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EDITOR-IN-CHIEF COLUMN

**Dear Colleagues!**

In your hands you hold the second issue of the «Yakut Medical Journal» for 2019.

Time, by the nature of things, goes forward. Spring has passed in work and care; it was time for nature to awaken from a long hibernation. Summer has come. Time of relax, active and creative. Ahead of us, our dear authors and users, the third and fourth issues of the «Yakut Medical Journal» are.

In accordance with the Charter of the publication "Yakut Medical Journal" is engaged in scientific coverage of biomedical, sanitary and epidemiological issues of public health of the Republic Sakha (Yakutia). This is its main task. Therefore, the journal, of course, responds to certain changes in the socio-political and socio-economic life of the republic, relating to public health.

In the post-soviet period in the Russian Federation attention to the

northern territories, in particular to the Arctic zone, has significantly weakened. But in recent years the situation has changed cardinally. The Russian Arctic has embarked on a path of rebirth. The great Lomonosov spoke prophetic words: "Russia's power will grow with Siberia and the Northern Ocean."

Currently, the Arctic zone of the Russian Federation includes 13 districts of Yakutia.

By decree of the Head of Yakutia, A.S. Nikolaev on December 30, 2018, the Ministry for the Development of the Arctic and the Peoples of the North of the Republic Sakha (Yakutia) was created to be engaged in the integrated development of the Arctic zone of the republic. Attention will be paid to the social problems of the Arctic zone, including the state of health of the population, who has lived and worked in difficult Arctic conditions for centuries.

The government of the republic is creating a program for the integrated development of the Arctic. In addition, an "Arctic" bloc will appear in each state republican program, funds will be directed to the implementation of various projects for the development of the Arctic zone.

The «Yakut Medical Journal» has already had its own "Arctic" block for many years - the "Arctic medicine" heading, which is active and fruitful from the very beginning.

In this issue you will get acquainted with the articles from this heading: Evseeva S.A. et al. "The analysis of nutrition of children of Anabarsky district of the RS

(Ya)", Sofronova S.I., Romanova A.N. et al. "Ethnicity-dependent evaluation of excessive body mass and obesity in the native population of northern Yakutia", A. Gudkov et al. "Seasonal functional organization of the external respiration system in children of senior school age, residents of the Arctic region."

And henceforth, in the "Yakut Medical Journal", the heading "Arctic medicine" will be one of the priorities for the editorial board of the publication, of course, and for the authors and users, for which we hope.

The «Yakut Medical Journal» is and remains to be a scientific and practical medical publication covering a wide range of health problems, prevention, detection and treatment of common diseases, promoting the achievements of medical science and medical education in one of the Arctic regions of the Russian Federation. This is its main focus. The doors of our journal are open to all those who are interested in the problems of the health of the population of our country.

I wish you, our dear authors and users, an active, healthy holiday!

Let the "Yakut Medical Journal" be an inseparable companion both at work and at rest!

Editor-in-Chief Anna Romanova

The editorial council and editorial board of the "Yakut Medical Journal" congratulate our active authors, regular users and readers on the Medical Worker Day!

We wish you good health, well-being, success in your difficult but noble work, and we expect interesting and useful articles from you!



ORIGINAL RESEARCHES

I.V. Averyanova

HEMODYNAMIC AND HEART RATE CHANGES THAT OCCUR IN RESPONSE TO AN ACTIVE ORTHOSTATIC TEST IN YOUNG MALE RESIDENTS OF DIFFERENT DISTRICTS OF RUSSIA'S FAR EASTERN REGION

The **purpose** of this research was to study the restructuring of the cardiovascular system, hemodynamics and heart rate in response to an active orthostatic test.

Material and methods: 69 young men who are students of the North-Eastern State University (Magadan) and 43 male students of the educational institutions of Chukotka Autonomous Okrug (Anadyr) took part in the research. The subjects were examined to study the main indices of the cardiovascular system and heart rate variability at rest (lying down) and in the process of performing an active orthostatic test.

Results: The conducted studies have shown that the process of prompt adaptation happens through the reorganization of the cardiovascular system and the parameters of the heart rate, which differ in persons living in different districts of the Far Eastern region.

Discussion: It has been found that autonomic maintenance of cardiac activity in response to an active orthostatic test is carried out by reducing the activity of the parasympathetic link, which is aimed at maintaining a sympathetic prevalence of vascular tone and heart necessary to realize the reserve capabilities of the cardiovascular system. Changes in the cardiovascular system in response to the orthostatic test were provided by a hypertensive reaction of diastolic blood pressure with a normotensive reaction vs. systolic blood pressure which was more pronounced in the group of Anadyr subjects. Of note that at the moment of transition to a vertical position, a significant decrease in the HF component of the heart rate was registered, which allowed to increase the activity of the sympathetic system and was more pronounced in the group of Anadyr young men. Against the background of a decrease in the LF component of the heart rate spectrum in the Anadyr subjects, also aimed at decreasing the inhibitory parasympathetic effect on sympathetic activity followed by activation of the tone of sympathetic vasoconstrictor fibers, this resulted in an increase in vasomotor tone and was manifested by a pronounced increase in diastolic blood pressure and total peripheral vascular resistance. Such post-exercise rearrangements in hemodynamics against the background of a decrease in the stroke volume with unchanged cardiac output testify to the vascular mechanism of maintaining hemodynamic parameters in response to the active orthostatic test. In the Magadan group the reaction to AOT was not noted. At the same time insignificant decrease in stroke volume against the background of post-exercise tachycardia led to a significant increase in cardiac output, which is a reflection of the circulatory mechanism for maintaining cardiovascular homeostasis.

Conclusion: The obtained results suggest the differences in the changes of hemodynamic parameters and heart rate in response to active orthostatic test can be considered as the regional feature of the functioning of cardio hemodynamics among representatives of the two far eastern regions of the seaside climatic zone.

Keywords: young male residents of the northeast of Russia, cardiovascular system, heart rate indicators, active orthostatic test.

Introduction. Being a method of influencing the venous return of blood to the heart, active orthostatic test (AOT) allows studying compensatory hemodynamic and autonomic shifts and thus to assess the function of the circulatory system as a whole [5]. Orthostatic tension causes consistent compensatory cardiovascular reactions to maintain homeostasis while the sympathetic nervous system, the parasympathetic nervous system, and the baroreflex mechanisms play an important role in this homeostatic response [17].

With a sharp movement of the body from a lying position to a standing position, due to the action of gravitational forces and greater venous compliance, a larger volume of blood remains in the lower part of the body, which leads to a decrease in venous return and unloading of arterial baroreceptors.

As a result, the sympathetic activation of both the heart and the vascular smooth muscle cells increases, and a significant decrease in the parasympathetic activity occurs, which in turn causes compensatory changes in the Heart Rate and the level of arterial pressure [16].

In this regard, the **purpose** of this work was to study the hemodynamic and cardiorhythm rearrangements in response to an Active Orthostatic Test (AOT) demonstrated by vago-normotonia Caucasoid young men living in the coastal climatic zone in two regions of Russia's Far East, Magadan Region and Chukotka Autonomous District.

Materials and methods. The study involved 69 young men aged 17–19 (18.1 ± 0.1 yrs) with an average body mass of 68.2 ± 0.4 kg and body length of 177.8 ± 0.2 cm being students in the Northeast State University (the city of Magadan) and 43 young men aged 17–19 (18.3 ± 0.2 yrs) with an average body mass of 67.8 ± 0.5 kg and body length of 178.1 ± 0.3 cm being students of educational institutions of Chukotka Autonomous District (the city of Anadyr). Cardiointervalograms were recorded continuously for 5 minutes at rest (lying position, baseline) and 5 minutes in a standing position (orthostasis). The recording of the cardiointervalogram was performed using the Varicard unit and the VARICARD-KARDi software [8] taking into account the guidelines of the

group of Russian experts [1].

The Total Power of the heart rate spectrum (TP) was calculated without taking into account the Ultra-Low Frequency component (ULF) based on the requirements of the correctness of the analysis of short time series using the Fourier transform method [4]. The following Heart Rate Variability (HRV) parameters were analyzed: mode (Mo, ms) as the most common value of the R-R interval; the difference between the maximum and minimum values of cardiointervals (MxD-Mn, ms); the number of pairs of cardiointervals with a difference of more than 50 ms in % of the total number of cardiointervals (pNN50, ms); standard deviation of the complete range of cardiointervals (SDNN, ms); mode amplitude with a class width of 50 ms (AMo50%, ms); Stress Index of regulatory systems (SI, standard units); Total Power of heart rate spectrum (TP, ms^2), spectrum power of the high-frequency component of Heart Rate Variability in the range of 0.4–0.15 Hz (respiratory waves) (HF, $\text{ms}^2\%$); spectrum power of the low-frequency component of Heart Rate Variability in the range

of 0.15–0.04 Hz (LF, $\text{ms}^2\%$); the power of the spectrum of the Very Low-Frequency component of heart rate variability in the range of 0.04–0.015 Hz (VLF, $\text{ms}^2\%$). At the same time, the period of the first minute of “active orthostasis” was excluded from the results presented below, since it represents a pronounced transient process, the analysis of which was not part of the objectives of our study.

Blood Pressure indicators were recorded with an automatic “Nessei DS – 1862” tonometer (Japan) at rest (lying position) and at 1st minute after going to the vertical position. At each stage of the experiment, the Starr Stroke Volume (SV, mL), the Cardiac Output (CO, L/min), the Total Peripheral Vascular Resistance (TPVR, $\text{dyne}^2 \cdot \text{s} \cdot \text{cm}^{-5}$) [13] were determined by calculation.

The initial type of autonomic regulation was determined at rest on the basis of the values of the following indicators: MxDMn, SI, TP, where the range of eutonia (normotonia) for MxDMn we took into account was from 200 to 300 ms, for SI – from 70 to 140 arb. units, for TP – from 1000 to 2000 ms^2 [9]. If the studied indices of MxDMn and TP were below these ranges, the autonomic balance was considered as sympathotonic, but with an increase in the values of this corridor it suggested to be vagotonia featured. On the contrary, as regards to the SI with an increase in its values of more than 140 arb. units (taking into account the other two indicators), the autonomic balance was referred to sympathicotonic one, and with a decrease of less than 70 const.

units, it was vagotonia featured. Due to the small number of sympathotonics in the sample, the functional indicators of young male subjects of this type were not analyzed in this series of studies. The sample for statistical analysis included individuals with the vagonormotonic type of autonomic regulation.

All examinations were carried out in a room with a comfortable temperature of 19–21° C, in the morning. The study was carried out in accordance with the principles of the Helsinki Declaration. The study protocol was approved by the Ethical Committee for Biomedical Research at the NESO of the Far Eastern Branch of the Russian Academy of Sciences (No. 004/013 dated December 10, 2013). Prior to inclusion in the study, all participants gave their written informed consent.

The results were statistically processed using the application package of Statistica 7.0. The check on the normal distribution of the measured variables was carried based on the Shapiro-Wilk test. The results of non-parametric processing methods are presented in the form of a median (Me) and an interquartile range of 25 and 75 percentiles. The results of parametric processing methods are presented as an average value and its error ($M \pm m$). In the case of comparing related samples, the statistical significance of differences was determined using the t-Student criterion for dependent samples with a normal distribution as well as using the non-parametric Wilcoxon test for samples with a distribution other than normal. When comparing unrelated

samples, the statistical significance of differences was determined using the t-Student test for independent samples with a parametric distribution and we used the non-parametric Mann-Whitney test for samples with a distribution other than normal. The critical level of significance (p) in the work was assumed to be equal to or less than 0.05 [3].

Results and discussion. It is known that the Blood Pressure rate is one of the main indicators of the cardiovascular system functionality, and keeping it optimal is provided by a complex set of neuro-humoral processes united by a network of interconnections. The evaluation of their individual contribution to the overall structure of regulatory mechanisms is very difficult [7]. Table 1 presents the main indicators of the cardiovascular system at rest and in the process of performing an active orthostatic test in young Caucasians from various districts of the Far Eastern region. As the data presented in the table indicate, the young men of the Chukotsky Autonomous District and Magadan Region have differences in the main characteristics of hemodynamics at rest which is manifested in significantly lower indices of systolic (BP_s) and diastolic (BP_d) blood pressure, as well as the TPVR in the Caucasian group of Anadyr subjects, which in general may indicate the formation of region-related features of the functioning of the cardiovascular system depending on the region of residence. In response to AOT in the young men of the two groups, there was a statistically significant increase in the BP_d and

Table 1

Indicators of the cardiovascular system in the young males of the FED in baseline and in the process of active orthostatic test (AOT), $M \pm m$

Studied parameter	Magadan Region (MR)			Chukotsky Autonomous District (ChAD)			Significance of difference baseline MR – baseline ChAD	Significance of difference AOT MR – AOT ChAD
	Stage of Experiment		Significance of difference baseline – AOT	Stage of Experiment		Significance of difference baseline – AOT		
	Indicators at rest (lying)	AOT		Indicator at rest (lying)	AOT			
BPS, mm Hg	123.9±1.0	125.7±1.7	p=0.17	118.9±2.0	118.5±2.2	p=0.75	p<0.05	p<0.01
BPD, mm Hg	64.4±0.9	76.6±0.9	p<0.001	61.4±1.2	76.7±1.2	p<0.001	p<0.05	p=0.94
HR, bpm	65.2±1.2	84.0±2.2	p<0.001	65.8±1.8	85.4±2.3	p<0.001	p=1.00	p=0.66
SV, mL	81.0±1.1	68.5±1.1	p<0.001	81.0±1.1	64.5±1.3	p<0.001	p=0.58	p<0.05
CO, L/min	5263.4±105.7	5721.4±163.7	p=0.07	5362.9±167.3	5490.7±167.3	p=0.38	p=0.61	p=0.69
TPVR, dyne2 • s • cm-5	1420.8±36.4	1430.7±42.1	p=0.30	1311.9±41.0	1419.0±53.2	p<0.05	p<0.05	p=0.+86

Table 2

Indicators of the Heart Rate Variability at rest and with AOT in young male vagotomotropic Caucasians residing in the FED, Me (25; 75-percentile)

Studied parameter	Magadan Region (MR)		Significance of difference baseline – AOT	Chukotsky Autonomous District (ChAD)			Significance of difference baseline MR – baseline ChAD	Significance of difference AOT – AOT ChAD
	Stage of Experiment			Stage of Experiment		Significance of difference baseline – AOT		
	Indicators at rest (lying)	AOT		Indicator at rest (lying)	AOT			
MxDMn, ms	330.4 (263.0;400.1)	280.6 (225.7;379.4)	p<0.05	370.0 (246.3;416.3)	228.0 (178.8;274.8)	p<0.001	p=0.80	p<0.01
RMSSD, ms	54.0 (38.5;63.4)	24.7 (16.6; 39.9)	p<0.001	60.1 (937.0; 82.5)	21.4 (16.3;28.9)	p<0.001	p=0.21	p=0.14
pNN50, %	30.0 (16.3;44.6)	4.5 (1.3;15.8)	p<0.001	37.7(11.6;55.2)	3.2 (1.0;7.6)	p<0.001	p=0.23	p=0.20
SDNN, ms	59.8 (45.9;71.2)	47.3 (36.9; 64.0)	p<0.001	70.6 (47.5;83.7)	48.9 (36.5;55.7)	p<0.001	p=0.13	p=0.59
Mo, ms	922.3 (824.4; 980.7)	631.8 (580.2; 724.2)	p<0.001	916.5 (772.0;997.5)	650.0 (606.0;691.3)	p<0.001	p=0.48	p=0.75
AMo50, ms	36.0 (28.1; 42.6)	45.4 (37.3; 51.7)	p<0.001	28.7 (23.3;44.0)	47.3 (39.5;57.9)	p<0.001	p=0.20	p=0.12
SI, arb. units	58.8 (37.6; 90.4)	122.7 (66.3; 182.8)	p<0.001	40.0 (30.4;127.2)	139.7 (100.0;263.8)	p<0.001	p=0.49	p<0.05
TP, ms2	2816.2 (1810.6; 4373.7)	1832.0 (1063.0; 3560.1)	p<0.01	3697.7 (1615.0;4103.0)	1685.3 (930.8;2163.3)	p<0.001	p<0.05	p=0.17
HF, ms2	921.3 (613.6; 1519.0)	231.9 (107.7; 454.2)	p<0.001	1244.3 (510.1;2 463.3)	224.3 (115.8;304.9)	p<0.001	p<0.05	p=0.56
LF, ms2	950.0 (647.3; 1325.5)	899.5 (504.6; 1714.3)	p=0.17	1346.8 (633.8;1 677.7)	1003.8 (423.7;1361.0)	p<0.05	p<0.05	p=0.65
VLF, ms2	395.6 (249.9; 711.7)	291.6 (187.6; 686.0)	p=0.47	715.3 (355.1;1086.1)	321.1 (196.1;473.6)	p<0.001	p<0.05	p=0.81
LF/HF, arb. units	1.0 (0.6;1.6)	4.6 (2.8;7.6)	p<0.001	1.2 (0.6;1.5)	4.7 (3.2;6.4)	p<0.001	p=0.98	p=0.96
IC, arb. units	1.5 (1.0; 2.3)	6.8 (3.8;10.6)	p<0.001	1.5 (1.1;2.3)	6.6 (5.0;8.3)	p<0.001	p=0.63	p=0.99

HR against the background of a decrease in Stroke Volume (SV), and the degree of their change was more marked in the Anadyr group. It is necessary to note the different nature of the responses to the test of Cardiac Output (CO) and TPVR in representatives of the two groups: in the group of Magadan young men, a statistically significant increase in the CO circulation was observed against the background of constant TPVR, whereas in the group of Anadyr surveyed, on the contrary, in response to AOT the increase in TPVR and the maintained CO baseline values were seen.

Studies have shown the increased diastolic blood pressure BP_D in response to AOT. The mechanisms underlying orthostatic hypertension remain poorly understood. D. H. Streeten and co-workers (1985) in their work [22] in patients with orthostatic hypertension found excessive accumulation of venous blood in the lower extremities and high levels of the blood noradrenaline in the standing position. This was apparently due to the fact that pronounced venous deposition had led to a significant reduction in cardiac output, with further sympathoactivation (possibly due to cardiopulmonary receptors) and excessive constriction of arterioles, but not venules, and increased BP_D. A higher level of norepinephrine and vasopressin in the standing position in persons with orthostatic hypertension compared with orthostatically normotensive subjects were also noted in studies by K. Kario and co-authors (2009, 2013) [18, 19].

Despite the fact that the vector of the general directionality of hemodynamic shifts in response to AOT in the two groups was similar with respect to the Blood Pressure and Heart Rate, we noted different mechanisms for maintaining the BP. So the transition to a standing position leading to a decrease in venous return and as a consequence of this decrease in the SV of the blood circulation, to a lesser extent expressed in the group of Magadan young male subjects. A less significant decrease in SV in this group due to an increase in the HR led to a significant increase in the CO of the blood circulation. This was not observed in the group of Anadyr boys.

Table 2 presents the characteristics of the heart rate variability at rest and at the peak of AOT in the subjects with the vagotonia-normotonia initial type of autonomic regulation from Caucasians living in different regions of the Far Eastern District. The analysis of the received data of the frequency characteristics of the HR

in response to orthostasis allowed us to establish a decrease in the activity of the parasympathetic ANS which manifests a statistically significant decrease in MxDMn, RMSSD, pNN50, SDNN, Mo, with a more pronounced decrease in the group of Anadyr young male subjects.

An analysis of the rearrangements of the HR spectral characteristics in the young men of the two groups revealed certain differences in the nature of the responses to orthostatic testing. The obtained results indicate that in response to the test in young men of the two groups, the high-frequency component of the HR decreases, but the decrease in this value was slightly more pronounced in the group of Anadyr young males. It is known that the reduction of parasympathetic activity during orthostatic exercise allows for relative sympathetic activation. This vagal "brake" is necessary so that the body can effectively respond to environmental disturbing factors. That is why vagal control of the heart manifested in the restructuring of the HRV indices can reflect not only autonomous and adaptive "flexibility", but also indicates the body's somatoregulatory capabilities [14].

It is indicated that after moving to a vertical position and redistributing the blood flow, afferentation from the baroreceptor zones of the main arteries decreases, their inhibitory effect on the vasomotor center of the brain stem decreases leading to an increase in sympathetic activity and a decrease in the efferent tone of the vagus nerves, while the main function of the sympathetic nervous system is maintaining the adequate blood circulation [10]. It is necessary to note the pronounced tendency of decrease in high-frequency oscillations of the Heart Rate in response to AOT, which reached 74% in the Magadan group, and 81% in the Anadyr group. In the work of A. N. Fleischman (1999, 2009) it was shown that a significant, more than 50% of the baseline values in the supine position, a decrease in the HF index in response to orthostasis indicates the compensatory nature of changes and, in turn, may indicate a violation of adaptation mechanisms. But a moderate decrease in this indicator, on average by 30% from the initial level in the supine position, is a reflection of the decrease in the tonic effect of the vagus on the heart and causes an increase in the chronotropic function of the heart [11, 12]. Apparently, such a significant decrease in parasympathetic activity during the orthostatic loading in young men can be considered, after the theory of "accented antagonism" [20], as aimed

at providing a certain level of sympathetic activation the main function of which will be maintaining optimal blood circulation.

LF-frequencies of the cardiorythm spectrum are currently considered to be an activator of arterial pressure rhythm oscillations implemented through baroreflex mechanisms [6]. In the 2nd group of young men, in contrast to the representatives of the 1st group, in response to AOT, there was a decrease in the LF component of the Heart Rate general spectrum, which is currently regarded as a manifestation of autonomic failure and may indicate a violation of sympathetic vasomotor innervation [12]. Based on the above, the nature of the resulting changes in the spectral characteristics of the Heart Rate in the Anadyr group indicates a decrease in impulses from baroreceptors (decrease in LF) at orthostasis, which in turn reduces the inhibitory vagotonic effect on sympathetic activity and activates the tone of sympathetic vasoconstrictive fibers [15], which leads to activation of vasomotor tone and is manifested by a pronounced increase in BP_D and TPVR. Apparently, baroreflex regulation activates sympathetic activity that is more pronounced in the Anadyr group as evidenced by higher values of the SI-test / SI-baseline ratio, the numerical value of which was 3.5 arb. units, against 2.1 arb. units in the group of Magadan subjects, that should be, based on the recommendations of N. A. Belokon' and M. B. Kuberger (1987), interpreted as "hyper-sympathicotonic reactivity" and "normal autonomic reactivity", respectively [2].

