcid.org/0000-0002-8050-3059

values for the day between subsequent days. The climatic factor exposure was assessed by the specialists of the Risk Analysis Department (Lear D. N., Head of the Department, Candidate of Medical Science).

218 children aged 4-7 years living in the subarctic climate areas (observation group) were examined. The comparison group consisted of 109 children exposed to milder climatic factors. The examination of children was carried out in compliance with the ethical principles of the Helsinki Declaration (WMA Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects, 2013) and approved by the Committee on Biomedical Ethics of the FBSI "Federal Scientific Center for Medical and Preventive Health Risk Management Technologies" . During this process, we collected informed voluntary consent of a legal representative, because it is a must. The conducted studies did not infringe on the rights, did not endanger the well-being of children, and did not harm their health.

Laboratory tests included biochemical and general clinical indicators reflecting possible negative effects of target organs: the level of red blood cells, white blood cells, hemoglobin, erythrocyte sedimentation rate (ESR) of blood, the content of apolipoproteins A1 (Apo A1) and B100 (Apo-B) with the determination of their ratio, the level of thyroid-stimulating hormone (TSH) and thyroxine (T4), serum cortisol, catecholamines (epinephrine, dopamine, norepinephrine, serotonin) in the blood plasma. The obtained values of indicators in children of the observation group were compared to the indicators in the comparison group. The results of the conducted studies are presented in the form of the mean value (X), the standard error of mean (SEM) and the interquartile range (Q_{25}-Q_{75}).

Children's diseases were analyzed based on the results of a comprehensive objective medical examination meeting the criteria of the International Statistical Classification of Diseases and Related Health Problems. What is more, the ICD-10 was used to determine the number of the diseases during the examination. The medical examination was carried out by specialists of the mobile team of the Department of Hygiene of Children and Adolescents (Valina S.L., Head of the Department, Candidate of Medical Sciences). To identify priority diseases from critical organs and systems, the following criteria were applied: the level of morbidity in the observation group that differs significantly from the level of morbidity in the comparison group ($p < 0.05$). To establish the relationship between the disease frequency (according to the Federal Compulsory Medical Insurance Fund) and the impact of a complex climatic factors, the dependencies were parameterized using the linear regression analysis method by the formula:

$$y = b_0 + b_1 \cdot x_1 + b_2 \cdot x_2 + b_3 \cdot x_3 + b_4 \cdot x_4 + b_5 \cdot x_5 \text{, (1)}$$

where y is the incidence of children population, sl./1000; x is a measure of the level of climate impact, °C, or hPa; b_0 is the parameter of the model intercept term; b_1 is the parameter characterizing the action of NEET; b_2 is the parameter characterizing the action of atmospheric pressure; b_3 is a parameter characterizing the effect of changes in NEET; b_4 is the parameter characterizing the effects of changes in atmospheric pressure; b_5 is the parameter characterizing differences in the incidence of children population between the areas of observation and comparison due to the other factors.

Modeling of cause-and-effect relationships was carried out by specialists of the Department of Mathematical Modeling of Systems and Processes (Kiryanov D.A., Head of the Department, Candidate of Technical Sciences). Statistical analysis of the data was carried out using the program Statistica 10. by nonparametric Mann-Whitney test. To assess the significance of the differences, the p -confidence criterion (≤0.05) was used [2].

Results and discussion. Our research showed that children living in the observation area are more exposed to adverse factors of the subarctic climate (a decrease of up to 4.3 times in the NEET values and an increase of up to 2.4 times in the daily changes in atmospheric pressure with a larger amplitude) relative to the comparison area.

Under exposure to the studied factors in the children of the observation group, a statistically significant increase of up to 1.7 times in the level of white blood cells and ESR of the blood relative to the indicators in the children of the comparison group was observed (Table. 1). It means the development of an inflammatory reaction of the target organs and systems, bronchopulmonary system in particular.