The dynamics of the Heart Rate spectral analysis in response to the AOT VLF components of the heart rhythm in the group of Anadyr boys, unlike the group of Magadans, was negative with a significant degree (by 55%), which may reflect the presence of energy-deficient processes at the tissue level [12].

Conclusion. Thus, the intergroup differences which we revealed in chronotropic, inotropic and vasomotor responses to orthostatic stress cause different degrees of rearrangements of hemodynamic parameters. A more pronounced afterload reduction in Stroke Volume in the group of Anadyr young men which was apparently associated with blood deposition in the peripheral veins and a decrease in venous return with an inadequate increase in heart rate due to insufficient sympathetic activation, leads to a constant load Cardiac Output as compared to the indicator at rest. Maintaining the blood pressure at an optimal level while reducing the Stroke Volume should

be compensated by the baroreflex mechanisms, which in turn should lead to an increase in total peripheral resistance (as was observed in the Anadyr group), otherwise blood pressure will decrease and may lead to syncope [21]. In this case we can see the vascular mechanism for maintaining hemodynamic values in response to the orthostatic test in the subjects of this sample. In the group of Magadan Caucasians, due to the high baseline values of the Total Peripheral Vascular Resistance, there was no vasoconstrictor reaction to Active Orthostatic Test. At the same time, a not so significant decrease in Stroke Volume against the background of the exercise tachycardia led to a significant increase in Cardiac Output as the integral characteristics of the blood circulation. Based on this, we can assume the formation of a circulatory mechanism for maintaining cardiovascular homeostasis in response to AOT among representatives of this group.

In general, at the moment of transition to the vertical position, the young men examined by us recorded an excessive decrease in the cholinergic HF component of the cardiac rhythm, which allowed us to increase the activity of the sympathetic system. This was largely revealed in the group of Anadyr youths and was expressed in a more significant increase in diastolic blood pressure, which, against the background of a decrease in the LF component of the heart rhythm spectrum, leads to an increase in the tone of the sympathetic vasoconstrictive fibers [15] and is manifested by a pronounced increase in diastolic blood pressure and TPVR.

It was established that the pattern of the Heart Rate Variability rearrangement is aimed at reducing the tonic inhibitory effect of the parasympathetic link of the Autonomic Nervous System, where urgent compensatory reactions are realized by reducing MxDMn, RMSSD, pNN50, SDNN, Mo, TP, and HF, which in turn made it possible to maintain sympathetic prevalence on vascular tone and heart, as well as to use baroreceptor regulation, which is generally aimed at the realization of the reserve capabilities of the cardiovascular system.

Based on this it can be assumed that the maintenance of Blood Pressure at a significant decrease in Stroke Volume among representatives of the Anadyr Caucasians is partly compensated by baroreflex mechanisms, which in turn leads to an increase in Total Peripheral Vascular Resistance, as well as a decrease in the low-frequency component of the

heart rate. The data obtained during the work enable us to conclude that the vector of rearrangements of the Heart Rate indicators in response to orthostatic load consists in the activation of sympathetic activity arising against the background of a significant decrease in parasympathetic influence with varying degrees of activation of the baroreceptor regulation of compensatory rearrangements of the cardiovascular system in representatives of the two groups. This result can be considered as a region-related feature of the rearrangements of hemodynamic parameters and heart rate in response to the orthostatic test among representatives of two Far Eastern regions of the seaside climatic zone of residence.

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CRYSTALLOSCOPIC ESTIMATION OF ORGANISM ADAPTATION TO DIFFERENT PHYSIOLOGICAL STRESSORS

ABSTRACT

The authors assessed modification of crystallogenic properties of human blood serum action under physical exertion and psychoemotional stress. Physical exertion was modeled with PWC170 test, and examination situation was a model of psychoemotional stress. This study was performed on 35 healthy volunteers. We got blood specimens three times (without any physical and phychoemotional stresses; after physical exertion and after examination) in all volunteers. Crystallogenic properties of blood serum were tested with teziocrystalloscopic method. Results of own and initiated crystallization were estimated with special semiquantitative criteria and spectrometric analysis. It is stated that physical exertion and psychoemotional stress cause increasing of crystallogenic activity of human blood serum. This trend is more pronounced for the first impact. This is confirmed both by the results of the visual metric evaluation of crystallograms, and by the data of their spectrometric studies.

Keywords: biocrystallogics, stress factors, blood serum.

Introduction. It is known that even physiological stressors can cause significant responses from regulatory (neuro-immuno-hormonal circuit) and effector (cardiorespiratory suprasystem) systems [7, 9, 10]. At the same time, the nature of metabolic changes occurring in the body during significant physical activity and psycho-emotional stress has not been studied in detail sufficiently [2, 3, 6].

Examination stress is a strong psychophysiological stimulus for a student with a socially determined significance and importance of the result, bringing many systems of the body out of balance for a long time, which remains after the answer to the examiner questions [1, 3, 10]. In this regard, this situation is a convenient model for assessing the emotional impact, including its influence on crystallogenic properties of the blood serum [5, 11, 12].

Currently, a number of standardized tests are known to study the physical performance of an individual [2, 7, 8]. One of the most common among them is the PWC 170 test, which allows to assess the functional reserves of the body in general and the cardiorespiratory system in particular, taking into account the age, sex and level of physical fitness of a person [2]. Moreover, the sample of Physical Working Capacity (PWC), developed by Shestrand at Karolinska University in Stockholm in the middle of XX century. In 1968 it has been recommended for determining the physical health of the person. This method (from the English Physical Working Capacity - "physical performance") is to determine the power of the standard load, in which the heart rate (HR) reaches 170 beats per minute. Its standardization and predetermined the

possibility of its application as a model of significant individualized physical activity.

The **aim of the study** was to evaluate the modification of crystallogenic properties of human blood serum under psycho-emotional and physical stress.

Material and methods. The assessment of crystallogenic and initiating activity of blood serum of 35 practically healthy students-volunteers (18-20 years old) before and after the influence of the stress factor, including physical activity and psychoemotional stress (passing the course exam). As a model of physical activity, the PWC 170 test was used in a variant of a veloergometric test. The power of the first and second loads was calculated from the tables taking into account anthropometric data, age and sex of the subjects [2].

To assess the impact of stress factors in all subjects, blood samples were obtained three times: in a calm state (in the intersessional period), after physical activity and immediately after the course exam. Whole blood serum was obtained by standard centrifugation. For the study of crystallogenic and initiating properties of a biological liquid was prepared microscope slide. according to the method of teziocrystalloscopy [4-6]. The basic substance in the teziographic test was 0.9% sodium chloride solution. Description of the results of own and initiated crystal formation of biological substrate was performed using a system of semi-quantitative parameters [5, 6]. The main indicators were evaluated in point scale. They were crystallizability (Cr; reflects the quantity of the crystallization – density of the crystalline elements in facies), the structure index (SI; characterized by the complexity of structureborne), the facia

destruction degree (FDD; it is an indicator of the qualitative side of the process and the correctness of the formation of structures) and the clarity of the marginal zone of the micropreparation (MB).

Visual morphometry of micro specimens dried serum supplemented spectrometric study crystalloscopic and teziographic facias are verified with spectrophotometry on PowerWave XS device (USA) at wavelengths of 300, 350 and 400 nm. To eliminate the influence of the characteristics of glass on the results of spectrometric studies of biocrystals introduced a correction for the optical density of the slide material (for crystalloscopy) or a control sample as a basic substance deposited on the same glass (for teziographic test).

Statistical processing of the results was performed using the program Statistica 6.0.

Results and discussion. On the basis of the obtained results, a comparative analysis of the influence of physical activity and psycho-emotional stress on the crystallogenic and initiating properties of blood serum was performed. In particular, it was found that these physiological stressors contribute to a significant transformation of the own crystal formation of the biological fluid in question (fig. 1 and 2).

At the same time, it is important to emphasize that the direction of shifts in all the main estimates for both variants of exposure is similar, due to the universality of the stress response of the body to the stimulus, but the severity of the shift in the value of the parameters is not the same. Thus, when performing the PWC 170 test, changes in the crystalloscopic pattern of blood serum were more distinct

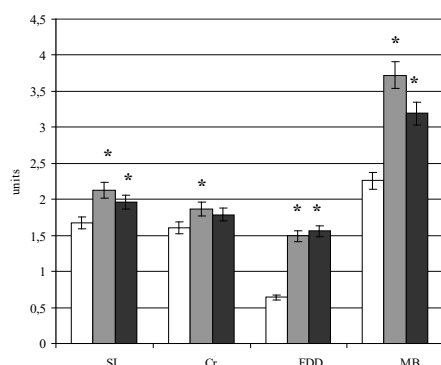


Fig. 1. Results of visuametric analysis of crystallograms of human blood serum under physical and emotional stress («*» – $p < 0.05$ to calm state)

□ - calm state, ■ - physical exercises, ■ - emotional stress.

and included a complication of the structural organization of crystal elements (due to the predominance of dendritic crystal formations with a minimum number of single structures), an increase in their density in the facias in combination with an increase in the degree of their destruction. This was manifested in a statistically significant increase in the level of structure index, crystallizability and facia destruction degree, respectively ($p < 0.05$). In addition, after the implementation of the veloergometric test, a significant expansion of the marginal zone of the micropreparation was observed, leading to an increase in the severity of the latter (MB), in which case the specified facias zone was wider not only compared with serum facias obtained at rest, but also under examination stress ($p < 0.05$). Taking into account the fact that the marginal zone of the micropreparation is formed by protein macromolecules, we can assume an increase in the concentration of proteins in the biological fluid entering the blood with the intensification of metabolism in muscle tissue.

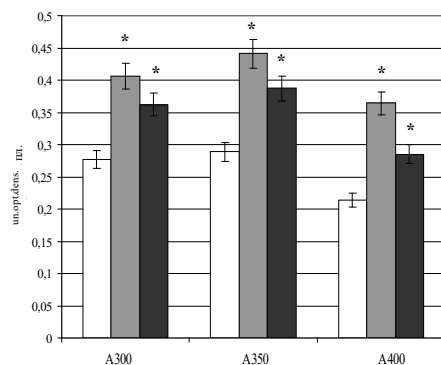


Fig. 2. Results of spectrometric analysis of crystallograms of human blood serum under physical and emotional stress («*» – $p < 0.05$ to calm state)

According to the results, emotional stress causes the formation of lesser shifts in the morphology of serum crystallograms (fig. 1). In particular, under examination stress there was a moderate but statistically significant tendency to complicate the organization of crystal structures (according to the structure index of facias; $p < 0.05$), but it was less significant than during exercise. With respect to the crystallizability of the biological medium (an indicator characterizing the quantitative side of crystallogenesis) the increase in the parameter level is registered only at the trend level ($p < 0.1$).

At emotional stress, as well as after the PWC 170 test, there was a significant expansion of the marginal zone of the micro-preparation of dehydrated blood serum ($p < 0.05$), but in this case it was less pronounced than in physical activity. In our opinion, this may be due to the transformation of the protein spectrum of the biological fluid without a significant change in the level of total protein in the blood serum of the subjects in the pre-examination period.

The shifts are recording by the method of visuametric analysis of crystalloscopic facias were verified by their subsequent spectrometric investigation at wavelengths of 300, 350 and 400 nm. It is established that in both variants of stress the optical density of crystallograms increases, and in the case of PWC 170 load test this tendency is more distinct at all used wavelengths, statistically significantly differing both from the level of the indicator registered at rest and immediately before the exam ($p < 0.05$). It should be noted that the increase in the optical density of facias in these cases is due to the increase in the number and complexity of the crystal elements that form the crystalloscopic picture of the biological fluid. Thus, multi-spectral data allow confirming the results parametric assess-

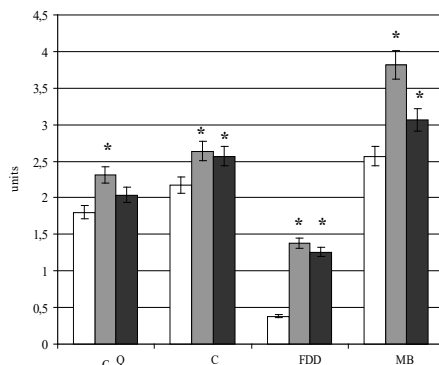


Fig. 3. Results of visuametric analysis of teziograms of human blood serum under physical and emotional stress («*» – $p < 0.05$ to calm state).

ment of crystalloscopic facias at rest and in the stress response.

A comprehensive assessment of the initiating properties of blood serum in healthy individuals in the implementation of the metabolic response to physical stress and psycho-emotional stress was also carried out (fig. 3 and 4). It is revealed that, as in the case of crystallogenic activity of the biological substrate, in teziographic test under the stress-response observed an increase in the values of most visuametric parameters, but the degree of this trend varies depending on the form of the corresponding stress factor (fig. 3). In particular, according to the level of the main quantitative indicator (the teziographic coefficient Q) directly after the physical activity, the increase in the initiator potential of the biofluid was recorded, as evidenced by a significant increase in this parameter ($p < 0.05$). In contrast, in the pre-examination period no substantial changes of the density of the crystal structures in blood serum teziograms of evaluated persons is not revealed. It should be noted that the value of the criterion under consideration after physical stress was higher than before the exam ($p < 0.05$). At the same time, both stressors contributed to the complication of the crystalline elements formed in the dried samples of biological fluid, which was indicated by a moderate increase in the level of crystallinity ($p < 0.05$ for both cases). Similar dynamics took place in relation to the facia destruction degree as a nonspecific marker of "correctness" of crystal formation. In our opinion, the nature of changes in these parameters reflects the universal component of metabolic stress response [6, 9].

The features of the formation of the marginal zone of the micro-preparation of dehydrated blood serum under the influence of the studied stressors are generally similar to those found for the

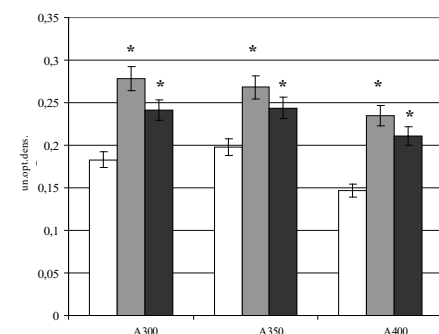


Fig. 4. Results of spectrometric analysis of teziograms of human blood serum under physical and emotional stress («*» – $p < 0.05$ to calm state).

main teziographic coefficient, but this parameter increases statistically both after physical activity and in the pre-examination period ($p < 0.05$). This allows us to assume the presence of rearrangements of serum proteome in both studied states, and when performing the PWC 170 test, these changes are more pronounced ($p < 0.05$).

These shifts in the initiated crystal formation of blood serum, as in the case of crystalloscopic facias of biological fluid, are fully confirmed by the results of spectrometric studies (fig. 4). Thus, for all used wavelengths, serum tezigrams demonstrate a higher level of optical density compared to dried samples of the biological medium obtained from the same people in a calm state ($p < 0.05$). At the same time at a wavelength of 300 and 400 nm the optical density of the facias of the blood serum of the subjects after exercise were significantly higher than that characteristic of the pre-exam period ($p < 0.05$).

Conclusion. In whole, the study demonstrated the direction of shifts in crystallogenic and initiating properties of blood serum of students under physical activity and psycho-emotional stress, but the severity of modification varies significantly. This allows us to conclude that the teziocrystalloscopic picture of human blood serum can be an indicator of various physiological states, which is reflected in the changes in the morphology of dried micro-preparations of the biological fluid, indicating shifts in the qualitative and quantitative composition of the latter.

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L.B. Masnavieva

ASSESSMENT OF THE CONTRIBUTION OF ENVIRONMENTAL FACTORS AND INTERLEUKIN-10 GENE POLYMORPHISMS TO THE FORMATION OF ITS SERUM LEVELS

ABSTRACT

Air pollution has an impact on the health of the population and leads to an increased risk of developing pathology, including the immune system. Genetic predisposition also contributes to the development of disorders in this system. The purpose was to study the contribution of the chemical inhalation load and gene polymorphisms of IL-10 in the formation of its serum levels in adolescents. Polymorphisms -1082G/A, -592C/A, -819C/T of gene IL-10 and the content of its protein product in the blood were studied in schoolchildren who live under conditions of varying levels of air pollution. It has been established that air pollution by immunotropic compounds plays the dominant role in the formation of the serum level of IL-10 in healthy adolescents. The effect of the polymorphic loci of the IL-10 gene (-592C/A and -819C/T) on the formation of its level is manifested in conditions of a high inhalation chemical load.

Keywords: gene polymorphism, interleukin-10, adolescents, air pollution.

Introduction. At the last time the data on the effect of air pollution on public health, the development of the pathology of the immune system is convincing. The impact of environmental factors of the same intensity and duration in some cases leads to the development of pathological processes, in other cases they do not lead to pathology. This is due to a combination of factors, among which the most important are the state of the body during impact and genetic predisposition or resistance to the development of certain diseases. The impact on the body of adverse environmental factors in critical periods of its development, which include the formation and restructuring of systems in childhood and adolescence, can cause the development of an inadequate response and cause the formation of pathology in the future.

The immune system plays an important role in the development of compensatory and adaptive reactions in response to the impact of external factors. In the development of the immune response, the production of inflammatory and anti-inflammatory cytokines (interleukins and interferons) is activated [10]. Changes in the level of cytokine synthesis, which is genetically determined, can lead to a decrease in anti-infective protection, the development of an excessive inflammatory or allergic process and cause the occurrence of pathology [2, 9, 13].

Based on the above-stated facts, this work purposed to study the contribution of the interleukin-10 gene polymorphism and chemical inhalation load to the formation of IL-10 serum levels in adolescents.

Materials and methods. The medical examination of adolescents was conducted after parents (legal representa-

tives) gave their written informed consent in accordance with the requirements of the Committee on Biomedical Ethics. The work consisted in conducting a one-stage survey of 650 schoolchildren of 14.76 ± 0.06 years who live in the territory of Eastern Siberia under the same climatic and geographical conditions, but with different levels of air pollution. Adolescents had no exacerbation of chronic diseases and acute respiratory infections at the time of the survey. Teenagers were divided into groups according to hazard index (HI) immunity disorders. When calculating the hazard index, a formula was used to estimate the dose chemical inhalation load [7]. We introduced personified data on each teenagers, data on admixture concentrations in the atmospheric air, and indoor concentrations of priority pollutants (both at home and in an educational organization) into a formula for calculating a dose chemical inhalation burden [4]. The first group was made up of 225 school students with HI lower than 2; the second group was made up of 359 teenagers with HI equal to 2 or higher, but less than 3, the third group include 66 adolescents with HI equal to 3 or higher.

We examined concentrations of interleukine-10 (IL-10) in blood serum. Cytokine levels were determined via ELISA tests with test-systems (Vector-Best, Novosibirsk). The allelic variants -1082G/A, -592C/A, and -819C/T of gene IL-10 were examined by PCR in real time in accordance with the protocol of the manufacturer of reagent kits (NPF Litekh, Russia). DNA for genetic studies was isolated from whole blood leukocytes with reagent «DNA-express» (NPF Litekh, Russia) using a modified method [1].

We analyzed the results statistically with "Statistica 6.0" applied software. A

check on the normal distribution of quantitative indicators was made using the Shapiro-Wilk test. The content of IL-10 in the blood of adolescents of groups I, II and III was compared by non-parametric tests of Kruskal-Wallis and the U-test of Mann-Whitey. We identified the dependence of the level of IL-10 on the inhalation chemical load and the polymorphisms of its gene were performed using nonlinear regression. The distribution of the genotypes was tested for compliance with the Hardy-Weinberg equilibrium in the program www.oege.org/software/hwe-mr-calc.shtml. the Hardy-Weinberg equilibrium calculator. The presence of differences in the distribution of the frequencies of the genotypes in the surveyed groups was evaluated according to the chi-squared test (χ^2). A p value equal to 0.05 was considered to be a critical statistical significance of discrepancies for Kruskal-Wallis tests, χ^2 test and regression analysis. For the Mann-Whitney U test, the level of statistical significance of the differences, taking into account the Bonferroni amendment, was 0.017. The research results are given as a median and 25 – 75 quartiles (Me(LQ-UQ)).

Results and discussion. It was found that the mean group values in blood IL-10 adolescents were within reference levels (0-10 pg / ml). These results confirm that the examined adolescents were practically healthy and did not have inflammatory processes. We found differences in its concentration depending on the level of inhalation load of immunotropic substances. The content of IL-10 in group II was statistically significantly higher than in group I ($2.51 (0.24 - 5.95)$ pg / ml, $p = 0.014$) and was $3.33 (1.36 - 6.44)$ PG / ml. The level of this parameter in group III was lower than in group II ($1.39 (0.01 -$

4.22) pg / ml, $p = 0.002$). Changes in the concentration of IL-10 may result from the activation of immunity at $2 \leq HI < 3$ and its stress at a higher level of air pollution by chemical compounds [6, 8, 12].

It is known that nucleotide substitutions at polymorphic loci -592 C/A and -819 C / T and -1082G / A of the *IL-10* gene are associated with low production of its protein. In this regard, the carriage of the minor alleles of these polymorphisms may cause a reduced concentration of IL-10, cause an imbalance between inflammatory and anti-inflammatory processes, change the course of the inflammatory response to external influences. [3, 5, 11]. We evaluated the frequency of genotypes of -592 C/A and -819 C/T and -1082G/A polymorphisms of the *IL-10* gene. The distribution of genotypes among schoolchildren in each group was in compliance with the Hardy-Weinberg equilibrium. There were no statistically significant differences in the levels of IL-10 in the blood of adolescents depending on the polymorphic variants of the gene (Table 1). This is understandable, since the observed schoolchildren were healthy and they did not have an activation of the synthesis of inflammatory and anti-inflammatory cytokines, in which there could be a decrease in protein synthesis due to the presence of minor alleles. It is possible that under conditions of increased chemical inhalation load with immunotropic compounds, which was accompanied by changes in the levels of IL-10 in the blood of adolescents, the contribution of genetic factors to the formation of its content will be more significant. Analysis of the content of IL-10 in schoolchildren with different HI immunity disorders depending on genotypes was carried out on the basis of this assumption (Table 1).