The effect of inflammation, including on the organs of the bronchopulmonary system, is characterized by damage and violation of the integrity of the bronchial mucosa, a decrease in the thickness of the alveolar-capillary membrane, the egestion of inflammatory mediators, and further progression of the process-, the development of morpho-functional changes in the respiratory parts of the lungs [7, 11]. In children of the observation group, a stress of thyroid function was observed. It was proved by a 1.4-times increase in the level of TSH in the blood serum relative to the same indicator in the comparison group (p=0.0001).

According to the data of annotated scientific sources, under the influence of low atmospheric temperatures, especially their differences, there is an increase in the level of thyroid hormones in the blood responsible for tolerance of low temperatures due to an increase in oxygen consumption and an increase in heat production [4, 6]. At the same time, steady stress of the thyroid function might lead to a violation of ventricular relaxation, the appearance of supraventricular arrhythmias, an increase in blood pressure and a further cascade of pathological processes. As a result, it may lead to vascular disorders and heart failure [15].

The assessment of indicators characterizing the risk of early development of vascular disorders in children of the observation group relative to the comparison group indicates a 1.2-times decrease in Apo A1 and an increase up to 1.3-times in the level of Apo-B and Apo-B/ApoA1 in the blood serum (p=0.0001). The found changes in lipoprotein levels are similar to the results of other studies devoted to the development of vascular disorders in children, which may result in the development of atherosclerotic changes in an older age group (younger than working age) when exposure to low temperatures keeps up [5].

It is known that all stages of the atherosclerosis development from early endothelial dysfunction to the formation of atherosclerotic plaques can cause myocardial hypoxia, pro-inflammatory cytokines leading to local arrhythmogenic activity. What is more, sympatho-adrenal regulation is also violated [10]. Therefore we should consider the change in the level of a number of hormones and neurotransmitters reflecting the dysregulation of the sympatho-adrenal system. Thus, in the children of the observation group relative to the comparison group, a decrease in the content of cortisol (1.2 times) and serotonin (2.5 times) (p = 0.0001-0.040) was found, with an increased level of adrenaline in the blood (p = 0, 0001). Low cortisol levels correlate with disorders in the central regulation of corticotropin-releasing factor production, which is carried out by the limbic structures of the brain associated with the production of neurotransmitters,

Table 1

The average value, the error of the average, the interquartile range of the studied indicators in the groups of examined children

Indicator	Observation group (n=218)		Comparison Group (n=109)		The significance of the differences p≤0.05
	X̄±SEM	Q_{25}-Q_{75}	X̄±SEM	Q_{25}-Q_{75}	
Blood					
Red blood cells, $10^{12}/dm^3$	4.71±0.06	4.5-4.9	4.41±0.07	4.2-4.6	0.0001
Hemoglobin, g / dm^3	132.87±1.72	127-139	132.71±1.63	128-137	0.900
White blood cells, $10^9/dm^3$	6.68±0.35	5.3-7.7	5.85±0.38	4.6-6.8	0.0001
ESR, mm / hour	7.53±0.65	5-10	4.35±0.38	3-5	0.0001
Blood serum					
TSH, mcm/cm^3	3.45±0.22	2.2-4.3	2.43±0.23	1.6-2.9	0.0001
T4 free, $pmol/dm^3$	12.37±0.29	10.92-13.62	13.76±0.32	12.71-14.73	0.0001
Apo-B/ApoA1, g/dm^3	0.57±0.027	0.5-0.62	0.45±0.035	0.32-0.53	0.0001
Apo A1, g/dm^3	1.42±0.03	1.35-1.50	1.69±0.09	1.35-2.02	0.0001
Apo-B, g/dm^3	0.82±0.03	0.72-0.89	0.72±0.04	0.63-0.76	0.0001
Cortisol, $nmol/cm^3$	241.59±18.71	160.5-318.9	281.85±31.89	178.6-362.4	0.040
Blood plasma					
Epinephrine, pg/cm^3	79.49±2.01	74.3-84.6	69.55±3.97	59.8-78.4	0.0001
Dopamine, pg/cm^3	58.44±2.9	50.7-65.9	59.35±3.91	52.4-66.8	0.710
Norepinephrine, pg/cm^3	383.99±19.29	328.4-422.7	384.23±24.22	341.8-455.0	0.990
Serotonin, ng/cm^3	99.18±13.57	66.5-133.1	250.06±29.05	188.4-290.9	0.0001