Differences in serum levels of IL-10 in adolescents of the first, second and third groups, depending on the presence of the major and minor alleles of the polymorphisms -1082G/A, -592C/A and -819C/T of the *IL-10* gene, were not detected. However, the content of this indicator in the blood of adolescents of group I differed from that in groups of teenagers who had the same genotypes, but were exposed to higher levels of air pollution. The concentration of IL-10 in the blood of adolescents with the GG and GA genotypes of the for polymorphic loci -1082G/A of gene *IL-10* of group II was higher than that of schoolchildren with the same genotypes from group I ($p = 0.0004$ and $p = 0.0101$, respectively). A similar situation was observed for the polymorphism

-592C/A.

Among individuals with CC genotype, the highest level of IL-10 was observed in group II ($p = 0.0002$ and $p = 0.023$ compared with groups I and III, respectively). Differences in the content of the protein product between groups were not observed if the adolescents had a minor allele A (genotypes CA and AA). The analysis the concentration of IL-10 in schoolchildren with different polymorphic variants in the -819 position revealed higher levels of this indicator were also found in individuals with genotypes CC and CT of group II compared with their peers from group I ($p = 0.006$ and $p = 0.033$, respectively) and III ($p = 0.030$ and $p = 0.053$, respectively).

Thus, it was found that the level of IL-10 among schoolchildren of Group I was lower than that of their peers, who have a greater inhalation chemical load. These differences were most pronounced in homozygous carriers of the "wild" allele (genotypes GG and GA polymorphism -1082G/A, genotypes CC and CA polymorphic locus -592C/A and genotypes CC and CT polymorphism -819C/T of the *IL-10* gene). Consequently, the polymorphisms -1082G/A, -592C/A and -819C/T of the *IL-10* gene make a significant contribution to the formation of the level of its protein product in adolescents with

an increased level of inhalation chemical load ($HI \geq 2$).

A regression analysis was performed to assess the contribution of genetic factors to the formation of IL-10 levels. It is important that adequate models describing the contribution of the -1082G/A polymorphism of the *IL-10* gene to the formation of IL-10 level in blood were not detected. We studied the combined effect of air pollution by chemical compounds and the presence of single nucleotide substitutions in the -592C/A and -819C/T loci of the *IL-10* gene on the blood cytokine content. It was found that at $HI < 3$, the values of β -coefficients were higher for variables that reflect the level of chemical inhalation load, compared with coefficients at indicators characterizing the contribution of the polymorphism -592C/A of the *IL-10* gene. This may indicate the dominant role of air pollution under the conditions of chemical inhalation load, which is no more than 3 times the reference levels ($HI < 3$). The regression equation for group I was as follows $IL-10 = 0,20 + 0,228 \cdot (HI)^2 - 0,10 \cdot (P_{592})^2$ ($R^2=0,06$, $p<0,005$, $F(2,18)=5,14$). Regression equations for group II and III are $IL-10 = 38,81 - 0,14 \cdot HI - 0,11 \cdot P_{592}$ ($R^2=0,03$, $p<0,051$, $F(2,17)=2,83$) and $IL-10 = -4,13 + 3,50 \cdot \Pi_{592} - 0,58 \cdot \Pi_{819} - 0,41 \cdot (HI)^2 - 2,82 \cdot (\Pi_{592})^2$ ($R^2=0,46$,

IL-10 concentrations in teenagers depending on genotype, pg/ml

Polymorphism	Genotype	Overall samplingn =650	including			P_1
			Group I n=225	Group II n=359	Group III n=66	
-1082G/A	GG	3.25 (1.31-7.71)	2.51 (0.14-6.19)	5.08 (2.76-6.97)*I	4.07 (1.39-4.86)	0.002
	GA	3.36 (0.89-6.45)	2.75 (0.14-5.95)	3.56 (2.20-6.95)*I	3.82 (0.27-8.82)	0.040
	AA	3.69 (1.17-6.71)	2.70 (0.27-5.49)	4.07 (3.05-9.54)	5.32 (1.02-9.61)	0.171
P_2		0.464	0.922	0.488	0.958	
-592C/A	CC	3.85 (1.62-7.30)	2.70 (0.25-5.95)	4.33 (2.70-7.50)*I	2.11 (1.02-4.86)##	0.000
	CA	3.56 (0.95-6.57)	3.09 (0.27-6.44)	3.88 (2.54-6.45)	4.22 (0.00-13.03)	0.165
	AA	3.39 (1.06-6.45)	2.07 (0.27-3.32)	6.60 (3.22-7.30)	4.07 (4.07-4.07)	0.150
P_2		0.766	0.851	0.489	0.647	
-819C/T	CC	2.78 (1.08-5.08)	2.70 (0.19-6.30)	3.56 (2.03-6.96)*I	2.11 (0.27-4.86)##	0.009
	CT	3.26 (0.81-6.45)	2.50 (0.22-5.76)##	3.54 (1.44-6.50)	1.02 (0.00-4.22)	0.030
	TT	3.32 (0.85-6.45)	1.35 (0.35-2.78)	4.77 (1.99-5.67)	3.57 (3.57-3.57)	0.116
P_2		0.879	0.733	0.602	0.751	

Note: p_1 – the level of statistical significance of differences between groups I-III; p_2 – the level of statistical significance of differences between subgroups of individuals with different genotypes; *I – the differences are statistically significant compared with the group I. $p<0.017$; ## – trend towards differences compared with group II. $0.017<p<0.033$.

$p < 0,016$, $F(4,19) = 4,20$ respectively. In these equations, R^2 is the coefficient of determination, F - Fisher's criterion, P_{592} and P_{819} are variables that characterize the polymorphic variants -592C/A and -819C/T of the *IL-10* gene. The values 1, 2, and 3 were used to encode them. The number 1 was used to encode homozygotes for allele 1, number 2 for heterozygotes, and 3 for homozygotes for allele 2. The influence of genetic factors on the level of IL-10 increased when $HI \geq 3$, and was more dependent on the presence of nucleotide substitutions in the polymorphic loci -592C/A and -819C/T. The equations that were presented confirm this.

The values of the coefficients of determination of equations for groups I and II were analyzed. The contribution of chemical air pollution by immunotropic compounds and nucleotide substitutions in polymorphic loci of the *IL-10* gene is 3-6% in the variability of IL-10 levels in practically healthy adolescents with personalized HI immunity disorders less than 3. With $HI \geq 3$, the role of chemical and genetic factors increases, and their combined effect causes changes in the serum IL-10 content in 41% of the schoolchildren examined.

Obviously, the presented regression models have a number of uncertainties associated with errors of analysis, a limited range of predictors, and the possibility of the modifying effect of unaccounted factors. Also, models have limitations. They can predict the contribution of these chemical and genetic factors to the variability of IL-10 levels with a probability of 95%, provided that adolescents have no acute infectious and inflammatory processes and personalized HI immunity disorders are less than 4. Also a necessary condition for the application of these regression equations is the similarity of the quantitative and qualitative composition of air pollutants with immunotropic effect, with that for which the model was made. These models allow us to prove the relationship between changes in the content of IL-10 in the serum of practically healthy adolescents and exposure to environmental factors, the polymorphism of the *IL-10* gene. Also, these models allow to establish the contribution of these factors to the formation of the level of IL-10, despite the limitations and uncertainties.

Conclusion. In general, the work found that the level of IL-10 changes in healthy adolescents when living in conditions of elevated levels of chemical inhalation immunotropic compounds. Differences in its content are most pro-

nounced in homozygous carriers of the "wild" allele (allele G is for polymorphism -1082G/A, allele C is for polymorphic loci -592C/A and -819C/T of the *IL-10* gene). Using regression models, it was found that the contribution of air pollution and the presence of minor alleles of the polymorphisms -592C/A and -819C/T of the *IL-10* gene contribute to the formation of IL-10 levels from 3 to 6% under the condition $HI < 3$. When $HI \geq 3$, the role of these polymorphisms increases, the contribution of the combined influence of chemical and genetic factors in the variability of IL-10 content reaches 41%.

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V. A. Balandin, I.A. Balandina, D. K. Garmaeva, A. A. Balandin MORPHOMETRIC CHARACTERISTICS OF CEREBRAL CORTEX GYRUS PRECENTRALIS IN THE MALES-MESOCEPHALIC ACCORDING TO CT - SCAN

ABSTRACT

The **purpose** of research was to determine the width of the precentral gyrus, to determine the thickness of the cerebral cortex and the X-ray density of the precentral gyrus neurons in males-mesocephalic according to CT-scan. The analysis of CT-scan study results of 55 males mesocrans, mesocephalics in age from 22 to 35 years without diseases and traumas of central and peripheral nervous system in anamnesis, with predominance of the right hand (right-handed) was done. Morphometric characteristics of the precentral gyrus the cerebral cortex, were determined at three points: above the upper temporal gyrus, at the level of the middle frontal gyrus and above the cingulate gyrus.

It is found that the maximum width of the precentral gyrus is determined above the upper temporal gyrus. Its minimum value was found above the cingulate gyrus. The largest indicator of the thickness of the cerebral cortex of the precentral gyrus is set at the level of the middle frontal gyrus, the lowest value is noted above the upper temporal gyrus. In the left hemisphere, the maximum X-ray density of neurons in the cerebral cortex of the precentral gyrus is set above the cingulate gyrus. In the right hemisphere, the limiting density of neurons was detected above the upper temporal gyrus. The lowest density of neurons in the cerebral cortex of the precentral gyrus was determined by CT-scan in both hemispheres of the brain at the level of the middle frontal gyrus.

Comparative analysis of the parameters of the width of the precentral gyrus, the thickness of the cerebral cortex and the X-ray density of the precentral gyrus neurons showed a statistically unreliable degree of interhemispheric differences with a tendency to reduce all indicators in the right hemisphere in comparison with the left one.

Keywords: precentral gyrus, cerebral cortex, X-ray density, morphometric characteristics, CT-scan, mesocephalic.

Introduction. The structure of the central nervous system is devoted to many works of both domestic and foreign scientists. Scientists have found that the cerebral cortex, which is a layer of gray matter in different departments has a different thickness. The surface of the crust is characterized by a complex relief, which includes numerous furrows and located between them elevations – convolutions [12, 14]. Of particular interest for various specialties doctors are information about the morphology of the precentral gyrus, since it originates the pyramid pathway responsible for arbitrary movements [13].

The possibilities of using such modern methods as CT-scan or magnetic resonance imaging in the diagnosis of various diseases impose new requirements to the level of knowledge about the parameters and structure of specific anatomical formations, taking into account the sex, age and typological characteristics of the subject [1, 5, 7]. In the scientific literature there is information about the anatomical characteristics and cytoarchitectonics of many areas of the cerebral cortex and

cerebellum, taking into account the specific period of postnatal human ontogenesis [2, 11, 15]. At the same time, detailed knowledge of the morphometric features of the precentral gyrus revealed by computed tomography is very scarce and has a fragmentary character.

The aim of the study was to determine the width of the precentral gyrus, to determine the thickness of the cerebral cortex and the X-ray density of the precentral gyrus neurons in males-mesocephalic according to CT-scan.

Materials and methods. The work is based on the analysis of the results of X-ray computer tomographic study of 55 men who underwent examination and treatment in the Department of radiology of the state Autonomous health institution of the Perm region «City clinical hospital №4». The age of the subjects ranged from 22 to 35 years inclusive. The research was approved by the ethical Committee of the E.A.Vagner Perm State Medical University (№10 from 22.11.2017). The examinees had no history of diseases and injuries of the Central and peripheral nervous system, noted the predominance

of the right hand (right-handed). All of them agreed to X-ray examination, which was carried out only according to the indications. Transverse-longitudinal (cranial) index of the subjects was $76.6 \pm 1.22\%$.

Review craniography was conducted in the standard projections (frontal and lateral) X-ray Chirana MP 15-B (Slovakia). Craniometrical study included the measurement of the longitudinal and transverse dimensions of the skull and the definition of craniata largest cross-longitudinal index. The study sample was made up objects with a skull of average form – mesocrans, mesocephalic, the value of the cranial index of which is varied in the range from 75,0 to 79,9. The longitudinal and transverse dimensions of the skull were measured at the extreme protruding points on the axial section and in 3D reconstruction mode. CT-scan was performed on 16-slice apparatus Optima CT 520 (General Electric – GE Healthcare, USA). Scanning was performed by a native with a slice thickness of 5 mm, with subsequent postprocessing reconstructions with a slice thickness of 0.65 mm in the mode of Head

and Bone with the use of the sharpen filters. The width of the precentral gyrus, the thickness of the cerebral cortex of the precentral gyrus and the X-ray density of neurons were determined at three points (T): in T1 – above the upper temporal gyrus, in T2 – at the level of the middle frontal gyrus, in T3 – above the cingulate gyrus. Statistical processing of the results was performed using the software system STATISTICA V. 6.0. The results were presented in the form of the arithmetic mean value (M), relative error (m), maximum and minimum values, variation coefficient, median. The significance of differences in mean values was assessed using the student's parametric t-test. The critical level of significance when testing statistical hypotheses was considered to be equal to 0.05, while the confidence interval, $p < 0.01$, indicating differences between the relative frequencies of the characteristic values was determined.

Results and discussion. Morphometric characteristics of the cerebral cortex of the precentral gyrus in males-mesocephalic are presented in the Table. Maximum width of precentral gyrus in men mesocephalic is inserted over the superior temporal gyrus (T1). It is 15.72 ± 0.04 mm in the left hemisphere and 15.68 ± 0.04 mm in the right hemisphere of the brain (Table). A minimum width of 11.41 ± 0.03 mm in the left hemisphere and 11.37 ± 0.03 mm in the right hemisphere was found above the cingulate gyrus (T3).

The greatest thickness of the cerebral cortex of the precentral gyrus was established at the level of the middle frontal gyrus (in T2). The smallest thickness of the cortex in both hemisphere was noted above the upper temporal gyrus (T1).

In the left hemisphere, the maximum X-ray density of neurons in the cerebral cortex of the precentral gyrus, equal to 33.45 ± 0.09 HU, was detected above the cingulate gyrus (in T3). In the right hemisphere, the limiting density of neurons reaches 33.32 ± 0.09 HU above the upper temporal gyrus (T1).

The lowest density of neurons in the cerebral cortex of the precentral gyrus was established by X-ray computed tomography in both hemispheres of the brain at the level of the middle frontal gyrus (T2).

When comparing the parameters of the width of the precentral gyrus, the thickness of the cerebral cortex and the X-ray density of the neurons of the precentral gyrus in both hemispheres, no statistically significant differences were found, with a tendency to reduce all indi-

cators in the right hemisphere compared to the left ($p > 0.05$).

Conclusion. In the available publications, the researchers noted that the more advanced evolution of the kinesthetic analyzer, located in the precentral gyrus, led mainly to the development of the right hand in humans [10]. In the modern literature there is information about the results of a comprehensive comparative analysis of the organization of cell groups, intercellular space, the area of neurons in the cerebral cortex of the precentral gyrus, performed in fetuses, newborns and infants with intrauterine growth retardation. It was determined that interhemispheric asymmetry is manifested in the cerebral cortex of the precentral gyrus by the predominance of the area of cell groups of the left hemisphere and the thickness of the cortex [8]. In our study, performed in men aged 22 to 35 years, on the basis of X-ray computed tomography, statistically significant interhemispheric differences in the width of the precentral gyrus and the thickness of the cerebral cortex of the precentral gyrus were not revealed. However, there is a tendency for parameters to prevail in the left hemisphere.

In the course of studies of quantita-

tive and qualitative characteristics of neuron-glial-capillary relationships in the upper frontal gyrus of the human cerebral cortex, taking into account gender, age and hemisphere, scientists have found that the density of glial cells increases with age regardless of gender. When calculating the glial-neuronal index, the researchers note that the ratio of glia-neuron in elderly people is one and a half times higher than in young people [9]. In this case, the density of capillaries throughout a person's life decreases. However, in both men and women there were no statistically significant differences in the indices of neurons, glia and capillaries between the right and left hemispheres of the brain [4].

Determination of the X-ray density of neurons in the cerebral cortex of the precentral gyrus, also did not show significant interhemispheric differences, while paying attention to the tendency to the predominance of parameters in the left hemisphere. The obtained results can serve as an equivalent of the age and sex anatomical norms of the brain precentral gyrus in men aged 22 to 35 years with a predominance of the right hand, which will allow using this data in further funda-

Morphometric characteristics of the cerebral cortex of the precentral gyrus in males-mesocephalic according to CT-scan (n=55)

Hemisphere	Point of measurement	M±m	Max	Min	σ	Cv	Me
Width of the precentral gyrus. mm							
Left	T1	15.72 ± 0.04	16.28	15.10	0.33	2.11	15.67
	T2	13.49 ± 0.04	14.09	12.92	0.33	2.47	13.54
	T3	11.41 ± 0.03	11.79	11.01	0.23	2.04	11.45
Right	T1	15.68 ± 0.04	16.29	15.11	0.33	2.11	15.69
	T2	13.46 ± 0.04	14.10	12.90	0.35	2.61	13.42
		11.37 ± 0.03	11.80	11.06	0.21	1.83	11.33
Thickness of the cerebral cortex of the precentral gyrus. mm							
Left	T1	4.43 ± 0.04	5.00	3.92	0.34	7.70	4.41
	T2	4.69 ± 0.04	5.24	4.10	0.34	7.28	4.72
	T3	4.48 ± 0.04	4.94	3.91	0.31	6.87	4.50
Right	T1	4.40 ± 0.04	4.96	3.90	0.32	7.17	4.38
	T2	4.66 ± 0.04	5.22	4.12	0.30	6.54	4.66
		4.43 ± 0.04	4.90	3.92	0.30	6.67	4.40
X-ray density of neurons in the cerebral cortex precentral gyrus. HU							
Left	T1	33.37 ± 0.09	34.55	32.02	0.70	2.11	33.38
	T2	32.86 ± 0.07	33.99	31.81	0.61	1.85	32.72
	T3	33.45 ± 0.09	34.62	32.13	0.76	2.27	33.55
Right	T1	33.32 ± 0.09	34.53	32.02	0.71	2.13	33.23
	T2	32.84 ± 0.08	33.93	31.82	0.64	1.95	32.75
		33.20 ± 0.08	34.58	32.17	0.65	1.95	33.11

mental researches and clinical work.

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STRESS HORMONES IN MEN WHOSE PROFESSIONAL ACTIVITIES ARE EITHER OFFICE-BASED OR OF AN EXTREME EMERGENCY NATURE

ABSTRACT

In this study we investigated cortisol, dehydroepiandrosterone sulfate and testosterone concentrations in the serum blood of healthy young (up to 40 years old) and mature (over 40 years old) men, and whose professional activities are either office-based or of an extreme emergency nature. We revealed a significant age-dependent decrease in hormonal parameters in those working in office conditions. In the group of men whose professional activity is of an extreme emergency nature, significant age-dependent changes in hormonal parameters were not found. Comparison of men of different working conditions showed significant changes in all three studied hormones only in the second age group (over 40 years old).

Keywords: cortisol, dehydroepiandrosterone sulfate, testosterone, stress, office-based employees, an extreme emergency nature of work.

Introduction. The endocrine system plays a key role in the regulation of the compensatory response mechanisms to extreme factors affecting the organism. The hypothalamic-pituitary-adrenal system is equally important in the development of stress reactions [7, 8, 16]. The active substances of this system (glucocorticoids) activate the processes of long-term adaptation in the organism. Excessive, prolonged exposure to damaging factors results in desadaptive disorders.

Thus, a persistent increase in cortisol concentration under stress causes various physiological, cognitive, and behavioral changes that are crucial for successful adaptation [5, 11]. The endogenous steroid dehydroepiandrosterone (DHEA) has an antiglucocorticoid activity. The buffer form of DHEA (dehydroepiandrosterone sulfate - DHEAS) at certain concentrations prevents the development of psychological disability and stress-induced diseases [14]. However, other systems of endocrine regulation (gonadal, thyroid) play a significant role in the maintenance of adaptive responses induced by stress [4, 9]. Extreme factors induce changes in the ratios of sex hormone concentrations result in enhanced catabolic processes [10]. Given the role of the endocrine system in the implementation of the stress response, one might expect significant changes in the endocrine system in people whose professional activity is closely associated with exposure to extreme stressors. In particular, a distinctive feature of the service of the employees of the Ministry of the Russian Federation for Civil Defense, Emergencies and Elim-

ination of Disaster Consequences is the presence of a large number of stress factors, emotional stress and constant dealing with danger – i.e. with life-threatening situations for themselves as well as for others. These circumstances in most cases have a negative impact on the health of those performing operational tasks and create conditions for the development of occupational stress [12].

In this regard, it is important to assess

the functional state of people whose professional activity is of an extreme and stressful nature. The **purpose** of this study was a comparative investigation of the stress hormones concentrations in men whose professional activities are office-based or of an extreme emergency nature.

Materials and methods of the research. The study was carried out in accordance with the Code of Ethics of

Table 1

Concentration of cortisol, DHEAS, and testosterone in healthy male office workers, Me (25%Q-75%Q)

Hormone	< 40 years old (n=33)	> 40 years old (n=14)	p-value
Cortisol (nmole/l)	601.04 (449.16-762.08)	453.92 (386.51-569.44)	P=0.048
DHEAS (µg/ml)	2.5 (2.08-3.14)	1.86 (1.37-2.24)	P=0.03
Testosterone (nmole/l)	19.5 (15.9-22.87)	11.53 (9.39-16.3)	P=0.03

* - p < 0.05 statistically significant by Mann-Whitney criteria

Table 2

Concentration of cortisol, DHEAS, and testosterone in healthy male employees of EMERCOM, Me (25%Q-75%Q)

Hormone	< 40 years old (n=117)	> 40 years old (n=27)	P по критерию Манна-Уитни
Cortisol (nmole/l)	567.12 (420.8-750.67)	615.37 (409.08-833.54)	P=0.176
DHEAS (µg/ml)	2.52 (2.09-3.56)	2.46 (1.69-2.91)	P=0.254
Testosterone (nmole/l)	16.08 (12.06-21.93)	18.66 (12.55-21.56)	P=0.675

the World Medical Association established for experiments involving humans (Declaration of Helsinki, revised in 2013 (World Medical Association, 2013)). Each person provided written informed consent after the study was approved by the Local Bioethics Committee of the Mental Health Research Institute in Tomsk. The total sample comprised 191 healthy men aged 19 - 60 years. Of these 47 were employees of higher educational and research institutions, so called office workers (the first group) and the second group consisted of 144 men, whose professional activity is of extreme emergency nature (employees of the EMERCOM of Russia in Tomsk region). Exclusion criteria were the presence of any mental disorders and somatic pathology in the acute stage.