including serotonin [12]. The imbalance between the secretion of catecholamines and serotonin in the blood under the influence of adverse climatic factors is likely one of the violation of the body's protective and adaptive response. It results in a decrease in resistance to hyperthermia, hypoxia, as well as deterioration of endogenous vasomotor activity in myocardial tissues and impaired cardiomyocyte metabolism [6, 13]. In turn, the imbalance of neurotransmitters has both direct and indirect effects on the activity of the hypothalamic-pituitary-thyroid system [8].

The found changes in indicators characterizing the negative effects of the respiratory, endocrine, nervous and circulatory systems are confirmed by the increased degree of incidence of the mentioned target systems. Thus, when compared to the comparison group, children of the observation group have an increased incidence of diseases of the circulatory system (sinus node weakness syndrome) up to 5.6 times (p=0.0001-0.007), the nervous system (functional disorders) up to 2.6 times (p=0.031), the respiratory system (tonsillar hypertrophy) up to 1.7 times (p=0.010-0.024), the endocrine system (unspecified thyroid disease) up to 1.2 times (p=0.033) (Table 2).

The established frequency of unspecified thyroid diseases (5.9 %) and cardiomyopathy in children in the observation group in the absence of these diagnoses in the comparison group (p=0.010) should be addressed. The obtained data in terms of the morbidity structure of examined children correspond to the results of Russian and foreign studies considering the influence of unfavorable climatic conditions on the formation of diseases of the respiratory system, neuro-endocrine system and circulatory organs [3, 7, 9, 14, 17, 18].

The found trends correlate with a 1.2-2.9-times increase in the primary in-

Table 2

Comparative analysis of the morbidity structure in children of the studied groups, %

Disease class/ Nosology (ICD-10)	Degree of incidence, %		Statistical significance in groups (p≤0.05)
	Observation group (n=218)	Comparison group (n=109)	
Respiratory diseases (J00-J99), including:	59.2	44.9	0.010
- hypertrophy of the palatine tonsils (J35. 1)	24.8	14.7	0.024
Circulatory diseases (I00-I99), including:	18.8	5.5	0.0001
- unspecified cardiomyopathy (R01. 0)	5.9	0.0	0.010
- Sinus node weakness syndrome (I49. 5)	10.1	1.8	0.007
Diseases of the endocrine system (E00-E920), including:	53.7	44.95	0.033
- thyroid diseases, unspecified (E07)	5.9	0.0	0.010
Functional disorders of the central nervous system and autonomic vegetative nervous system, including: - Autonomic dysfunction syndrome (G90. 8); - astheno-neurotic syndrome (G93. 8)	11.9	4.6	0.031

cidence rate of the children in the observation area (according to the data on the number of people seeking medical care during the analyzed period) in terms of diseases of the endocrine, nervous and circulatory systems. The analysis of the relationship between the frequency of the disease and the complex impact of adverse climatic factors enabled us to determine a reliable dependence increase in eventual developing of diseases due to the complex influence of adverse factors of subarctic climate, including: nervous system (functional disorders) (R^2=0.12-0.80; 6.71≤b_0≥114.99; -0.001≤b_1≥-0.09; 0.01≤b_2≥-0.15; 0.006≤b_4≥=0.08; 1.31≤b_5≥ 2.29; p=0.0001)endocrine system (R^2=0.32; b_0=37.58; b_2=-0.048; b_4=0.17; b_5=2.22; p=0.0001), and the circulatory system (cardiac conduction disorder) (R^2=0.35; b_0=-4.24; b_2=0.008; b_4=0.09; b_5=2.65; p=0.0001).