Hormonal status was studied taking into account the age factor. According to previous research, the DHEAS and testosterone concentrations increase up to 40 years old, and decrease after 40 years old. For these reasons we divided the subjects into 2 age groups: of young (up to 40 years old) and mature age (over 40 years old) (Alcor Bio, product catalog 2018).

The material for the study was blood serum. Blood samples from all examined individuals were drawn after an 8-h overnight fast into tubes with a clot activator (CAT) to isolate the serum (BD Vacutainer).

The cortisol, dehydroepiandrosterone sulfate (DHEAS) and testosterone concentrations were measured in serum by enzyme immunoassay (ELISA) using reagent kits from AlcorBio. Reactions were carried out according to the manufacturer's instructions with the obligatory control of the standard positive and negative samples included in the test systems. The ELISA results were evaluated on the Epoch BioTek Instruments (USA) automatic microplate spectrophotometer at a wavelength of 450 nm.

Statistical analysis was carried out using the SPSS 22.0 for Windows software package. The normality of the distribution of the values of the variables was checked by the Kolmogorov-Smirnov criterion. Data were expressed as medians, upper and lower quartiles. The statistical significance of differences between groups was determined by Mann-Whitney criteria (for two independent samples). Differences were considered significant at $p < 0.05$.

Table 3

Concentration of cortisol, DHEAS, and testosterone in healthy men over 40 years old whose professional activities are either office-based or of an extreme emergency nature, Me (25%Q-75%Q)

Hormone	Healthy male office workers	Healthy male employees of EMERCOM	P по критерию Манна-Уитни
Cortisol (nmole/l)	453.92 (386.51-569.44)	615.37 (409.08-833.54)	P=0.017
DHEAS (µg/ml)	1.86 (1.37-2.24)	2.46 (1.69-2.91)	P=0.05
Testosterone (nmole/l)	11.53 (9.39-16.3)	18.66 (12.55-21.56)	P=0.02

* - $p < 0.05$ statistically significant by Mann-Whitney criteria

Results and discussion. Our study showed significant age dependent changes of hormonal levels in male office workers. In this group the cortisol concentration was statistically lower in men aged 40 years or more compared to men younger than 40 years old ($p = 0.048$) (Table 1). DHEAS concentrations in the mature age group were significantly lower compared to the young age group ($p = 0.03$). The testosterone level in male office workers also decreased significantly with age ($p = 0.03$).

Another pattern was observed in the employees of EMERCOM of Russia in the Tomsk region. We did not find any age-dependent significant differences in the concentrations of the studied hormones in men whose professional activity is of an extreme emergency nature (Table 2). Though the cortisol concentration was slightly higher in men over 40 years old in comparison to those under 40 years old, the difference did not reach statistical significance ($p = 0.176$).

The lack of significant changes in endocrine indices in different age groups among employees of extreme emergency professions is probably related to the main physiological functions of the studied hormones. Cortisol is the main adaptive hormone that mediates the physiological response of the organism to various extreme factors [5]. Its increase under conditions of prolonged and repeated stress provides optimal adaptive changes of the body. According to previous research, changes in the level of cortisol and testosterone in law enforcement

officers and rescuers are associated with the level of professional stress and length of work, which is associated with disturbances of the pituitary regulation [1-3].

The comparative analysis of groups of men under the age of 40 whose professional activity is of an office or extreme emergency nature did not reveal any significant differences.

Significant changes in all three studied hormones were observed when results from the two groups of men aged 40 years or more were analyzed. In the older age group, cortisol ($p = 0.017$), DHEAS ($p = 0.048$) and testosterone ($p = 0.02$) were significantly higher in employees of EMERCOM of Russia in the Tomsk region compared with the office workers (Table. 3).

Such age-related features of hormonal regulation in men whose professional activity is of an extremely stressful nature can be explained by the theory of allostasis. With age, the mechanisms and driving forces of mental development change, primarily due to changes in the brain's energy and neurodynamic parameters of mental activity in the form of a shift in the balance of neurodynamic parameters of mental activity towards the predominance of inhibitory processes [6]. As a result, hormonal changes those are protective when young (allostasis) become non-adaptive later. Allostatic stress, manifested in over-activation of regulatory systems, with age makes a person less able to additionally respond to adaptive stress, which leads to vulnerability, and not to sustainability [13, 15]. Another ex-

planation could be quite opposite. Employees of EMERCOM are actually fitter with more physical activity than the more sedentary office workers. Changes with time in office workers might be seen as age-related deterioration which is not seen in the group of rescuers.

Conclusion

1. In the group of healthy men whose professional activity is office based, a significant decrease in the concentration of cortisol, DHEAS and testosterone in the blood serum with age was found.

2. In the group of healthy men whose professional activity is of an extreme emergency nature, there were no significant age dependent changes in the concentration of the blood serum cortisol, DHEAS, and testosterone.

3. A comparative analysis in groups of men aged 40 years and more showed significantly higher concentrations of cortisol, DHEAS, and testosterone in the blood serum of men whose professional activity takes place in extreme emergency conditions compared to men whose professional activity is of an office nature.

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PEROXIDATION INTENSITY IN YAKUTIA RESIDENTS IN ZONES WITH A HIGH RATE OF ONCOLOGICAL MORBIDITY

ABSTRACT

In order to study the peculiarities of free-radical processes in the organism of residents of the Republic of Sakha (Yakutia) living in areas with a high oncological diseases index, some indicators of lipid peroxidation and antioxidant system have been determined. We surveyed 75 rural residents of the Lensky district of the southern zone (high oncological diseases) and 88 rural residents of the Anabarsky district of the Arctic zone (growth of liver cancer) were examined. The intensification of lipid peroxidation in residents of the southern zone, especially in non-indigenous women, has been established. In the non-indigenous population, the intensification of free-radical processes causes the activation of low molecular weight antioxidants, and the indigenous population activates the enzymatic link of the antioxidant system. The reduced activity of antioxidant protection indicators was also noted in non-indigenous women, which puts them at risk of developing oxidative stress, as one of the main factors in the development of pre-pathologies and pathologies, including tumors.

Keywords: lipid peroxidation, antioxidant protection, disadaptation, cancer incidence.

Introduction. The severity of environmental stress can be determined by indicators of the increase in mortality of the working age population in a specific area [3]. According to the Ministry of Health of the Republic of Sakha (Yakutia), in the structure of causes of mortality, neoplasms rank third (15%) after circulatory system diseases and external causes of death. In 2018, the death rate from neoplasms increased by 4.4% and amounted to 143.1 per 100 thousand population (2017 - 137.5) [2]. Under the conditions of increasing anthropogenic and technogenic environmental pollution, the growth of environmentally caused diseases can be considered as a result of a decrease in the adaptive reserves of the body. One of the important factors in the impairment of adaptation and the development of many diseases is the activation of lipid peroxidation processes with impairments in the prooxidant-antioxidant system [5,

6]. Therefore, the assessment of the state of lipid peroxidation and antioxidant protection of the organism of the population living in areas with a high incidence of tumors, is an important task to find the reasons underlying the growth of cancer and the adoption of appropriate preventive measures.

The aim of the study was to identify and compare the features of free-radical processes in the inhabitants of the Southern and Arctic zone of the Republic Sakha (Yakutia) with a high rate of oncological morbidity.

Material and research methods. We carried out the determination of indicators of POL-AOS in a sample of 75 rural residents of the Southern zone RS (Ya), where a high oncological morbidity rate is registered (Lensky district). The average age of the investigated was 46.1 ± 0.25 years. In the Arctic zone, where the number of liver, respiratory organs, lym-

phatic and hematopoietic tissues cancer is growing, the sample was 88 rural residents (Anabarsky district), the average age was 44.1 ± 0.34 years. The intensity of free radical oxidation of lipids was determined spectrophotometrically by the accumulation of malonic dialdehyde (MDA) [8]. The antioxidant defense indicators of the body were determined by the total content of low molecular weight antioxidants (LMWA) [7], catalase (Kat) [4].

Statistical data processing was performed using the SPSS Statistics 17.0 applied statistical software package. Standard methods of variation statistics were used: calculation of averages, standard errors, medians, 95% confidence interval. The data in the tables are presented as $M \pm m$, where M is the average, m is the average error. The significance of differences between the mean values was assessed using Student's t

test and Kolmogorov-Smirnov test, single-factor analysis of variance (ANOVA). The probability of the validity of the null hypothesis was taken at $p < 0.05$. Correlation analysis was performed by the method of Pearson and Spearman.

Results and discussion. The non-parametric Spearman correlation method revealed the interrelation of indicators of POL - AOS with the area of residence: MDA (-0.364 ; $p < 0.01$), LMWA (0.629 ; $p < 0.01$), catalase (0.146 ; $p < 0.05$). It has been established that the intensity of lipid peroxidation processes is higher among residents of the southern zone. The level of MDA in the examined individuals in the Southern zone was 2 times higher than that of the residents of the Arctic zone ($p = 0.000$) (Table 1).

Intensification of peroxidation always causes activation of the body's antioxidant defense system. It should be noted that the inhabitants of the southern zone is characterized by the strengthening of the non-enzymatic link of antioxidant protection. Thus, the level of LMWA among the residents of the Arctic ($p = 0.000$). At the same time, the nature of the interrelationships of the parameters of the two systems was expressed by the following correlation: between MDA and LMWA at the level of $r = 0.348$; $p < 0.01$, between LMWA and catalase at the level $r = -0.251$; $p < 0.01$. The inhabitants of the Arctic zone more pronounced enzymatic AOS: catalase activity was 15% higher than in the southern zone ($p = 0.024$).

The greater contribution to the high MDA value among the residents of the southern zone belongs to woman, since their MDA content was 1.5 times higher than that of men ($p < 0.05$). It should be noted that the intensity of POL in women of the Arctic zone is 2.2 times lower than

in women in the southern zone ($p < 0.05$). In men of the Arctic zone, the intensity of POL is at the same level as in women (Fig. 1.).

The compensatory increase in the antioxidant system of the body of women in the Southern zone is less pronounced than in men, as evidenced by significantly lower levels of LMWA in women (0.106 ± 0.024 vs. 0.185 ± 0.049 mg * eq / ml eryt) with the same catalase activity (Fig. 2).

Comparison of the level of antioxidants depending on gender and place of residence showed that the men of the southern zone had a level of LMWA that was 2.4 times higher than that of men in the Arctic zone, which indicates a greater intensification of the non-enzymatic antioxidant system in response ($p < 0.05$). In the inhabitants of the Arctic, the antioxidant protection of the body by sex did not have significant differences, but it should be noted that men have higher levels of LMWA and catalase with the same levels of MDA.

The alien population mainly lives in the southern zone and one of the adaptation reactions of the body in cold climates is the acceleration of metabolic processes, including free radical oxidation processes, as evidenced by the slight correlation of MDA with ethnicity ($r = 0.232$; $p < 0.01$). In non-indigenous men, MDA levels were 2.5 times higher than in indigenous men ($p < 0.05$). Also, for non-indigenous women, the MDA level was slightly higher than for indigenous women (Table 2).

However, a comparison of the MDA level of the indigenous people of the two zones showed that in the Southern zone, the level of MDA among the indigenous people is significantly higher than in the Arctic zone ($p < 0.05$). The balance in the POL-AOS system is better preserved

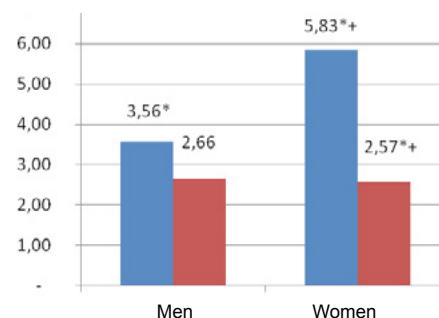


Fig.1 Indicators MDA depending on gender and area of residence.

■ - South Zone ■ - Arctic Zone

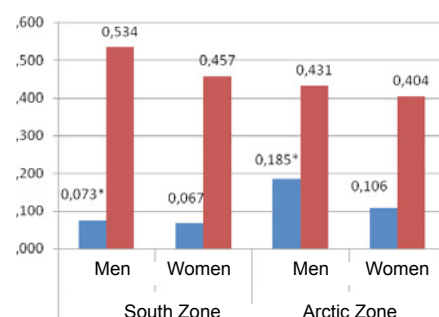


Fig.2. The concentration of antioxidants depending on gender and area of residence.

■ - LMWA ■ - Catalase

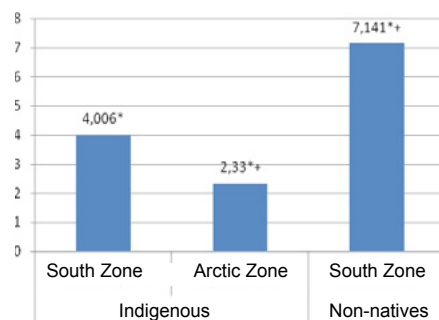


Fig. 3. Concentration MDA in indigenous and non-indigenous people.

■ - MDA

Table 1

The dependence of the concentration of POL - AOS indicators from the area of residence

Statistics	Zone	M±m	St. dev.	Mediana	95% CI	p
MDA, μmol/L	South	5.042±0.506	4.112	4.116	4.031 - 6.054	0.000
	Arctic	2.593±0.132	1.477	2.349	2.331 - 2.854	
LWMA, mgEq / ml * eryt	South	0.134±0.017	0.145	0.108	0.098 - 0.169	0.000
	Arctic	0.068 - 0.002	0.024	0.065	0.064 - 0.074	
Catalase, μCat/L	South	0.413 - 0.031	0.254	0.355	0.350 - 0.475	0.024
	Arctic	0.479±0.020	0.235	0.459	0.439 - 0.520	
K _{AO/LP}	South	0.278- 0.031	0.258	0.202	0.214 - 0.341	0.009
	Arctic	0.331 - 0.033	0.376	0.275	0.264 - 0.397	

among the indigenous men of the southern zone and among the population of the Arctic zone, this is evidenced by a higher K_{AOS} / POL score (Table 2).

The data obtained that a decrease in the adaptive reserves of the body is more characteristic of the inhabitants of the southern zone. It is known that in the Lensky and Anabarsky areas there is an intensive development of natural resources, as a result of which the pressure on the environment increase in the degree of contamination of the OS of the Southern and Arctic zones, the incidence rates of the population of malignant neoplasms significantly increase [10,11]. In the Lensky district, residents consume drinking water with high mineralization

Table 2

POL-AOS Indicators among indigenous and non-indigenous people

South				Arctic	
Men		Women		Men	Women
Indigenous N=18	Non-indigenous N=10	Indigenous N=26	Non-indigenous N=16	Indigenous N=12	Indigenous N=23
MDA, $\mu\text{mol/L}$					
2.69 \pm 0.60*	6.70 \pm 0.73*	5.06 \pm 0.49	7.28 \pm 0.63	3.05 \pm 0.76	2.07 \pm 0.53
LWMA, mgEq / ml * eryt					
0.205 \pm 0.02*	0.116 \pm 0.03	0.105 \pm 0.02*	0.109 \pm 0.02*	0.072 \pm 0.03	0.060 \pm 0.02
Catalase, $\mu\text{Cat} / \text{L}$					
0.448 \pm 0.05	0.368 \pm 0.06	0.357 \pm 0.04	0.495 \pm 0.06	0.569 \pm 0.06	0.416 \pm 0.05
$K_{\text{AOe/LP con.un.}}$					
0.459 \pm 0.09*	0.187 \pm 0.02*	0.227 \pm 0.02	0.193 \pm 0.01	0.311 \pm 0.03	0.314 \pm 0.03

[7]. And pollution of surface water and soil by production waste can lead to pollutants entering the human body. Heavy metals tend to accumulate and initiate intensification of peroxide processes and the formation of free radicals (SPO) [1]. Oxidative stress becomes one of the leading pathogenetic mechanisms in the development of severe pathologies, including neoplasms [12, 13].

Conclusion. Thus, the intensity of lipid peroxidation is higher in the population of the southern zone, especially, in non-indigenous women, in whom a reduced level of antioxidant protection shows a decrease in the adaptive reserves of the body, and places them at risk of developing oxidative stress as one of the main factors in the development of pre-pathologies and pathologies, including neoplasms. Antioxidant protection is not the indigenous population is characterized by the intensification of low molecular weight antioxidants, and the indigenous population by the intensification of the AOS enzymatic link.

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TERMS OF FUNCTIONAL CLOSING OF AN ARTERIAL CHANNEL AT NEWBORN WITH CONGENITAL HEART DISEASES IN THE REPUBLIC SAKHA (YAKUTIA)

ABSTRACT

In the article results of closing of the functioning arterial channel at newborns with congenital heart diseases in the Republic Sakha (Yakutia) are presented. For the purpose of studying of functional closing of an arterial channel at newborns with congenital heart diseases in the Republic of Sakha (Yakutia) 162 medical records are analyzed. Standard anthropometrical parameters, gestation term, ultrasonographies are considered. A retrospective assessment of a number of anamnestic factors on the part of parents was also conducted. We did not reveal statistically reliable distinction among such indicator as age of the father, gestation term, body weight and length of a body at the birth. Also statistically not confirmed results of median values of the functioning arterial channels are received. Statistically not confirmed indicators of association of a factor of presence of congenital heart disease at mother in group of children with the functioning arterial channel were received. As a result of a research possible terms of closing of the functioning arterial channel at newborns are established.

Keywords: patent ductus arteriosus (PDA), congenital heart disease, functioning arterial channel, newborns.

Introduction. Patent ductus arteriosus (PDA) is a vessel, connecting aorta and a pulmonary artery, kept structure, normal for a foetus, after the expiration of its closing. PDA is the most widespread defects: according to clinical data, frequency is it 10-18% of all congenital heart diseases. Existence of the open arterial channel at which its functioning is followed by noticeable violations of the central and regional hemodynamics can be designated by the term of a hemodynamic the significant functional arterial channel. Probability of its long functioning of subjects is more, than less gestational age of the child, his body weight and then serious condition of the newborn. According to Razumovsky A.Y., by results of a Doppler echocardiography, at the full-term children in the first day of life the arterial channel was completely fallen down in 50% of cases, in 48 hours – 90%, and by 96 hours of the life – it was not defined. At the body weight equal of 1500 up to 2000 grams, to this age the PDA remains at 7% of children, at the body weight from 1000 to 1500 gram of 21% and less than 1200 grams, demanding intensive therapy, the channel remains open in 85% of cases. According to some information, regardless of gestational age, the medical and obstetrical center complicates 35% of long artificial ventilation of lungs at newborns.

Terms of functional closing of an arterial channel at newborns with congenital heart diseases are insufficiently studied in the Republic Sakha (Yakutia). This research was conducted for the first time.

Research objective. To study possible terms of PDA at newborns with congenital heart diseases in the Republic

Sakha (Yakutia) according to repeated research.

Materials and methods. This research was conducted on the basis of Republican hospital №1-National center of Medicine. The database was made on the basis of results of the analysis of 162 medical records. They were filled within two periods: 2001-2003 years and 2013-2015 years. Congenital heart diseases were registered according to nomenclature headings Q20-Q28 of International classification of diseases-10.

All newborn took measurement of growth and body weight, ultrasonography, echocardiography with a Doppler for the purpose of assessment of anatomical structure, function of heart and canal vascular. Functioning of an arterial channel was determined according to color Doppler by criteria of identification of an additional stream in a vascular projection – trunk of a pulmonary artery. By results of ultrasonography were allocated two groups: 1) group without additional channel in a projection of a trunk of a pulmonary artery – not functioning arterial channel; 2) group, with the revealed systolic-diastolic or systolic dumping into projections of a pulmonary artery.

The retrospective assessment of a number of the anamnestic factors was carried out from parents: age of parents at the time of the child's birth with congenital heart diseases, gestation term at the birth, the weight and length of a body. The age of parents of the newborns included in a sample was: mothers – from 17 up to 40 years, father – from 17 to 48 years.

Gestation term at the time of the birth of children with congenital heart diseases

was from 25 week to 41 weeks of pregnancy. Body weight at the birth was: minimum value – 564 gram, maximum – 4500 gram. Body length at the birth was: the minimum value – 30 gram, maximum – 58 gram.

When carrying out statistical processing of the database the χ^2 -criterion and Mann-Whitneys U-criterion were used.

Results and discussion

We carried out statistical processing of cases of repeated researches on an occasion of congenital heart diseases among newborns. Among all selection of repeated researches (162 cases) it is revealed that at 62 cases of congenital heart diseases additional dumping in a trunk of a pulmonary artery at the first and repeated surveys was not revealed, closing of a channel happened at 24 children, at 76 dumping of blood through an arterial channel remained. Among cases of the PDA examined in dynamics (n=100) reduction of dumping of blood on the functioning arterial channel in dynamics occurred in 34% of cases, increase in dumping of blood on the functioning arterial channel is revealed in 34% of cases, closing of an arterial channel happened at 24% of cases, at 4% of the examined cases dynamics is not revealed. The group of nonfunctioning arterial channels made 53,1%, the group of the PDA made 46,9%. The minimum quantity of day at repeated ultrasonography was 2 days, maximum – 82 day. Results are presented in table 1.

According to the data provided in Table 1 statistically not confirmed result of median values of closing of the PDA are received. In 50% of cases of the closed arterial channels dumping of blood in not

revealed in the period from 16,5 days to 35 days, in 25% of cases of signs of functioning of a channel it was not revealed from 2 to 16,5 days and with 35 more than a day. Median values of closing of the functioning arterial channel at a repeated research were 25,5 days. Median values of reduction of dumping of blood on the PDA – 22 day, median values of increase in blood – 21 day.

Statistical processing of maternal was carried out. Results are presented in Table 2.

Deduction:

We did not reveal statistically reliable distinction among such indicator as age of the father, gestation term, body weight and length of a body at the birth. It is revealed that median values of age mother among the PDA was slightly more senior (26 years), than in group of nonfunctioning.

Statistically not confirmed results of median values of the PDA are received. In 50% of cases of the closed arterial channels dumping of blood is not revealed during the period from 16,5 to 35 days. Median values of closing of arterial channels at a repeated research were 25,5 days.

Statistically not confirmed indicators of association of a factor of presence of congenital heart disease at mother in group of children with the PDA were received.

Conclusion: By results of the carried-out statistical analysis possible terms of closing of the PDA at newborns were revealed.

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Table 1
Dynamics of dumping of blood of arterial channels

Percentile	Dynamics of dumping of blood of arterial channels (days)					p=
	0 (n=62)	1(n=34)	2(n=33)	3 (n=24)	4 (n=9)	
25	15.5	17.75	14.0	16.5	15.0	0.168
50	23.0	22.0	21.0	25.5	20.0	0.168
75	30.0	29.25	24.0	35.0	30.5	0.168

Note: 0 – signs of the PDA at the first and repeated research are not revealed; 1 – reduction of dumping of blood at a repeated research (step-0,1sm); 2 – increase in dumping of blood at a repeated research (step-0,1sm); 3 – dumping of blood at a repeated research is not revealed, closing of the PDA; 4 – lack of dynamics of the amount of dumping of blood at the first and repeated research.

Table 2

The indicators influencing groups of arterial channels

Indicator	1)		2)		P=
	n	Me (Q1; Q3)	n	Me (Q1; Q3)	
Age of mother, years,	86	23 (23; 33,25)	75	26 (22; 31)	0.049
Age of father, years	75	29 (25; 36)	68	28,5 (25; 35,5)	0.261
Week of gestation	86	38 (36; 40)	76	39 (36; 40)	0.641
Weight (g)	86	2975,00 (2237,50; 3482,50)	76	3215,00 (2278,75; 3567,50)	0.360
Length (sm)	85	50 (46,5; 52)	75	51 (48; 53)	0.135

Note: p – the reached significance value of distinctions when comparing group with use of criterion of Kraskell-Willice.

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COMPARATIVE FEATURES OF METABOLISM AND FUNCTIONING OF THE EXTERNAL RESPIRATION IN YOUNG MALE RESIDENTS OF DIFFERENT CLIMATIC AND GEOGRAPHICAL AREAS OF RUSSIAN NORTHEAST

ABSTRACT

The environmental and climatic conditions of the North impose a special effect on the functioning of the body systems placing high demands on maintaining the internal constancy of the human body. Special attention should be paid to the system of external respiration which is the first to be adversely affected by cold air as well as possible changes in the metabolism of people who live under these climatic extremes for a long time. The varying degree of exposure to environmental factors, from moderate cold pressure to extreme combined effects, which have an influence on the whole body should be taken into account. The **purpose** of this work was to identify the peculiarities of metabolism rearrangements as well as the respiratory system functioning in young healthy individuals permanently residing in different climatic and geographical zones of northeastern Russia which differ significantly in the weather severity index.

Based on a study of spirometry and indirect calorimetry, a comparative study was conducted among 17-19 year old 678 young men from the North born Caucasians in their 1st and 2nd generations residing in Magadan region and Chukotka Autonomous Region. An analysis of the data showed that compensatory adaptive changes in physiological systems were observed in young men of all the examined groups. However most of all they were typical for residents of the continental part of Magadan region whose adaptive shifts were aimed at minimizing the pronounced cold effect of this climatic area. At the same time, the young men of this group were found to have the highest daily energy consumption indicators that ensure the maintenance of the increased heat production. Besides, they demonstrated the maximum permeability of the distal bronchioles among all the young surveyed men, which is necessary both for adequate oxygen supply to the body and protection from low ambient temperatures.

Keywords: young males, external respiration system, indirect calorimetry, metabolism, North.

One of the leading abiotic factors of the North which can lead to the depletion of compensatory and regulatory mechanisms as well as to disorders in constancy of the internal environment is the cold factor [2]. At the same time, the special structure of the climate of northern regions undoubtedly increases the "price of adaptation" which is not always experienced successfully by everybody [8]. Northeastern Russia is a vast territory, significantly different in environmental and climatic conditions as well as the degree of impact of these abiotic factors on humans. Magadan Region (MR) can be divided into significantly different sub-zones: the coastal part with the city of Magadan which is cyclonic and characterized by constant winds and relatively high air temperatures in winter (-15°C), and the continental part with the town of Susuman suggesting the almost absence of the wind exposure, but extreme temperatures in both summer ($+36^{\circ}\text{C}$) and winter (-53°C) as well as relatively low humidity [10]. It should be distinguished the coastal zone of Chukotski Autonomous District (CAD, Anadyr) referring to the sub-arctic climate zone. These unfavorable conditions force humans to use additional means of protection against the influence of the above environmental factors [13]. However, with respect to the respiratory system, this practice is

not applicable and it is that very system which is the first to be exposed to the negative effects of cold air. In this regard, the purpose of our work was to identify peculiarities of respiratory system rearrangements as well as metabolism of people permanently residing in different climatic and geographical zones of northeast Russia.

Materials and methods. To achieve this goal, 622 healthy young men aged 17-21 were comprehensively examined, all being Caucasians born in the North in the 1st and 2nd generations, permanently residing in the northeast of Russia. The first group were permanent residents of the city of Magadan (the coastal part of Magadan Region), the second group included persons from the town of Susuman (the continental part of Magadan Region), and the third group was made up of the young men from the city of Anadyr (the coastal part of the Chukotski Autonomous District).

The study was conducted in a room with a comfortable temperature. The method of spirometry was used to assess the function of external respiratory (FER), which is the main instrumental method to determine the possible presence of any diseases of the respiratory system [15]. Indicators of respiratory function were recorded in an open system on the principle of "volume-flow" using a computer

spirometry KM AP 01 "Diamant-S" (Russia). Due values were calculated using the method of R. F. Clement (et al.) being the generally accepted standard in the Russian Federation for the evaluation of spirometric samples [3]. The following indicators were analyzed: the time taken to perform a calm expiration that is Vital Capacity, (T_{VC} , s), and forced expiration that is Forced Vital Capacity, (T_{FVC} , s); Vital and Forced Capacity of the lungs (VC, FVC, L); Peak Expiratory Flow (PEF, L/s); Forced Expiratory Volume in the first second (FEV_1 , L); Forced Expiratory Flows at 25%, 50%, 75% ($FEF_{25\%}$, $FEF_{50\%}$, $FEF_{75\%}$, L/s); Medium Expiratory Flow ($MEF_{25-75\%}$, L/s) as well as two Indices of bronchial obstruction, Tiffno and Gensler (IT, IG, %).

The levels of metabolic processes in the body as well as some indicators of external respiration were estimated using the Medgraphics VO2000 metabolograph (USA) based on the "indirect calorimetry" method [14]. Energy consumption was determined at rest in a day (REE/day, kcal) both in kilocalories and as a percentage of the norm (REE/Pred, %). The Respiratory Rate (RR, cycle/min), Body Temperature and Pressure Saturation Volume (V_t BTPS, mL), Minute Volume of Body Temperature and Pressure Saturation (V_E BTPS, L), Respiratory Quotient (RQ, arb. units), Oxygen Consump-

tion and Carbon Dioxide Emission (VO_2 , VCO_2 , mL/min), the relative concentration of carbon dioxide and oxygen in exhaled air (FET CO_2 , FET O_2 , %), the proportion of Fats and Carbohydrates in the energy substrate (Fat/REE, CHO/REE, %), Oxygen Consumption per kilogram of weight, (Ox. Cons/kg, mL/kg), Oxygen Utilization Factor (Ox. Util. Fact., mL/L).

The study was carried out in accordance with the principles of the Helsinki Declaration. The study protocol was approved by the Ethical Committee for Biomedical Research at the NESC of the Far-Eastern Branch of the Russian Academy of Sciences (December 4, 2012; Protocol No. 3). All young men underwent research voluntarily.

Statistical data processing was performed using Microsoft Excel 2013. The average values of indicators (M) and average errors ($\pm m$) were calculated. Significance of differences was assessed by Student's t-test for independent samples. The null hypothesis of the presence of differences among the presented samples was accepted at $p < 0.05$.

Results and discussion. Table 1 presents indicators of the function of external respiration in young men of different cli-

matic and geographical zones. From the presented data it is clear that the smallest part of the differences was recorded for regions with a coastal climate, and the largest one when compared with the continental climate region. In the absence of significant differences in the vital capacity of the lungs, the Susuman residents had the lowest values for the forced capacity, the forced expiratory volume in the first second and the peak expiratory flow. The maximum values of them were observed in the residents of Anadyr. It should be noted that this was noted both in terms of actual and relative (as a percentage of the proper indicator) values. Considering the fact that the respiratory airways have the greatest surface contact with the external environment, this fact of reducing of the main characteristics of the bronchopulmonary system should be considered as a protective reaction of the body against the extremely low atmospheric air of Susuman [11]. At the same time, the indicated decrease in airflow of the upper structures of the lungs was compensated by the expansion of the distal bronchioles ($\text{FEF}_{75\%}$) the diameter of which in Susuman residents reached 150 % increase. The increase in the patency of the small

bronchi was also observed in the young men of the cities of Magadan and Anadyr, but such high values in $\text{FEF}_{75\%}$, as compared to the inhabitants of the central European part of Russia, could be observed only in the inhabitants of the continental part of Magadan Region. In addition to increasing in the amount of warm air remaining in the lungs, this increase in bronchopulmonary should certainly be considered as a mechanism to protect the lungs from pneumosclerotic manifestations, when in conditions of very low temperatures of Susuman there is an elevated production of surfactant necessary for moistening and warming the dry cold air [9]. Besides, an increase in the caliber of the distal bronchi contributes to the sustainable maintenance of the more efficient laminar nature of the air flow, which ultimately has a positive effect on the diffusion processes in the respiratory zone of the bronchopulmonary tree [1].

Table 2 shows the indicators of indirect calorimetry of the examined young men. Analysis of the data shows that, as in the case of the characteristics of the function of external respiration, most of the differences were observed among groups of young people from the continental and

Table 1

Indicators of the function of external respiration in 17-21 year old male residents of Magadan, Susuman and Anadyr ($M \pm m$)

Indicator	Habitat of the examinees			Significance of differences among groups		
	Magadan (1) n = 359	Susuman (2) n = 63	Anadyr (3) n = 42	1-2	2-3	1-3
T_{VC} , s	1.78 \pm 0.05	1.62 \pm 0.05	1.89 \pm 0.07	$p < 0.01$	$p < 0.01$	$p = 0.21$
VC, L	5.12 \pm 0.04	5.13 \pm 0.1	4.99 \pm 0.14	$p = 0.93$	$p = 0.42$	$p = 0.37$
VC, %	103 \pm 0.6	103 \pm 1.58	103 \pm 2.06	$p = 1$	$p = 1$	$p = 1$
T_{FVC} , s	1.38 \pm 0.04	1.13 \pm 0.05	1.8 \pm 0.06	$p < 0.001$	$p < 0.001$	$p < 0.001$
FVC, L	4.94 \pm 0.04	4.71 \pm 0.1	5.07 \pm 0.14	$p < 0.05$	$p < 0.05$	$p = 0.37$
FVC, %	102 \pm 0.64	97 \pm 1.65	108 \pm 2.2	$p < 0.01$	$p < 0.001$	$p < 0.01$
FEV_{12} , L	4.51 \pm 0.03	4.26 \pm 0.07	4.5 \pm 0.14	$p < 0.01$	$p = 0.13$	$p = 0.95$
FEV_{12} , %	106 \pm 0.6	101 \pm 1.31	107 \pm 2.59	$p < 0.001$	$p < 0.05$	$p = 0.71$
T_{PEF} , s	0.14 \pm 0.01	0.26 \pm 0.01	0.13 \pm 0.1	$p < 0.001$	$p = 0.36$	$p = 0.92$
PEF, L/s	9.92 \pm 0.08	9.12 \pm 0.16	10.17 \pm 0.29	$p < 0.001$	$p < 0.01$	$p = 0.41$
PEF, %	108 \pm 0.81	100 \pm 1.54	113 \pm 2.44	$p < 0.001$	$p < 0.001$	$p = 0.06$
$\text{FEF}_{25\%}$, L/s	8.91 \pm 0.08	8.51 \pm 0.17	8.73 \pm 0.27	$p < 0.05$	$p = 0.94$	$p = 0.52$
$\text{FEF}_{25\%}$, %	109 \pm 1	104 \pm 1.87	108 \pm 2.64	$p < 0.05$	$p = 0.22$	$p = 0.72$
$\text{FEF}_{50\%}$, L/s	6.32 \pm 0.1	6.31 \pm 0.15	5.73 \pm 0.2	$p = 0.96$	$p < 0.05$	$p < 0.01$
$\text{FEF}_{50\%}$, %	113 \pm 1.18	111 \pm 2.54	106 \pm 3.71	$p = 0.48$	$p = 0.27$	$p = 0.07$
$\text{FEF}_{75\%}$, L/s	3.81 \pm 0.05	4.16 \pm 0.13	3.32 \pm 0.15	$p < 0.05$	$p < 0.001$	$p < 0.01$
$\text{FEF}_{75\%}$, %	131 \pm 2.5	150 \pm 4.63	114 \pm 5.3	$p < 0.001$	$p < 0.001$	$p < 0.001$
$\text{MEF}_{25-75\%}$, L/s	6.34 \pm 0.06	6.29 \pm 0.13	5.54 \pm 0.2	$p = 0.73$	$p < 0.01$	$p < 0.001$
$\text{MEF}_{25-75\%}$, %	115 \pm 1.02	113 \pm 2.17	112 \pm 3.57	$p = 0.41$	$p = 0.81$	$p = 0.42$
IT, %	88 \pm 0.42	84 \pm 0.99	86 \pm 0.89	$p < 0.001$	$p = 0.14$	$p = 0.12$
IG, %	93 \pm 0.5	93 \pm 0.75	88 \pm 0.85	$p = 1$	$p < 0.001$	$p < 0.001$

Table 2

Indicators of indirect calorimetry in 17-21 year old male residents of Magadan, Susuman and Anadyr (M ± m)

Indicator	Habitat of the examinees			Significance of differences among groups		
	Magadan (1) n = 84	Susuman (2) n = 51	Anadyr (3) n = 23	1-2	2-3	1-3
REE/day, kcal	2145±59.5	2344±63.6	2048±74.5	p<0.001	p<0.01	p=0.31
REE/Pred, %	117±2.92	131±3.02	115±4	p<0.01	p<0.01	p=0.69
RQ, arb. units.	0.86±0.01	0.79±0.01	0.89±0.03	p<0.001	p<0.01	p=0.35
RR, cycle/min	14.5±0.49	18.2±0.72	14.7±0.8	p<0.01	p<0.01	p=0.83
Vt BTPS, mL	686±26.4	544±18.2	640±28.5	p<0.001	p<0.01	p=0.24
VE BTPS, L/min	9.22±0.31	9.08±0.27	9.2±0.56	p=0.74	p=0.85	p=0.98
V CO ₂ , mL/min	263±9.47	267±8.34	253±10.8	p=0.75	p=0.31	p=0.49
V O ₂ , mL/min	304±8.05	338±9.2	290±11	p<0.01	p<0.01	p=0.31
FET CO ₂ , %	3.59±0.05	3.72±0.07	3.6±0.11	p=0.14	p=0.36	p=0.93
FET O ₂ , %	16.68±0.07	16.24±0.09	16.7±0.19	p<0.001	p<0.05	p=0.92
CHO/REE, %	52±4.52	33±4.01	53±6.36	p<0.01	p<0.01	p=0.9
Fat/REE, %	48±4.48	67±4.01	47±6.33	p<0.01	p<0.01	p=0.9
Ox. Cons/kg, mL/kg	4.27±0.1	5±0.13	4.2±0.16	p<0.001	p<0.001	p=0.71
Ox. Util. Fact., mL/L	33.8±0.6	37.8±0.83	33.3±1.72	p<0.001	p<0.05	p=0.79

coastal areas. No significant differences through the groups from Magadan and Anadyr were found. The energy consumption at rest (REE) among the young men of all the three examined groups was higher than the proper values calculated using the Harris-Benedict formula [12]. It is noteworthy that the highest values of metabolism (131%) were demonstrated by the residents of Susuman which was achieved due to the more energy efficient lipid type of metabolism (Fat/REE). Under the North conditions, the transition of basic metabolism from carbohydrate to fat type is observed in aboriginal ethnic groups. The latter type, in conditions of extremely low temperatures of the continental climate zone, allows synthesize ATP more efficiently, optimally implementing the mechanism of maintaining the thermal balance of the internal environment of the body [5]. In the groups of the cities of Magadan and Anadyr, carbohydrates were the predominant energy substrate, which is also evident from the higher rates of respiratory quotient (RQ).

Of special note that, against the background of increased oxygen consumption by the bodies of young men from Susuman (by indicator of FET O₂), maintenance of VE BTPS was achieved not due to a more effective BTPS volume, but due to an increase in economically less favorable respiratory rate [7]. Apparently, a significant V_t BTPS decrease found in them compared to the young men of oth-

er groups is explained by the implementation of the strategy to protect the lung tissue from the effects of low ambient air temperatures. It is noteworthy that an increase in RR in this case cannot compensate for the lost volume of air entering the respiratory zone of the bronchial tree since shallow and frequent breathing results in ventilation of mostly anatomically dead space while the alveolar portions of the lungs remain unaffected. It becomes obvious that the mechanism for maintaining an adequate level of oxygen supply to the body at simultaneous protection of the lung structures from exposure to exogenous factors is the improved oxygen utilization by the body's tissues seen in oxygen utilization index (Oh. Util. Fact.) [6]. A significant increase in this value shown by the subjects from Susuman against the background of a growth in O₂ consumption per kg of the body weight (Ox. Cons/kg) indicates an increase in the diffusion of oxygen between the alveolar air and blood, which fully ensures the increased energy costs of the organism at low temperatures of the continental natural climatic zone.

Conclusion. Thus, the conducted studies have shown that the adaptive shifts in the body system functioning observed in permanent residents of north-eastern Russia increase with increasing the extremes of environmental and climatic factors. At the same time, for most indicators of the function of external res-

piration and energy metabolism, there were no significant differences among the young men living in the coastal climatic zones of Magadan Region and the Chukotski Autonomous District. The vector of functional rearrangements in persons living in the continental climate zone is aimed at protecting the lungs from obstructive and sclerotic lesions (limiting the depth of breathing, reducing the lung volume characteristics) on the one hand, and adequately providing of the body needs with increased oxygen and improving its delivery to organs and tissues (elevated O₂ Cons. and Ox. Util. Fact.) on the other hand. At the same time, this interaction of functional systems under conditions of extremely low temperatures is an example of effectively maintaining of the homeostatism of the internal environment of the body, which is bringing the residents of this territory closer to the "polar metabolic type" [4].

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THE ROLE OF DEFICIENCY OF THE CONTENT OF CIRCULATING LEUKOCYTES IN THE CONSERVATION OF IMMUNE STATUS IN PEOPLE IN LIFE CONDITIONS ON THE SPITZBERGEN ARCHIPELAGO

ABSTRACT

The **purpose** of the study is to establish the role of the deficiency in the content of circulating leukocytes in preserving the immune status of people in the conditions of life on the Svalbard archipelago. We surveyed 74 able-bodied residents of the village of Barentsburg Arch. Svalbard, 45 women and 29 men, aged from 20 to 60 years and 77 healthy people at the time of the survey, living in Arkhangelsk, 64 of them women and 13 men, aged 21 to 55 years. The hemogram, neutrogram, monocytoqram and lymphocytoqram were studied in blood smears stained according to the Romanovsky-Giemsa method, neutrophil phagocytic activity, lymphocyte phenotypes (CD3 +, CD4 +, CD8 +, CD10 +, CD19 +, CD23 +, CD71 +, CD95 +) by the method of indirect immunosypoxy. The content of cytokines IL-1 β , TNF- α , IL-6, irisin, endothelin-1 and Nt-pro-BNP was determined by ELISA. The concentration of the CEC - by the method of precipitation using PEG-6000. It has been established that neutropenia (32.43%), monocytopenia (28.38%) and lymphopenia (18.92%) are recorded in the working-age population living in the Spitsbergen archipelago. The decrease in the content of circulating neutrophils and monocytes is associated with a sharp increase in the activity and intensity of phagocytosis. On the background of neutropenia and monopenia, there is a deficiency in the content of mature T-lymphocytes (91.89%), activated T-cells with a receptor for transferrin and T-helper cells (44.59%). Against the background of T-cell deficiency, the levels of irisin (45%), Nt-pro-BNP (20%) and endothelin-1 (10%) are increased. Signs of compensatory proliferation of myeloid cells and lymphocytes are not installed. The decrease in the content of neutrophils occurs due to functionally active cells, low concentrations of monocytes, mainly promonocytes, lymphocytes - mostly of small forms, which constitute the majority of recycle cells. It has been established that the risk of T-helper immunodeficiency is very high. An increase in the activity of phagocytes does not fully compensate for the deficiency of their content in the blood, since elevated concentrations of the CEC are very often recorded at 55.41-100%.

Keywords: monocytes, mature T-lymphocytes, T-helpers, activated T-lymphocytes, neutrophil phagocytosis, irisin, brain natriuretic peptide (Nt-pro-BNP), endothelin-1.

Introduction. The influence of adverse climatic factors on the human body is associated with pronounced fluctuations in the functional activity of various systems with the expansion of the limits of fluctuations of almost all physiological parameters, reduction of the reserve capacity to regulate homeostasis. This concerns, first of all, the neuro-immuno-endocrine regulation of the functions of the cardiovascular system. The earliest reactions are from the side of catecholamines and short peptides, which alter the hemodynamics, frequency and strength of heart contractions. Thus, the short peptide endothelin-1 has a powerful vasoconstrictor effect [16]. The brain natriuretic peptide (Nt-pro-BNP) ensures the preservation of intracellular pressure by keeping sodium in the cell against the density gradient [10]. Irisin induces the activation of thermogenin in the cells of brown adipose tissue [14]. One of the pathogenetic factors of cardiovascular crises is the systemic effect of proinflammatory cytokines. Pro-inflammatory cytokines are secreted by any cell in response to a negative factor that threatens the integrity and functional activity of the cell. The physiological effect of cytokines is mainly local, but with an increase in their concentration in the blood, systemic damage may develop. Damage to endothelium cells during an inflammatory reaction is accompanied by their retraction

and the formation of gaps [8]. The instability of the immune system during a long stay in the polar region is accompanied by the formation of environmentally dependent immunodeficiencies. It is known that the T-cell homeostasis system is very stable and capable of self-preservation even with the elimination of 15% of the cells [11]. A secondary violation of the T-cell repertoire, up to immunodeficiency, usually develops through a violation of T-cell clonal equilibrium due to prolonged or extreme predominance of activation. The aim of the work is to establish the role of the deficiency in the content of circulating leukocytes in preserving the immune status of people in the conditions of life on the Svalbard archipelago.

Material and methods of research.