Conclusion. Under the influence of adverse factors of the subarctic climate, children aged 4-7 years suffer from changes in the level of biochemical and general clinical indicators characterizing the development of negative effects in the form of stress of thyroid function, the formation of the inflammatory process, the risk of early vascular disorders, deterioration of endogenous vasomotor activity in myocardial tissues and neuro-endocrine regulation. 1.2-5.6-times increased frequency of functional disorders of the nervous, endocrine and circulatory systems proves the negative effects regards the target organs. This might happen due to the complex impact of adverse factors of the subarctic climate. The found indicators of negative effects should be used to monitor the health state and improve the effectiveness of the development of medical and preventive measures for children living under the influence of adverse (extreme) factors of the subarctic climate.

Reference

1. Бутьева И.В. Методические вопросы интегрального анализа медико-климатических условий / И.В. Бутьева, Т.Г. Шейнова // Комплексные биоклиматические исследования. - 1988. - С. 97-108 [Butieva IV, Sheynova T.G. Methodological issues of integral analysis of medico-climatic conditions. *Kompleksnye bioklimaticheskie issledovanija [Complex bioclimatic research].* 1988: 97-108. (in Russ.).]

2. Гланц С. Медико-биологическая статистика / С. Гланц. - М.: Практика; 1998. - 459 с. [Glantz S. Primer of biostatistics. *Mediko-biologicheskaja statistika [Medical biological statistics].* - M.: Praktika; 1998. 459 p. (in Russ.).]

3. Григорьева Е.А. Климатическая дискомфортность Дальнего Востока России и заболеваемость населения / Е.А. Григорьева // Региональные проблемы. - 2018. - № 21(2). - С. 105–112 [Grigorieva EA. Climatic discomfort and morbidity at the Russian Far East. *Regional'nye problemy [Regional problems].* - 2018; 21(2): 105–112. (In Russ.).]

4. Губина А.Е. Сезонные изменения показателей иммунной и эндокринной систем спортсменов в природно-климатических условиях Среднего Приобья / А.Е. Губина, Ан.П. Койносов // Экология человека. - 2018. -№ 2. - С. 31–36 [Gubina AE, Koynosov AnP. Seasonal Changes in Indicators of the Immune and the Endocrine Systems of Athletes in the Natural and Climatic Conditions of the Middle Ob Region. *Ecologiya cheloveka [Human Ecology*]. 2018; 2: 31-36. (in Russ.).]

5. Климатогеографичекие особенности ханты-мансийского автономного округа – Югры и их влияние на здоровье населения / Т.Я. Корчина, В.И. Корчин, И.В. Лапенко [и др.] // Вестник угроведения. - 2014. - № 3(18). - С. 166-174 [Korchina TYa, Korchin VI, Lapenko IV et al. [Climatic and geographical features of the Khanty-Mansiysk Autonomous Okrug – Yugra and their impact on public health. *Bulletin of Ugric studies.* 2014; 3(18): 166-174. (in Russ.).]

6. Кубасов Р.В. Гормональные изменения в ответ на экстремальные факторы внешней среды / Р.В. Кубасов // Вестник РАМН. - 2014. - № 9–10. - P. 102-109 [Koubassov RV. Hormonal Changes in Response to Extreme Environment Factors. *Annals of the Russian Academy of Medical Sciences.* 2014; 9–10: 102–109. (in Russ.).]