We surveyed 74 able-bodied residents of the village of Barentsburg Arch. Svalbard, 45 women and 29 men, aged from 20 to 60 years, during the polar day (July-August 2017) and 77 healthy people at the time of the survey are people living in Arkhangelsk, 64 of them are women and 13 are men aged 21 to 55 years. All studies were carried out with the consent of the volunteers and in accordance with the requirements of the Helsinki Declaration of the World Medical Association on the ethical principles of medical research (2000). The complex of immunological research included the study of the number and ratio of cells of

hemogram, neutrogram, monocytoqram, lymphocytoqram, phagocytic activity of neutrophilic peripheral blood leukocytes in blood smears stained by the Romanovsky-Giemsa method. The selection of mononuclear cells from peripheral blood was performed according to the method of A. Boum [6]. Phagocytic activity of neutrophils was studied after incubation of 100 μ l of citrated blood and an equal amount of reagent with Reactlex production latex at 37 ° C for 30 minutes. The phenotypes of peripheral blood lymphocytes (CD3 +, CD4 +, CD8 +, CD10 +, CD19 +, CD23 +, CD71 +, CD95 +) were studied by indirect immunoperoxidase reaction (Sorbert reagents, Moscow). The content of cytokines IL-1 β , TNF- α , IL-6, irisin, endothelin-1 and brain natriuretic peptide (Nt-pro-BNP) was determined by enzyme immunoassay in the serum on an automated immuno-enzyme analyzer "Bio-RAD" (Germany). The concentration of circulating immune complexes was determined by the standard precipitation method using 3.5%; four%; 7.5% PEG-6000. Mathematical and statistical analysis of the research results was carried out on a IBM / AT-Pentium 4 computer using the Microsoft Excel 2010 (USA) and Statistica 7.0 application software (StatSoft, USA).

Results and discussion. The inhabitants of the Spitsbergen archipelago have a lower total leukocyte count in pe-

peripheral venous blood (5.07 ± 0.18 and $5.80 \pm 0.19 \times 10^9$ cells/l; $p < 0.01$) due to neutrophilic granulocytes (2.48 ± 0.11 and $2.96 \pm 0.14 \times 10^9$ cells/l; $p < 0.05$) mainly with 2 and 3 segments of the nucleus (respectively, 0.62 ± 0.03 and $0.85 \pm 0.05 \times 10^9$ cells/l; $p < 0.01$ and 1.02 ± 0.05 and $1.24 \pm 0.06 \times 10^9$ cells/l ($p < 0.01$); neutropenia is registered in 32.43% of the patients (24 people). The deficit of active phagocytes is set at 14.71% and only in 4.48% of cases coincides with neutropenia. In individuals with neutropenia, a high level of phagocytic protection was recorded: $71.33 \pm 4.66\%$ with an intensity of phagocytosis - 9.67 ± 1.74 pcs. The residents of the village. Barentsburg increased neutrophil phagocytic activity level was detected in 30.88% (29 people) and averaged $91.0 \pm 1.38\%$ with phagocytosis intensity - 17.9 ± 1.75 pcs. It is known that adverse environmental factors in the early stages increase the activity of phagocytes, but further, reducing the reserve capacity, reduce the activity of phagocytosis and its intensity [1]. In the structure of the hemogram in the examined individuals of the Arctic settlement, the content of monocytes is lower (0.22 ± 0.02 and $0.37 \pm 0.03 \times 10^9$ cells/l; $p < 0.001$) mainly due to promonocytes (0.03 ± 0.002 and $0.16 \pm 0.02 \times 10^9$ cells/l; $p < 0.01$) and lymphocytes (2.19 ± 0.09 and $2.33 \pm 0.11 \times 10^9$ cells/l; $p < 0.05$) of mostly small forms (1.20 ± 0.05 and $1.42 \pm 0.08 \times 10^9$ cells/l; $p < 0.01$), which are known not only to circulate intensively, but are also capable of recycling [7]. Monocytopenia and lymphopenia were detected in 28.38 and 18.92% of the examined individuals, respectively. It is known that a decrease in the content of leukocytes is the main signal for admission of the corresponding cells from the depot to the circulation [7]. So, the main neutrophil depot is the lung capillary network. The tissue pool of monocytes is 3.5 times higher than the content of tissue neutrophils [13], so the migration processes of monocytes from the blood may seem less intense and appear less pronounced. There is an assumption that monocytes are recyclable [7]. Practically in all examined persons (91.89%), there was a deficiency in the content of mature T-lymphocytes (CD3+), the average level of which was $(0.61 \pm 0.03) \times 10^9$ cells/l. The low level of activated T-cells with transferrin receptor (CD71+) ($0.32 \pm 0.02 \times 10^9$ cells/l) is noteworthy, in 87.83% of cases there was a deficit of these cells, which makes it possible to judge the intensity of anaerobic metabolism in people living in the arctic territory. 10.81% of the inhabitants of the archipelago increased the content of cytotoxic lymphocytes (CD8+), the average

level of which was $(0.38 \pm 0.02) \times 10^9$ cells/l. In 44.59% of the examined, there was a deficiency in the content of T-helper cells, the average content of which was $(0.48 \pm 0.03) \times 10^9$ cells/l. A low content of immunocompetent cells labeled for programmed death by the Fas receptor was established, which corresponds to a low level of lymphoproliferation activity. Thus, the content of lymphocytes with the CD95 receptor was $(0.34 \pm 0.02) \times 10^9$ cells/l and in 87.83% of cases the level of these cells was lower than 0.6×10^9 cells/l. Against the background of insufficient content of mature T cells in the inhabitants of the archipelago, only 13.51% of cases showed signs of increased lymphocyte proliferative activity with an increase in the content of lymphocytes with CD10 receptor in the peripheral blood ($0.44 \pm 0.03 \times 10^9$ cells/l, as well as elevated levels of B lymphocytes with the CD19 receptor and the Fc receptor for IgE (0.43 ± 0.03) and $(0.38 \pm 0.03) \times 10^9$ cells/l, registered respectively in 14.86 and 20.27% of cases. Against the background of T-cell deficiency, residents of Spitsbergen most frequently recorded elevated concentrations of short peptides: irisin in 45% of the subjects, brain natriuretic peptide (Nt-pro-BNP) and endothelin-1, respectively, in 20 and 10% of cases. The content of Nt-pro-BNP, endothelin-1 and irisin among residents of the Arctic village, as well as among residents of the city of Arkhangelsk, is in a very wide range of fluctuations (respectively, 0.56 - 219.72 and 1.713 - 267.87 fmol/ml; 0.05 - 3.84 and 0.073 - 7.018 fmol/ml; 0.001 - 14.59 and 0.605 - 24.328 µg/ml). The most dramatic differences are very often established with respect to irisin; in other words, the problem of heat production is the most important. In the background are the problems of preserving the osmotic pressure of the cell by preserving sodium against the density gradient on the part of the brain natriuretic peptide and on the latter the dysregulation of vasoconstriction with endothelin-1. It is known that the content of irisin is interconnected with the concentrations of the main pro-inflammatory cytokines - TNF-α and IL-6 [12]. Indeed, individuals living in Spitsbergen archipelago have a higher concentration of pro-inflammatory TNF-α (14.05 ± 0.70 and 2.85 ± 0.37 pg/ml, $p < 0.001$) unchanged on the side of IL-1β (11.24 ± 3.22 and 9.63 ± 0.54 pg/ml) and IL-6 (5.59 ± 0.32 and 5.80 ± 0.52 pg/ml). Orientation toward inflammatory cytokines suggests a higher level of reactive oxygen metabolites, a sharp increase in phagocytosis. TNF-α plays an extremely important role in the first moments of the inflammatory reaction, because it acti-

vates the endothelium and promotes the expression of adhesive molecules, which leads to the adhesion of granulocytes to the inner surface of the vessel. Under the influence of TNF-α, the transendothelial migration of leukocytes occurs in the tissue [15]. On myocardiocytes there are specific receptors for irisin. Through these receptors, irisin is capable of enhancing metabolic processes, increasing mitochondrial biogenesis and increasing oxygen consumption and energy expenditure in myocardial cells, which is accompanied by inhibition of cell proliferation, but also contributes to their differentiation [9]. To prevent the loss of the extracellular pool and maintain the hydrodynamic pressure of the cells, the influence of the brain natriuretic peptide is activated [2]. At the same time, an increased level of Nt-pro-BNP is a risk of hemodynamic disturbances with possible signs of myocardial overload, left ventricular hypertrophy and renin-angiotensin system insufficiency, which provides the level of tissue oxidation [17]. Inhibition of lymphoproliferation and differentiation of lymphocytes with an increase in the content of brain natriuretic peptide in the blood is associated with a deficiency of IL-2 and is due to an increase in the concentration of IL-10. In the blood of the inhabitants of arch. Svalbard recorded elevated levels of circulating immune complexes. Thus, the average content of the CEC IgA is 3.9 ± 0.23 g/l, in 55.41% of cases elevated levels are noted. In 81.08% of the examined individuals, elevated concentrations of IgM CIC were detected with an average content of $6. \pm 0.40$ g/l. Anomalous CIC IgG values were established for all villagers, exceeding the upper limit of the norm by a factor of 13 - 45.3 ± 2.03 g/l. It is known that long-term circulation in the blood of the CEC contributes to the formation of their deposits in the tissues, on the basement membrane of small vessels and capillaries and leads to disruption of microcirculation, blockage of vessels, damage and necrosis of tissues [4]. This is facilitated by violations of blood flow, triggering the adhesion and aggregation of platelets, the release of vasoactive amines and an increase in vascular permeability. Thus, 56.76% of the examined individuals recorded platelet aggregation and their lysis. The CEC interacts with cells that have membrane Fcγ receptors for the components of the complement system, which enhances platelet aggregation with the involvement of collagen and fibrin in this process. Abnormally high levels of the CEC can disrupt microcirculation, accompanied by impaired blood supply, changes in migration, exudation and

transudation [3]. **Conclusion.** Thus, neutropenia (32.43%), monocytopenia (28.38%) and lymphopenia (18.92%) are recorded in the working-age population living in climatic and geographical conditions of the Spitsbergen archipelago. The decrease in the content of neutrophils occurs due to functionally active cells, low concentrations of monocytes, mainly promonocytes, lymphocytes - mostly small forms, which, according to the literature, constitute the majority of recycled cells. Small lymphocytes that retain information of antigens and which are predominantly T-cells of the reserve pool, are capable of being recycled, and are capable of further blast transformation and differentiation [5]. The decrease in the content of circulating neutrophils and monocytes is associated with a sharp increase in the activity and intensity of phagocytosis. An increase in phagocytic activity is likely to compensate for a decrease in the concentration of phagocytes in the blood and, possibly, is a reflection of the activity of the reactions of the microcirculatory bed. Against the background of neutropenia and monopenia, there is most often a deficit in the content of mature T-lymphocytes (91.89%), activated T-cells with a receptor for transferrin and T-helper cells (44.59%), i.e. The risk of T helper immunodeficiency is very high. Against the background of T-cell deficiency, the levels of irisin are increased (45%), which indicates the need to increase heat production. Signs of compensatory proliferation of myeloid cells and lymphocytes have not been established: the content of stab neutrophils, promonocytes, as well as large lymphocytes, CD10 + and CD95 + is not increased. The increase in the activity of phagocytes, in all likelihood, does not fully compensate for the deficiency of their content in the blood, since elevated concentrations of CIC are recorded very often (CIC IgA 55.41%, IgM 81.08% and IgG 100%). The voltage of hemodynamic regulation reactions is not so rare; elevated concentrations of Nt-pro-BNP and endothelin-1 were recorded, respectively, in 20 and 10% of the examined individuals.

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EVALUATION OF PHYSICAL DEVELOPMENT OF 3-7 YEARS CHILDREN IN THE MURMANSK REGION

ABSTRACT

The social and economic conditions that have changed dramatically in recent times have led to a change in the way of life of the indigenous peoples of the North and those who have lived there within ten generations. Such peoples in the Murmansk region include the Sami (Lovozer district) and Pomors (Tersk district). This change has a particularly strong impact on the younger generation. Evaluation of physical development of children is an external integral manifestation of the adequacy of the processes of growth and development to the changing conditions of existence of the organism. It is therefore necessary to monitor the growth and development of children and to obtain timely information on the physical development of children in changing conditions.

Materials and methods. Assessment of physical development of children aged 3-7 years was carried out in 2017-2018 in two districts of the Murmansk region – settlement Lovozero (Lovozer district) and Umba (Tersk district). All in all 237 children, including 116 girls and 121 boys residing and attending kindergarten were surveyed. The inclusion criterion was children with the first or the second group of health, with minor functional disorders, without chronic pathologies. All parents of the examined children were acquainted with the purpose and conditions of the study and gave their written consent to their child's participation in this study. The study of physical development parameters was carried out taking into account the requirements of the unified methodology and the use of one-dimensional centyl scales for children aged 3-17 years in accordance with the age group. To assess the contribution of socio-economic conditions, perinatal and neonatal periods, personal data provided by the parents of the surveyed children were used.

Results and conclusions. Analysis of physical development of children aged 3-7 years showed that the lowest rates of length and weight of the body are observed in children in Lovozero regardless of gender and age, which explains the ethnic characteristics of the Kola Saami. The largest jump in growth is observed in children aged 5.5 years. Sharply disharmonious physical development is observed in more than 30% of the surveyed children regardless of gender, age and place of residence. The main contribution to disharmonious development of the children of s. Lovozero makes the lack of mass and body length, and the children of s. Umba is overweight, and in girls it is more pronounced.

Keywords: physical development, children, preschoolers, length weight, body weight, centile tables, harmonious development, Murmansk region.

Introduction. Nowadays, the Arctic is a zone of claim of the international community, including the Arctic countries and recently the so-called "non-Arctic" countries. State policy in the field of subsoil use and the presence of industrial companies in the Arctic regions has a powerful impact on the livelihoods of the population, determining the need to adapt to changing conditions and largely to the socio-economic ones, which leads to a change in the way of life of indigenous peoples of the North and those who have lived there within ten generations. Such peoples in the Murmansk region include the Sami (Lovozer district) and Pomors (Terek district). This has the greatest impact on the child population. Evaluation of physical development of children is an external integral manifestation of the adequacy of the processes of growth and development to the changing conditions of existence of the organism [1, 4, 8, 11, 12, 15]. Any significant deviations from the norm in the physical development of children indicate a relative disadvantage in the health of the individual, subsequently determining the main features of the health of this generation in old age, including the transfer of appropriate qualities to the next generation. Social and environmental factors do not act in isolation, but in a complex interaction with biological ones, including

hereditary factors [3, 5, 9, 13, 14]. This determines the dependence of morbidity in children and adolescents both on the environment in which they live, and on the genotype and biological patterns of growth and development. Therefore, it is necessary to monitor the growth and development of children and obtain timely information about physical development as an integral indicator of morphological and functional processes in the growing body, especially in the Arctic.

Research material and methods. Assessment of physical development of children aged 3-7 years was carried out in 2017-2018 in two districts of the Murmansk region s. Lovozero (Lovozer district) and Umba (Tersk district). All in all, 237 children, including 116 girls and 121 boys residing and attending kindergarten were surveyed. In Lovozero, 127 children were examined, which accounted for 67% of the total number of children of this age, among them 64 boys and 63 girls; and in Umba - 110 children (50 %), among them 57 boys and 53 girls. All examined children had the first or the second group of health, with minor functional disorders, without chronic pathologies. According to the principles of medical ethics, approved by the UN General Assembly (1992), the Council of Europe Convention on Bioethics (1997) and the Council on Bioethics of the RCHAA KSC

RAS (18.01.2017), all parents of the examined children were acquainted with the purpose and conditions of the study and gave their written consent to their child's participation in this study

The study of physical development parameters was carried out taking into account the requirements of the unified methodology and the use of one-dimensional centyl scales for children aged 3-17 years in accordance with the age group. Indicators lying in the 25-75 cent range are referred to the variants of the norm, 10-25 and 75-90 are the border zones of quantitative characteristics of length and weight of the body, indicators lying outside the 90th and 10th centiles to low and very low values, while indicators lying above 97 and below 3 centiles reflect a clear pathology or disease [10]. Assessment of the degree of harmonic development was performed using the analysis of the difference of rooms and corridors (centiles) between the considered indicators, where: difference of not more than 1 corresponded to the harmonic development, 2 – moderate development there is disharmony; 3 or more points - disharmonious or heterochronic development [7]. Due to the fact that the rate of change in the indicators of physical development of the child varies in different periods of life, the age group for children 3-7 years was carried out at in-

Table 1

**Physical development of preschool childrens settlement Murmansk region
(Lovozero and Umba)**

Age	Lovozero				Umba			
	Body weight, kg		Body length, cm		Body weight, kg		Body length, cm	
	M±m	δ	M±m	δ	M±m	δ	M±m	δ
girls								
3,0	11.8±.7*	1.5	90.0±5.7*	11.4	13.8±0.8	1.7	95.8±1.8	3.5
3,5	13.8±0.6	1.2	93.5±1.2	3.3	14.6±0.6	1.7	96.0±1.6	4.2
4,0	13.6±0.9*	2.3	93.1±2.9*	7.7	16.7±0.4	1.0	103.7±1.3	3.1
4,5	14.9±0.6*	3.8	96.3±2.2	7.2	19.1±1.5	3.3	104.2±0.9	2.1
5,0	17.1±0.6	1.4	102.9±1.6	3.7	18.3±2.7	6.1	104.4±3.0	6.8
5,5	18.2±0.6	2.0	106.2±1.6*	5.0	20.0±0.8	1.9	114.4±1.2	2.9
6,0	19.6±2.0	5.0	109.1±3.5	8.6	23.2±2.0	4.9	118.7±1.3	3.2
6,5	19.6±2.2	5.8	110.3±3.9	10.4	24.1±2.1	6.4	118.8±2.0	6.1
7,0	21.1±1.5*	4.4	116.2±1.6*	4.9	27.7±3.6	8.0	123.6±1.5	3.3
boys								
3,0	12.3±0.4*	1.0	91.9±1.8*	4.3	13.7±0.3	0.6	95.2±1.7	3.4
3,5	14.5±0.5	1.3	95.6±1.7	4.7	14.5±0.5	1.5	95.4±1.6	4.8
4,0	13.7±0.2*	0.5	94.2±1.5*	3.2	17.7±0.9	2.4	101.4±1.3	3.4
4,5	16.4±0.5	1.7	101.7±1.5	4.9	17.9±0.9	2.3	102.8±1.9	4.9
5,0	16.4±0.6	1.2	107.7±0.6	1.1	19.1±1.5	4.1	107.9±2.0	5.4
5,5	19.9±1.8	5.5	111.7±2.0	7.1	19.2±0.8	2.0	111.6±1.7	4.2
6,0	20.1±1.0	2.1	113.1±1.2	2.8	21.4±1.5	3.0	116.3±2.2	4.4
6,5	22.6±1.3	2.9	116.1±1.8	4.1	22.6±1.5	3.9	116.7±2.1	5.5
7,0	23.3±1.5	5.1	117.2±1.5	5.1	23.4±0.7	1.5	117.9±1.8	4.0

Note. * – The significance of the differences (Mann-Whitney test) between the Lovozero and Umba

tervals of 6 months. The group of 5 year olds included children aged 4 years and 8 months to 5 years and 2 months, and the group of children 5.5 years of children from 5 years 3 months to 5 years 8 months etc.

To assess the contribution of socio-economic conditions, perinatal and neonatal periods, personal data provided by the parents of the surveyed children were used. Statistical analysis was performed using the software package "STATISTICA 6.0". U Mann – Whitney test was used to identify the significance of intergroup differences. Criterion U is the median of possible differences between the elements of the first and the second sample, and p is the level of significance of differences, which in this paper corresponded ($p < 0.05$).

Results and discussion. Measures of length and body weight of preschool children (3-7 years) showed that mostly regardless of gender and age of children the average length and weight of boys and girls in s. Lovozero is lower in comparison with children from Umba (table 1). The significance of differences in body length in the same age groups between girls from Lovozero and Umba was revealed only in three age groups of 4 ($p < 0.01$), 5.5 ($p < 0.001$) and 7 ($p < 0.01$) year-old children. Boys aged 3 ($p < 0.01$) and 4 ($p < 0.002$) years respectively. The average body length of girls in s. Lovozero varied from 90.0±5.7 cm to 116.2±1.6 cm and from 95.8±1.8 cm to 123.6±1.5 cm in Umba. In boys, changes in body length ranged from 91.9±1.8 cm to 118.2±1.5 cm in Lovozero and from 95.2±1.7 cm to 116.9±1.8 cm in Umba, respectively. The greatest increase is observed in children aged 5.5 years, and in girls from Umba it increased by 9%. The body weight of girls living in Lovozero varied from 11.8±0.7 to 21.1±1.5 kg in Lovozero and from 13.8±0.8 to 27.7±3.6 kg in Umba. In boys, respectively, from 11.8±0.7 to 21.1±1.5 kg in Lovozero and from 13.8±0.8 to 27.7±3.6 kg in Umba (table 1).

The assessment of the body length of children aged 3-7 years according to the centyl tables showed that mainly about 55% of children living in these settlements get into the 25-75 cent range, with the exception of girls from Lovozero 33.3% (table 2). There, about 49.2% of girls have values below 10 cents, which corresponds to low and very low body length values.