7. Луговая Е.А. Оценка коэффициента напряжения адаптационных резервов организма при хроническом воздействии факторов Севера / Е.А. Луговая, И.В. Аверьянова // Анализ риска здоровью. -2020. - № 2. - P. 101–109 [Lugovaya EA, Averyanova IV. Assessing tension coefficient of body adaptation reserves under chronic exposure to factors existing in polar regions. *Health Risk Analysis.* 2020; 2: 101–109. (in Russ.).] DOI: 10.21668/health.risk/2020.2.11.eng

8. Klimaticheskaja diskomfortnost' Dal'nego Vostoka Rossii i zabolevaemost' naselenija. Regional'nye problemy. – 2018; 21(2): 105–112 [Grigorieva E.A. Climatic discomfort and morbidity at the Russian Far East. *Regional problems*. 2018; 21(2): 105–112. (in Russ.).

9. Ревич Б.А. Климатические изменения как новый фактор риска для здоровья населения российского севера / Б.А. Ревич // Экология человека. - 2009. - № 6. - P. 11-16 [Revitch BA. Sezonnye izmenenija pokazatelej immunnoj i endokrinnoj sistemy sportsmenov v prirodno-klimaticheskih uslovijah Srednego Priob'jaю Jekologija cheloveka [Climatic changes as new risk factor for population health in Russian North. *Human Ecology.* - 2018; 2: 31–36.). 2009; 6: 11-16. (in Russ.).]

10. Ярославская Е.И., Аксенова К.В. Коронарный атеросклероз и нарушения ритма сердца / Е.И. Ярославская, К.В. Аксенова // Сибирский медицинский журнал. - 2019. - № 34(2). - С. 21–25 [Yaroslavskaya EI, Aksenova KV. Coronary Atherosclerosis and Cardiac Arrhythmias. *The Siberian Medical Journal*. - 2019; 34(2): 21–25. (in Russ.).] DOI: https://doi.org/10.29001/2073-8552-2019-34-2-21-25

11. AltitudeOmics: effect of reduced barometric pressure on detection of intrapulmonary shunt, pulmonary gas exchange efficiency, and total pulmonary resistance. F.A. Petrassi, J.T. Davis, K.M. Beasley [et al.]. *Journal of Applied Physiology*. - 2018. - No 124(5). - P. 1363–1376. DOI:10.1152/japplphysiol.00474.2017

12. Ehlert U. High and low unstimulated salivary cortisol levels correspond to different symptoms of functional disorders / U. Ehlert, U.M. Nater, A. J. Böhmelt. *Psychosom. Res*. - 2005. - № 59(1). - P. 7–10. DOI: 10.1016/j.jpsychores.2005.03.005

13. Eiden L.E. Neuropeptide-Catecholamine Interactions in Stress. *A New Era of Catecholamines in the Laboratory and Clinic*. USA, Elsevier Inc. - 2013. - № 68. - P. 399–404. DOI: 10.1016/B978-0-12-411512-5.00018-X

14. Identification of weather variables sensitive to dysentery in disease-affected county of China // J. Liu, X. Wu, C. Li [et al.]. *Science of The Total Environment*. - 2017. - No 575. - P. 956–962. DOI: 10.1016/j.scitotenv.2016.09.153.

15. Kaminski G. The Influence of Subclinical Hyperthyroidism on Blood Pressure / G. Kaminski, K. Makowski, D. Michałkiewicz [et al.]. *Heart Rate Variability, and Prevalence of Arrhythmias. Thyroid*. - 2012. - № 22(5). - P. 454–460. DOI:10.1089/thy.2010.0333

16. Missenard A.L. 'Homme et le climat. - Paris. - 1937. - 186 pp.

17. Seasonal variations in cardiovascular disease / S. Stewart, A.K. Keates, A. Redfern, J.J.V. McMurray. *Nature Reviews Cardiology*. - 2017. - No 14. - P. 654–664. DOI: 10.1038/nrcardio.2017.76.

18. Shiue I. Physically equivalent temperature and mental and behavioural disorders in Germany in 2009-2011 / I. Shiue, D. R. Perkins, N.J. Bearman. *Ment. Health*. - 2016. - No 25(2). - P. 148–153. DOI: 10.3109/09638237.2015.1101431.