By body weight, the percentage of children corresponding to the average value (25-75 centyl range) does not exceed

40% in s. Lovozero and 50% in Umba. The lowest values (range <10 centiles) by body weight are observed in children from s. Lovozero girls - 33.3%, boys – 25%. Low values of physical development of 49.2% of girls and 25% of boys from Lovozero village are associated with ethnic specificity of body size typical for the Saami of the Kola North [6]. It is so? because physical development and physique are about 70 % determined by heredity and only 30% by environmental factors in which growth and development takes place. Analysis of the parents' sur-

vey showed that 75% of the interviewed parents were born in Lovozero and identify themselves as Sami, if not both parents, then one of them. The literature notes that the small size of the body of the Saami children is preserved throughout the period of growth and development of the child and does not exceed the 50th percentile of the all-Russian standards in body length and is typical not only for the Kola, but also for other groups of Saami. Thus, the body length of 9-year-old Sami children Inari and Kautokeino practically coincide with the

Table 2

Evaluation of physical development of childrens 3-7 years old by centile tables, (%)

Inhabited locality	Body length					Body weight				
	<10	10-25	25-75	75-90	>90	<10	10-25	25-75	75-90	>90
girls										
Lovozero n=63	49.2	11.1	33.3	4.8	1.6	33.3	15.9	39.7	7.9	3.2
Umba n=53	7.5	3.8	56.6	24.5	7.5	9.4	9.4	49.1	17.0	15.1
boys										
Lovozero n=64	25.0	14.1	54.7	3.1	3.1	23.4	26.6	32.8	10.9	4.7
Umba n=57	15.8	14.0	54.4	14.0	1.8	10.5	17.5	49.1	10.5	12.3

Table 3

Evaluation of preschoolers 3-7 years old by harmonious physical development according to centile tables

		centile on body length									
		Girls					Boys				
		<10	10-25	25-75	75-90	>90	<10	10-25	25-75	75-90	>90
centile on body weight		Lovozero									
	<10	30.2		1.6	1.6		14.1	4.7	4.7		
	10-25	11.1		1.6	1.6		12.5	6.3	9.4		
	25-75	4.8	11.1	17.5				4.7	26.6		
	75-90	3.2	3.2	7.9	1.6			1.6	7.8		1.6
	>90			1.6		1.6		4.7			1.6
		Umb									
	<10	3.8	1.9	3.8			7.0	3.5			
	10-25	1.9		3.8	3.8		3.5	3.5	8.8	1.8	
	25-75	1.9	1.9	28.3	3.8	1.9	3.5	7.0	29.8	7.0	
	75-90			11.3	11.3	1.9			8.8	1.8	1.8
	>90			11.3	5.7	1.9	1.8		7.0	3.5	

values of only the 25th percentile of US NCHS standards, as in the Sami children of Lovozero [16, 17]. At the same time, for boys after 4.5 years, the difference in growth between cities is smoothed. The length of the body height above the average prevailed at the girls Umba, and accounted for the age of 5.5 years, when they had the greatest increase in growth. The highest percentage of children with high body weight (range >90 centiles) is noted in children of Umba approximately 15.1% of girls and 12.3% of boys, which is considered the highest degree of deviation of physical development from the norm regardless of the length of the body [10]. This may be a consequence of malnutrition or lack of some components (vitamins, essential amino acids, trace elements, etc.), as chronic diseases metabolic disorders have not been identified. In the questionnaires, parents noted that the percentage of consumption of vegetables and fish in the diet of children at home has decreased; the consumption of carbohydrates (flour products, sweets) has increased. However, for a full assessment, an individual assessment of the degree of harmony of the child's development is needed.

Individual assessment of the degree of harmony of the child's development was carried out by analyzing the difference between the numbers of corridors (centiles) between the indicators (length and weight). Analysis of the degree of harmony showed that no more than 30% of the surveyed children have a harmonious physical development. The lowest percentage of 17.5% is observed in girls in Lovozero (table 3).

Sharply disharmonious physical development is observed in more than 30% of the surveyed children regardless of gender and age. Moreover, in children from the village of Lovozero, the main contribution is made by the lack of weight and length of the body. While in children from Umba disharmonious development is manifested in excess body weight, and in girls it is more pronounced, which differs from the structure of the contribution to the deviations of the Russian Federation, where more boys are overweight, and girls have lack of weight [2].

Conclusion. Thus, the analysis of physical development of children aged 3-7 years showed that the lowest rates of length and weight of the body are observed in children in Lovozero regardless of gender and age, which explains the ethnic characteristics of the Kola Saami. The largest jump in growth is observed in children aged 5.5 years. Sharply disharmonious physical development is observed in more than 30% of the surveyed children regardless of gender, age and place of residence. The main contribution to disharmonic physical development in children from Lovozero village is the lack of body weight and length, and in children from Umba this contribution is overweight, and in girls it is more pronounced.

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INFLUENCE OF CEMENT PLANT EMISSIONS ON MEDICINAL PROPERTIES OF MEDICINAL PLANTS IN CENTRAL YAKUTIA

ABSTRACT

The work is devoted to the study of the influence of cement dust on the medicinal properties of plants, namely the content of flavonoids in plants of Central Yakutia. Flavonoids being evolutionarily adequate to the human body, cause antioxidant, angioprotective, hepatoprotective, choleretic, diuretic, neurotropic, anti-oncological and other important pharmacological properties. The plants were collected in areas of high and medium pollution with cement dust. The study found that the plants of each species collected in different environmental conditions, different levels of flavonoids. In the zone of severe pollution with cement dust (at a distance of 500 m from the plant), the most pronounced decrease in the content of flavonoids in plants than in other study areas was noted. From the above data it can be seen that the spectrum of the content of substances of secondary synthesis varies in plants growing in conditions of atmospheric pollution, depending on the zone of influence of cement dust emissions. All species we study collected in the technogenic zone produce fewer flavonoids than plants collected in the control area. That is connected, in all probability, with the need to develop adaptive systems to change the cement environment. This fact is a consequence of the response to stress factors of plant organisms.

Consequently, it can be assumed that the content and accumulation of flavonoids depends on the presence and concentration of anthropogenic impurities in the atmosphere. According to the literature data, it was found that at a distance of 20 m from the plant there was the excess of biogenic elements B, Zn, Cu. Their high concentration in the soil is manifested in inhibition of growth, increase of lipid peroxidation and permeability of plant membranes.

Keywords: flavonoids, dietary supplement, cement dust.

Introduction. One of the directions of development of the pharmaceutical industry is to increase the range of new medicines, which include medicinal plant materials and products dietary supplemented on it. Currently, out of hundreds of thousands of medicines used in world medical practice, medicinal preparations from plants make up over 30%.

It has been established that with increasing extremes of climatic growing conditions in the tissues of a number of plant species, a greater number of bio-

logically active substances (DIETARY SUPPLEMENT) are synthesized [5, 7].

Intensive industrial development of natural resources has a negative impact on natural ecosystems. Due to emissions of solid particles, especially ash, soot, cement dust into the atmospheric air, dust layers are formed, which slow down the processes of photosynthesis. Cement dust, penetrating through the stomata during the gas exchange of leaves into plants, affects not only the surface, but also the cells inside the plant. The more

available moisture reserves from the soil are consumed, the earlier the plants experience a water deficit [3]. Photosynthetic activity decreases with an increase in leaf temperature and the onset of water deficiency [6].

"Yakutcement" is the largest cement plant of republican significance in Yakutia. The plant is located in the village of Mokhsogollokh Khangalassky district. Currently, the plant produces up to 300 thousand tons of cement per year, over 500 thousand tons of crushed stone.

Aerial emissions from this plant, along with oxides and nitrogen dioxide, sulfur dioxide, carbon dioxide and organic combustion products, contain a significant amount of cement, slurry and clinker dust, which is capable of alkalizing the environment [8].

We have conducted a study of plants collected in the zones of influence of cement dust and motor vehicle exhaust gases on the accumulation of flavonoids in them. A comparative phytochemical analysis of vegetation growing on technologically polluted sites is of great importance in terms of studying the mechanisms of plant adaptation to the negative effects of a polluted environment. Therefore, phytochemical studies are an essential part of the study of the biological resources of Yakutia.

Material and research methods. We studied 8 plants growing in Central Yakutia as the object of study: ordinary tansy *Tanacetum vulgare* L. (leaves, flowers), fireweed *angustifolia* *Chamaenerion angustifolium* (L.) Holub. (leaves, flowers), lanka astalavista *Linaria acutiloba* Fisch. ex. Reichenb. (leaves), Mongolian wormwood *Artemisia mongolica* (Bess.) Fisch. ex. Nakai (leaves), yakut wormwood *Artemisia jacutica* Drob. (leaves), elecampane British *Inula britannica* L. (leaves), dandelion horned *Taraxacum ceratophorum* (Ledeb.) DC. (leaves), yarrow ordinary *Achillea millefolium* L. (leaves), growing in Central Yakutia.

Plant samples were collected from communities in the vicinity of the "Yakutcement" plant in Moksogollokh, Khangalassky district, at a distance of 500 m, 1000 m and 2000 m in a linear, north-eastern direction. In total, 4 areas were selected for collecting plants.

Area number 1 is located on an artificial sand dump 500 meters from the "Yakutcement" cement plant. There are 14 species in the community, of which *Tanacetum vulgare* L., *Chamaenerion angustifolium* (L.) Holub., *Artemisia mongolica* (Bess.) Fisch. ex. Nakai., *Linaria acutiloba* Fisch. ex. Reichenb., *Taraxacum ceratophorum* (Ledeb.) DC. dominate. The total projective vegetation (TPV) cover is 30%.

Area number 2 is located 1000 meters from the cement plant "Yakutcement", adjacent to the highway. The objects of study are located in the larch-for-bury-cranberry forest with birches and willows. The stumps from the felling of trees is marked in the forest and there is an undergrowth of larch. *Larix dahurica* Turcz. ex. Trautv., *Betula pendula* Roth., *Salix bebbiana* Sarg. are noted in the

tree layer. The closeness of tree crowns is 5%. In the shrub layer, there are *Rosa acicularis* Lindl., *Vaccinium vitis-idaea* L., *V. uliginosum* (L.) In the grassy layer, there are 16 plant species, dominated by *Tanacetum vulgare* L., *Chamaenerion angustifolium* (L.) Holub., *Linaria acutiloba* Fisch. ex. Reichenb., *Vicia amoena* Fisch., *Inula Britannica* (L.). The TPV cover is 40%.

Area number 3 is located 2000 meters from the plant "Yakutcement" and 50 meters from the road. In the steppe grassy meadow, 15 plant species are noted, of which *Poa angustifolia* L., *Taraxacum ceratophorum*, *Chamaenerion angustifolium* Holub., *Tanacetum vulgare* L., *Hordeum jubatum* L., *Linaria acutiloba* Fisch. ex. Reichenb., *Artemisia mongolica* dominate. The TPV cover is 40%.

Area number 4 (control area) is located 67 km from the "Yakutcement" in the district of the village of Tabaga. The meadow is periodically trampled and eaten by cattle. The community includes 12 plant species dominated by *Geranium pratense* L., *Elytrigia repens* (L.) Nevski, *Acetosa thysiflora* (Finger.) A. Love et D. Love, *Tanacetum vulgare* L., *Chamaenerion angustifolium* (L.) Holub., *Potentilla bifurca* L., *Linaria acutiloba* Fisch. ex. Reichenb. The TPV cover is 90%.

Research methods. Geobotanical descriptions of communities are made according to the generally accepted method [4].

Quantitative determination of flavonoids was made using the standard method Shelyuto [9]. The dietary supplementis of this method is the ability of flavonoids to complex with aluminum chloride, with measurement of the optical density of the complexes in the visible region at a blue light filter, at a wavelength of 410 nm. In this case, we used cells with a layer thickness of 0.75 mm. The study was conducted using a spectrophotometer Specord - 40. Measurements were performed at a multiplicity of 3 times, 70% ethyl alcohol was used as an extractant. The calculation of the number of flavonoids was carried out according to a calibration schedule built according to the routine.

The plant material was collected in dry weather, during flowering, during the greatest accumulation of biologically active substances, namely in the first decade of July. Preparation of raw materials was carried out in a dark, ventilated area. The loss of raw material mass during drying was about 90%.

Statistic analysis of the data was performed using by Statistica 19 software. Standard methods of variation statistics

were used: the calculation of mean values, standard errors, 95% confidence interval. The data in the tables are presented in the form $M \pm m$, where M is the average, m is the average error. To assess the statistically significant differences in the data obtained, non-parametric methods, Student criterion, Spearman correlation analysis were used. The probability of the validity of the null hypothesis was taken at $p < 0.05$.

The discussion of the results. Near the plant, the area is subject to anthropogenic impact, which affects the density of the projective cover of vegetation. Plant communities are found in dry disturbed habitats covered with mud and cement dust. Currently, the vegetation in the village and its surroundings is mainly represented by anthropogenic ruderal communities. Birch disturbed highlighted by the presence and dominance in the community such synanthropic species as: ordinary tansy, wormwood Yakut, fireweed *angustifolia*, quack grass, lankaastalavista, dandelion ergonomy, melilotus officinalis, etc.

According to the Pokrovskaya Hydro-meteorological Service of the Republic of Sakha (Yakutia), northeast winds prevail in the study area [8]. This is due to the fact that the village is located on the open and high banks of the Lena River. Winds from the river side (south-west), as a rule, carry air masses in the northeast direction. Therefore, we chose the northeast direction from the cement plant as a place to gather plants.

The study found that plants of each species, collected in different environmental conditions, differ in the content of flavonoids.

Thus, a statistically significant decrease in the content of flavonoids was observed in flowers (Table 2) of plants. The most pronounced decrease in 2.5 times in the leaves and 2.2 times in the flowers was noted in *Tanacetum vulgare* L., and the smallest in the flowers of *Chamaenerion angustifolium* (L.) Holub. (1.13 times).

In the second section, there was a significant increase in the level of flavonoids compared with the first section of the study, but it remaining lower than in the control section. The greatest accumulation of flavonoids in 1.9 times was observed in *Tanacetum vulgare* L. It should be noted that an increase in their content in the leaves and flowers in this area occurred identically.

In the third study area, there was a decrease in the content of flavonoids in comparison with the second area. Per-

Content of flavonoids in the leaves (upper digits) and flowers (lower digits) of plants growing in different distances from the cement plant "Yakutcement"

Type of plant	500 m	1000 m	2000 m	Control area
Ordinary tansy <i>Tanacetum vulgare</i> L.	0.2821±0.0006* 0.2254±0.0006*	0.5397±0.0001*+ 0.4356±0.0001*+	0.4779±0.0001*++ 0.3947±0.0004*++	0.7105±0.0073 0.4001±0.0001
Fireweed angustifolia <i>Chamaenerion angustifolium</i> (L.) Holub.	0.5258±0.0003* 0.2417±0.0003*	0.788±0.0009*+ 0.3568±0.0001*+	0.6340±0.0006*++ 0.3223±0.0211*++	1.0614±0.0006 0.2754±0.0001
Lanka astalavista <i>Linaria acutiloba</i> Fisch. ex. Reichenb.	0.2974±0.0001* 0.3425±0.0003*	0.3786±0.0004*+ 0.4125±0.0003*+	0.3389±0.0006*++ 0.2138±0.0006*++	0.4878±0.0028 0.5628±0.0009

* - significance of differences $p < 0.05$ in comparison with the control area;

*+ - significance of differences $p < 0.05$, compared to the MCP at a distance of 500 m;

*++ - significance of differences $p < 0.05$, compared to the MCP at a distance of 1000 m.

haps this decrease is due to the fact that at a distance of 2000 meters from the Yakut Cement plant, plants are less susceptible to the effects of cement dust, as evidenced by their higher content than in the first section. At the same time, this site is located in the immediate vicinity of the highway (50 meters) and, most likely, vehicle exhaust emissions are also likely to contribute to this accumulation.

The data show that the spectrum of the content of substances of secondary synthesis varies in plants growing under conditions of atmospheric pollution, depending on the zone of influence of emissions of cement dust. All species studied by us collected in the technogenic zone produce less flavonoids than plants collected in the control plot. This is due, in all likelihood, to the need to develop adaptation systems to change the cement environment. Therefore, it can be assumed that the content and accumulation of flavonoids depends on the presence and concentration of man-made impurities in the atmosphere. The reduced production and accumulation of flavonoids are a consequence of the response of plant organisms to the presence of emissions of the cement plant (MCP) in the atmosphere.

In the process of technogenic impact on the soil cover in the area of the cement plant there are significant changes in the chemical composition of soils, increases their alkalinity and increases the accumulation of heavy metals, which subsequently affect the growth and development of plants [2].

It should be noted that the soil cover is one of the contributors to pollutants. The level of anthropogenic accumulation of chemical elements in soils is explained by their concentration, volumes and duration of emissions into the atmosphere. The study of the chemical composition of cement dust and its comparison with

the quantitative chemical composition in the control sod-carbonate soil in the impact zone of emissions from the "Yakutcement" plant were carried out by M.M. Shashurin. As a result of the studies, the excess of cement dust content was found in comparison with the soil: Sr – 700 mg/kg in cement dust (in the control soil 200 mg/kg); Ti – 2000 against 1250 mg/kg; Pb – 30 against 20 mg/kg; Zn – 400 against 100 mg/kg; Cu – 50 against 8.5 mg/kg in the control soil [8, 11].

The high concentration of these elements in the soil is manifested in inhibition of growth, increase of lipid peroxidation and permeability of plant membranes [3, 6]. In visual assessment, the main symptoms of poisoning plants with the above substances are: yellow tops of leaves, necrosis of plant tissues (begins with the edges of the leaves) [6, 15].

Any biotic or abiotic stress (exposure to pathogenic fungi, bacteria, viruses, temperature changes, mechanical damage, bright light, ultraviolet radiation, imbalance of mineral components in the soil, drought, salinity, exposure to ozone, herbicides, heavy metal salts) can lead to intensification of flavonoid biosynthesis in various anatomical parts of the plant [9, 13].

In the implementation of the stress-protective effect lie the antioxidant properties of these compounds. Any abiotic stress causes hyperproduction of hydrogen peroxide in chloroplasts, mitochondria and peroxisomes of the plant cell, along with the release of peroxidase and catalase by these organelles [10]. Significant amounts of H_2O_2 diffuse into vacuoles - the main location of flavonoids [12], which are able to effectively neutralize H_2O_2 and other active oxygen forms [14]. Their protective function is also carried out through the formation of barriers to infection or mechanical damage (tannins, lignins) and inherent antibiotic activity in

many of them.

A number of authors suggest that flavone compounds increase the tolerance of plants to adverse environmental conditions [1, 9]. It is known that in non-typical habitats its flavonoid complex, reflecting a specific type of secondary exchange, varies significantly and does not coincide with similar profiles characteristic of the species in this region [1, 13]. In addition, the objectives of the study included the study of the flavonoid complex for the analysis of ecological and cenotic number of communities growing in the territory of the Mokhsogollokh Cement plant. All the above mentioned factors of plant growth in Yakutia undoubtedly affect the accumulation of dietary supplement.

Conclusion. The therapeutic properties of medicinal, pharmacopoeia plants studied by us in Central Yakutia are greatly reduced in the areas of strong and medium pollution with cement dust, as evidenced by the small accumulation of flavonoids in these areas than in the control area. At the same time, in these two areas, tansy ordinary *Tanacetum vulgare* L. can serve as an indicator of pollution, since the content of flavonoids in it is most significantly reduced than in other plants. Man-made loads on the natural environment around industrial enterprises depend on many factors. This should take into account, first of all, the volume of emissions into the air and discharges into surface and groundwater of substances that pollute the environment, the area of direct mechanical destruction of soil and vegetation cover in the area of industrial enterprises, local industries, the duration of man-made load, natural conditions.

As the distance from the cement plant for a distance of up to 2 km, the General condition of the vegetation improves, the plant organs have no external signs of damage or weakening. It can be as-

sumed that the content and accumulation of flavonoids depends on the presence and concentration of anthropogenic impurities in the atmosphere. Reduced production and accumulation of them are a consequence of the response of plant organisms to the presence in the atmosphere – the emission of MCP. Collection of medicinal plants near cement plants is not recommended, as the medicinal properties of medicinal plants, grown in such conditions, are reduced. Since there is an accumulation of carcinogenic substances, carbonates, which can harm human health and the environment as a whole.

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DIAGNOSTIC AND TREATMENT METHODS

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DYNAMICS OF THE RESISTANCE TO ANTIMICROBIAL DRUGS IN THE MULTIDISCIPLINARY SURGICAL HOSPITAL FROM 2006 TO 2016

ABSTRACT

The analysis of the structure and resistance to antimicrobial agents of purulent-inflammatory disease pathogens in patients in a multidisciplinary surgical hospital has been carried out. It was revealed that *Escherichia coli*, *Klebsiella pneumoniae*, *Klebsiella oxytoca* are leading in the structure of pathogens of purulent-inflammatory diseases. The statistical forecast assumes a further increase in the proportion of microorganisms of the *Enterobacteriaceae* family and an increase in the proportion of pan-resistant strains of *Klebsiella pneumoniae*. According to the results of microbiological monitoring, it is necessary to use protected aminopenicillins and levofloxacin as the starting empirical therapy for the treatment of infections caused by *E. coli*, and for *K. oxytoca*, *Kl. pneumoniae* - levofloxacin, IV generation cephalosporins and carbapenems.

Keywords: microbiological monitoring, antimicrobial drugs.

Introduction. Purulent-septic diseases occupy one of the leading positions in the morbidity structure in the multidisciplinary surgical hospital. Number of patients with purulent-septic diseases is about one-third of all surgical patients. The modern range of surgical treatments (abdominal and thoracic surgery, bones and joints, vessels, etc.) create the danger of suppuration of postoperative wounds, which often leads to direct threat to patients' lives. More than half of all deaths after surgery are associated with the development of infectious complications.

Treatment of purulent-septic diseases is multipurpose and necessarily includes the use of antimicrobial drugs.

Discovery of antibiotics in the XX century leads to a significant decrease in severity and mortality from purulent-septic diseases. However, in recent years, the growth of microorganisms' resistance to antibiotics has become an urgent public health problem [2]. Its importance is determined by the fact that antimicrobial resistance affects many aspects. The spread of resistant microorganisms in hospitals leads to an increase of hospitalization, treatment costs, and lethality, especially in high-tech interventions (heart surgery, transplantation, oncohematology) [1].

The economic importance of antibiotic resistance is determined by compulsory usage of antibiotics with wider spectrum, which cost higher than the traditional drugs for treating infections caused by

sensitive microorganisms. The social aspect is determined by the increase of population morbidity, disability, and by the need of using more expensive drugs.

The data of microorganisms' resistance to antibiotics in specific hospital is unique, because there are significant differences in consumption of antibiotics, implementation of medical care standards, and use of the infection control programs in different hospitals. Regarding to the above, there is a need to conduct a local monitoring of antibiotic resistance to optimize the pharmacotherapy for patients with purulent-septic diseases [5].

Aim of the research. To analyze the structure and resistance to antibiotics of purulent-septic diseases pathogens and determine exact treatment for primary empirical antibacterial therapy.

Research problems

1. To analyze dynamics of causes' structure of purulent-septic diseases in the multidisciplinary surgical hospital.

2. Determine the indicators of resistance to antibiotics.

3. Construct a short-term mathematical prognosis about the dynamics of purulent-septic diseases etiology to improve the effectiveness of primary empirical antibacterial therapy.

Research materials and methods. A retrospective complete copy of effective research from the journals of the bacteriological laboratory was taken during the period from 2006 to 2016. (2006. n = 610, 2009. n = 504, 2012. n = 476, 2014. n =

468, 2016. n = 748) about the identification of pathogens and their antibacterial resistance indicators obtained from patients undergoing treatment in a multidisciplinary surgical hospital. Identification of bacteria was carried out according to the documents which regulate the work of bacteriological laboratories. Determination of the of microorganisms' sensitivity to antibiotics was made using the disk-diffusion method. Interpretation of sensitivity indicators was done according to the clinical recommendations "Determination of microorganisms' sensitivity to antibiotics" (approved at the 16th International Congress on Antibiotic Chemotherapy MAKMAX / ESCMID, 21-23 May 2014, Moscow) [3]. Clinical Hospital №10 in Khabarovsk is a modern well-equipped multi-specialized clinic. The hospital is represented by departments of surgical and therapeutic profile. The hospital bed capacity is more than 450 beds, the main type of emergency care provided is surgical, the number of bed - days spent by patients is more than 150 thousand per year, about 15 thousand patients are hospitalized annually. The statistical analysis of the results was counted using descriptive statistics methods in MS Office EX-CEL 2003 and the χ^2 method. The significant differences level was taken as $p < 0.05$.

Results and discussion. Analysis of etiological agents causing purulent-septic diseases in the Clinical Hospital №10 over 10 years showed an increase in the proportion of gram-negative microorgan-

isms of the *Enterobacteriaceae* family, which summary composed over 50% in 2016 (Fig. 1).

With the construction of a prognosis until 2020, further increase in the proportion of microorganisms of *Enterobacteriaceae* family was expected. Whereas it's going to be a decrease in the proportion of gram-positive microorganisms ($p < 0.05$). At the same time, the relative low proportion of non-enzyme-forming gram-negative microorganisms attracts attention.

Among the microorganisms of the *Enterobacteriaceae* family *Escherichia coli*, *Klebsiella pneumoniae*, *Klebsiella oxytoca* occupy leading positions (Pic. 2). The proportion of *Escherichia coli* in 2006 was 17.2%, and in 2016 increased to 22.5% ($p > 0.05$), *Klebsiella pneumoniae* 6.1% and 22.6% ($p < 0.05$), *Klebsiella oxytoca* 3.6% and 5.5% ($p > 0.05$) respectively.

The most significant increase was observed in *Klebsiella pneumoniae*. The proportion of which rised by more than 4 times during the studied time period.

Number of *Proteus mirabilis* and *Proteus vulgaris* ($p > 0.05$) remains almost unchanged.

Number of *Pseudomonas aeruginosa* also remains unchanged. Showed 1.6% ($n = 10$) in 2006, and 1.9% ($n = 14$) in 2016 ($p > 0.05$).

Among gram-positive microorganisms, there was a significant decrease in the number of *Staphylococcus epidermidis* from 38.4% to 8.2% ($p < 0.05$) over the studied period. A similar situation is observed with *Staphylococcus aureus*. Its' number showed a tendency to fall from 22.5% to 19.9% ($p > 0.05$).

Indicators of *E. coli* resistance to antibiotics (2006-2016) demonstrate high levels of resistance to the β -lactam group. As for aminopenicillins this indicator is numbered 100% in 2016. For cephalosporins of the third generation there was an increase in resistance indices for cefotaxime from 32.4% in 2006 to 73.2% in 2016 ($p < 0.05$), and for ceftazidime from 54.0% in 2009 to 60.7% in 2016 ($p > 0.05$) (Table 1). Attention is paid to the persistent low rates of resistance to protected penicillins, which showed 25.5% in 2009. and 19.0% in 2016 ($p > 0.05$), which is probably due to the extended spectrum of β -lactamase production by *E. coli*, in which there

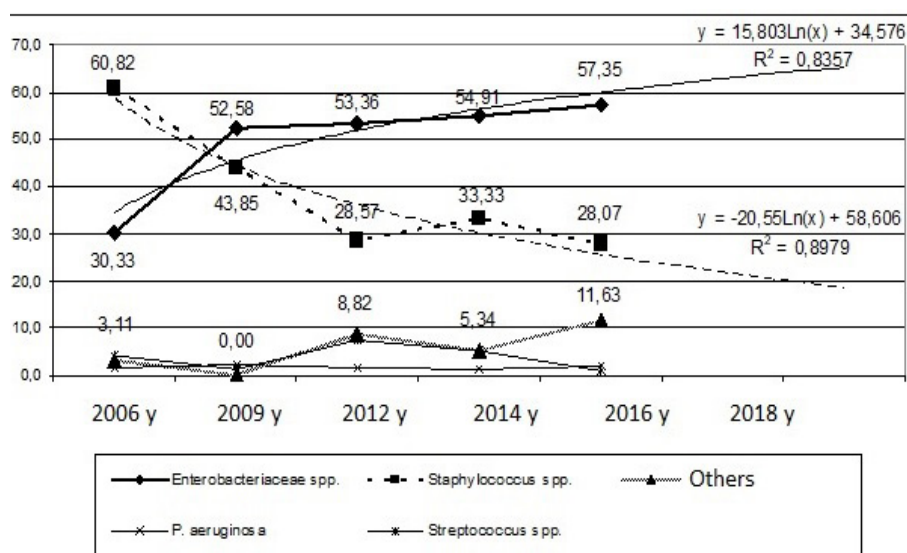


Fig. 1. Structure of microorganisms, selected in samples in 2006 – 2016, predicted to 2020

is a resistance to cephalosporins of I-IV generations and sensitivity to protected aminopenicillins remains [4]. At the same time, over 10 years, a decrease in *E. coli* resistance to fluoroquinolones for ciprofloxacin was noted from 73.3% in 2006 to 19.0% in 2016 ($p < 0.05$) and levofloxacin from 87.6% in 2006 to 20.8% in 2016 ($p < 0.05$). Low levels of resistance in *E. coli* are noted for meropenem 4.7% and amikacin 10.7% in 2016.

In 2006-2016 *Klebsiella oxytoca* showed high levels of resistance to the group of β -lactam antibiotics: for aminopenicillin in 2016 this indicator amounted to 100%, for cephalosporins of the third generation an increase in resistance indices was observed to cefotaxime from 13.6% in 2006 to 78.05% in 2016 ($p < 0.05$) and to ceftazidime from 18.2% in 2006 to 61% in 2016 ($p < 0.05$) (Table 1). The level of *Klebsiella oxytoca* resistance to protected aminopenicillins dynamically

increased from 0% in 2006 to 48.8% in 2016 ($p < 0.05$), which is fundamentally different from *E. coli*. Perhaps, it is an indicator of the *Klebsiella oxytoca* production of gram-negative bacteria chromosomal β -lactamase class C. During the research period there was a decrease in *Klebsiella oxytoca* resistance to ciprofloxacin from 81.8% in 2006 to 31.7% in 2016 ($p < 0.05$) and the increase in resistance to levofloxacin from 22.7% in 2006 to 31.7% in 2016 ($p > 0.05$). In 2016 low levels of resistance among *Klebsiella oxytoca* was noted only to meropenem 7.3%.

In 2006-2016 similar indicators of resistance also noted among *Klebsiella pneumoniae*. An increase in resistance percentage was shown for cefotaxime from 51.4% in 2006 to 75.0% in 2016 ($p > 0.05$), ceftazidime from 51.4% in 2006 to 68.0% in 2016 ($p > 0.05$), amikacin from 0% in 2006 to 45.0% in 2016 ($p < 0.05$), to

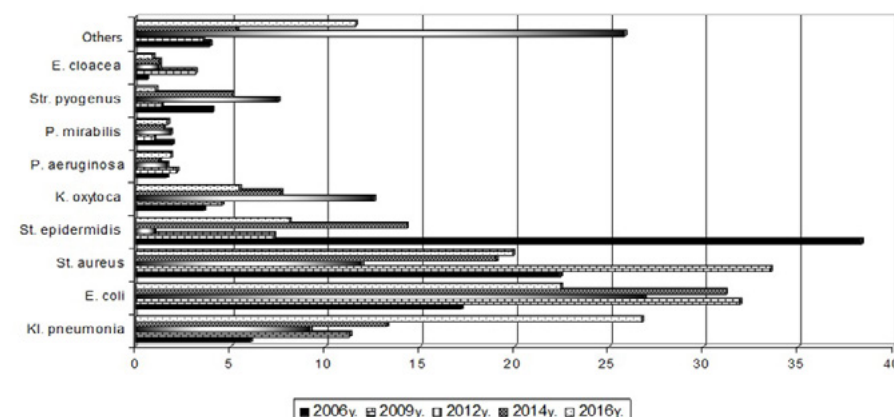


Fig. 2. The etiological causes' structure of the purulent-septic diseases in the multidisciplinary surgical hospital, 2006 – 2016, %

Table 1

The resistance of *E. Coli*, *Klebsiella oxytoca* and *Klebsiella pneumonia* to antibiotics in the multidisciplinary surgical hospital in a multidisciplinary surgical hospital 2006-2016, %

Antibiotic	<i>E. coli</i>					<i>K. oxytoca</i>					<i>K. pneumonia</i>				
	2006	2009	2012	2014	2016	2006	2009	2012	2014	2016	2006	2009	2012	2014	2016
	n=105	n=161	n=128	n=146	n=168	n=22	n=23	n=60	n=36	n=41	n=37	n=57	n=44	n=62	n=200
Ampicillinum	100.00	97.52	92.19	95.21	100.00	4.55	100.00	100.00	88.89	100.00	100.00	100.00	100.00	98.39	100.00
Amoxitilinum/clav. acid	-	25.47	27.34	15.75	19.05	0.00	17.39	6.67	16.67	48.78	48.65	45.61	43.18	38.71	53.50
Cefuroximium	-	-	44.53	67.81	-	-	-	43.33	61.11	-	-	-	43.18	82.26	100.00
Cefotaximum	32.38	45.34	67.97	58.90	73.21	13.64	13.04	50.00	47.22	78.05	51.35	63.16	34.09	72.58	75.00
Ceftazidime	-	54.04	38.28	52.74	60.71	18.18	21.74	50.00	52.78	60.98	51.35	50.88	20.45	61.29	68.00
Cefepimum	-	0.00	22.66	37.67	51.79	-	-	16.67	38.89	51.22	-	-	13.64	37.10	62.50
Meropenem	-	16.15	4.69	1.37	4.76	-	13.04	6.67	0.00	7.32	-	19.30	11.36	9.68	29.00
Ciprofloxacinum	73.33	57.14	82.81	25.34	19.05	81.82	73.91	75.00	61.11	31.71	81.08	68.42	70.45	51.61	51.50
Levofloxacinum	87.62	53.42	57.03	33.56	20.83	22.73	34.78	73.33	41.67	31.71	94.59	78.95	63.64	46.77	49.00
Amicacinum	0.00	34.16	45.31	35.62	10.71	27.27	43.48	56.67	55.56	29.27	0.00	59.65	43.18	29.03	45.00
Doxycyclinum	8.57	20.50	67.19	41.78	62.50	36.36	39.13	46.67	30.56	63.41	45.95	40.35	45.45	38.71	95.50

Meropenem from 19.3% in 2009 to 29.0% in 2016 ($p > 0.05$). Negative predictive occasion for a medical organization is the identification of pan-resistant strains (PDR (pandrug resistance) - resistance of microorganisms to all antibiotics) *Klebsiella pneumonia*. For the first time, pan-resistant strains of *Klebsiella pneumonia* were detected in 2014 (among three patients) - 4.8%, but already in 2016 these strains were seen already among 46 patients - 23% ($p < 0.05$).

More advantageous situation with levels of resistance to antibiotics is noted in *Staphylococcus aureus*. Despite the increase in the number of oxacillin-resistant strains of *Staphylococcus aureus* (MRSA) from 0.7% in 2006 to 39.6% in 2016 ($p < 0.05$), only one vancomycin-resistant strain was detected in 2016.

Conclusions

1. The main position in the cause structure of purulent-septic diseases is occupied by *Escherichia coli*, *Klebsiella pneumoniae*, *Klebsiella oxytoca*, *Staphylococcus aureus*.

2. Predictively the increase in density of *Enterobacteriaceae* family and panresistants strains of *Klebsiella pneumonia* is expected.

3. The sensitivity of strains of *Staphylococcus aureus* demonstrates a high number of oxacillin-resistant strains (MRSA).

4. According to the results of microbiological monitoring protected aminocillin and levofloxacin should be used as the primary starting therapy for *E. coli* and levofloxacin, cefalosporins IV generation and carbapenem should be used for *Kl. oxytoca*, *Kl. Pneumonia*.

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Table 2

The resistance of *St.aureus* to antibiotics in the multidisciplinary surgical hospital in a multidisciplinary surgical hospital 2006-2016, %

Antibiotic	<i>S. aureus</i>				
	2006	2009	2012	2014	2016
	n=137	n=169	n=57	n=89	n=149
Ciprofloxacinum	6.6	39.6	70.2	69.7	35.6
Levofloxacinum	2.9	34.9	42.1	62.9	34.2
Amicacinum	13.1	68.0	70.2	75.3	36.9
Doxycyclinum	8.8	16.0	22.8	69.7	40.9
Lincomycinum	89.1	87.0	59.6	60.7	34.9
Erythromycinum	100.0	68.6	84.2	87.6	41.6
Oxacillinum	0.7	39.1	54.4	68.5	39.6
Vancomycinum	0.0	0.0	0.0	3.4	0.7
Linezolidum	-	-	0.0	0.0	0.0

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THE DIAGNOSTICS AND TREATMENT OF ENDOGENOUS INTOXICATION IN PATIENTS WITH MANDIBLE TRAUMATIC OSTEOMYELITIS

ABSTRACT

Quite often standard methods of treatment of traumatic osteomyelitis of the lower jaw do not lead to a suppression of the purulent-inflammatory process in the bone tissue and the disease acquires a lukewarm torpid nature of the flow with periodic exacerbations. An important task of clinical medicine is to determine the presence and assessment of the severity of endogenous intoxication. For diagnostics, it is usually proposed to determine the level of endotoxin substances and parameters of the cellular composition of the blood, special indexes of intoxication are calculated for facilitating the interpretation of these changes in populations and subpopulations of blood cells, but a sufficient evidence base to facilitate the interpretation of laboratory data is not yet formed.

The **aim** of the study was to determine the diagnostic efficiency of laboratory parameters in endotoxemia caused by traumatic osteomyelitis of the lower jaw, as well as the development of a diagnostic algorithm and complex treatment depending on the stage of chronic endogenous intoxication. Patients with traumatic osteomyelitis of the lower jaw at the age of 18 to 65 years were examined. In addition to the traditional clinical and laboratory examination, an assessment of the nature and severity of chronic endogenous intoxication was carried out using the developed test suite.

As a result of the study, it was found that the most informative in the prognostic plan is the definition of the level of "medium-mass molecules", diene conjugates and the sorption capacity of erythrocytes. Other parameters investigated, including integral leukocyte indices of intoxication, are inferior to them for diagnostic value. Analysis of the results of clinical and laboratory studies shows the important role of chronic endogenous intoxication in the imbalance of homeostasis systems that caused atypical or torpid manifestations of the disease. The results of the study showed that the most informative methods for detecting the presence and subsequent dynamic monitoring of the level of endogenous intoxication should be recognized as the definition of sorption capacity erythrocytes and the level of "medium-mass molecules". Integral leukocyte indices of intoxication can be used to identify patients at risk of a complicated course of the disease, who need an in-depth biochemical examination.

Keywords: traumatic osteomyelitis, sorption capacity of erythrocytes, leukocyte indices of intoxication, endotoxemia.

Introduction. Increasing the effectiveness of treatment of traumatic osteomyelitis of the lower jaw (TOLJ) continues to be one of the urgent problems of maxillofacial surgery. Quite often the standard methods of treatment do not lead to the suppression of the purulent-inflammatory process in the bone tissue and the disease acquires a torpid nature of the flow with periodic exacerbations [1, 2, 5].

Long-term presence of microorganisms and their toxins in the bloodstream,

accumulation of under-oxidized metabolic products lead to the development of chronic metabolic stress of the patients' body. Endogenous intoxication is extremely important, and with a certain phase of the disease it becomes a leading pathogenetic element of many chronic inflammatory diseases of the maxillofacial region. According to the definition, endotoxemia is a complicated autocatalytic process that eventually acquires a universal character, that less

and less depends on the mechanisms that triggered it. During an endotoxemia unbalanced biologically active substances are becoming aggressive agents. The term of "endogenous toxic substances" means substances of biological origin, which accumulating in the body above the normal level, have a damaging effect on organs and systems [3]. In this case, the basic systems of biotransformation and toxic substances get unbalanced, that lead to the development of

chronic endogenous intoxication in the compensated, subcompensated or decompensated stages [1, 2, 8, 9]. In this connection, the conventional complex therapy of TOLJ often turns out to be ineffective, and the disease acquires a torpid flow with frequent exacerbations and recurrences. Such a course of the disease determines an unfavorable clinical prognosis and requires more detailed clinical and laboratory diagnosis and the introduction of new methods of treatment [1, 7, 8].

Determination of the presence and assessment of the severity of endogenous intoxication is an important task for clinical medicine. For the diagnosis of endotoxemia is usually suggested to determine the level of some endotoxic substances [3] and the parameters of the cellular composition of the blood, which, apparently, reflect the protective reaction of the organism. Moreover, in order to facilitate the interpretation of these changes in populations and subpopulations of blood cells, it was suggested to calculate specific indices of intoxication [4]. Along with this, despite a rather large number of studies, the evidence base, which will facilitate the interpretation of laboratory data has not yet been formed.

The purpose of this study is to determine the diagnostic efficacy of laboratory indicators for endotoxemia caused by traumatic osteomyelitis of the lower jaw, as well as the development of a diagnostic algorithm and complex treatment, depending on the stage of chronic endogenous intoxication.

Materials and methods of research.

We examined 468 patients with traumatic osteomyelitis of the lower jaw at the age of 18 to 65 years. With the simple randomization method, patients were divided into two clinical groups: the main (with the inclusion of the efferent therapy in the complex treatment scheme) and the comparison group, where patients were treated with a traditional set of therapeutic measures. The criteria for inclusion in the study were: a clinically established and radiologically confirmed diagnosis of traumatic osteomyelitis of the lower jaw, the patient's consent to participate in the study. A group of practically healthy people aged from 20 to 62 years was examined, in order to determine the regional indicators of the norm. Formed groups were representative and comparable to each other in terms of age and sex.

In addition to the traditional clinical and laboratory examination, we evaluated the nature and severity of chronic en-

dogenous intoxication with the help of the complex of tests, which were developed by us [1, 2, 8, 9].

The level of toxemia was determined by the content of average molecular weight (AMW) in blood plasma by spectrophotometric method [3], the level of accumulation in the blood plasma of primary (diene conjugates) and final (dienketones) products of lipid peroxidation - modified Z method Placer et al. (1976), the content of malonic dialdehyde - by the method of M. Mihara, M. Uchiyama (1978).

To determine the degree of membrane damage, the sorption capacity of erythrocytes (SCE) was determined according to A.A. Togaibaevu (1988).

To assess the condition of the antioxidant system, the total antioxidant activity of plasma (P. Prieto et al. 1999), the activity of superoxide dismutase (VA Kostyuk et al., 1990) and catalase (MA Korolyuk et al., 1988) in serum and erythrocytes of peripheral blood were determined.

To assess the changes at the system level, the analysis of changes in hemogram and leukocyte formula of the blood was carried out, as well as the calculation of a number of integral indicators: hematological index of intoxication by V. S. Vasiliev (1983), leukocyte index of intoxication (LII) by I. Y. Calf-Caliph (1941), hematological index of intoxication by G. N. Karabanov (1993).

Patients with associated somatic pathology in the stage of decompensation or remission of less than 3 months were excluded from the study. Materials for the biochemical study were erythrocytes and blood serum, blood draw was carried out from the cubital vein. The multiplicity of studies was determined by the following parameters: at the time of hospitalization before the beginning of surgical treatment, on the 3rd -4th and on the 8-10th day after the operative intervention. To characterize these indicators, their predictive value (positive predictive value), specificity and sensitivity were determined by R. Fletcher et al. [6].

To define the difference between the compared averages, the t-test of the Student was used, the differences were significant for $p < 0.05$.

Results and its discussion. The clinical picture of traumatic osteomyelitis of the lower jaw among the patients of both clinical groups was characterized by a long torpid course of disease (from 2.5 months to 1.5 years) with repeated relapses (up to 35% in the comparison group), the absence of a clear delineation

of the stages of the disease, mild general symptoms of the inflammatory process, lack of correlation between general and local manifestations of the disease.

As a result of the study, it was found that the most informative in the prognostic plan is the definition of the level of "medium-mass molecules", diene conjugates and the sorption capacity of erythrocytes. The value of these indicators exceeded 91%. Other parameters, including integral leukocyte indices of intoxication, were inferior in diagnostic value. In this case, the sensitivity of determining the level of "medium-mass molecules" and the sorption capacity of erythrocytes was absolute, and the specificity was 82% and 91%, respectively. While the sensitivity of determining diene conjugates was only 70%. The predictive value of the determination of TBA-positive products did not exceed 60%, and the total antioxidant activity - 80%.

Analysis of the results of clinical and laboratory studies has convincingly demonstrated the important role of chronic endogenous intoxication in the imbalance of homeostasis systems, which caused atypical or torpid manifestations of the disease.

The received data pushed us to a revision of the traditional scheme of treatment of traumatic osteomyelitis of the mandible in the direction of expanding the methods of a fight against existing endotoxemia. For each stage of chronic endogenous intoxication, we have developed the concept of complex treatment, in addition to traditional therapy, we have included various methods of extracorporeal detoxification, (discrete plasmapheresis, intravenous laser irradiation of blood, indirect electrochemical oxidation of blood, reinfusion with ultraviolet irradiated blood, enterosorption), application of antihypoxic drugs, according to the medical evidence - etiotropic antibiotic therapy, and a new approach for choose the right time of surgical operations. As a result, among the patients of the main group with a sub- and decompensated stage of chronic endogenous intoxication, the level of endogenous intoxication on the 8th day after the operation was significantly decreased in comparison with the corresponding parameters in the comparison group (Table 1).

The results of the remaining studies also indicated a significant decrease in the level of chronic endogenous intoxication.

The proposed scheme of complex treatment of patients with sub- and de-

Table 1

Dynamics of indices of endogenous intoxication among the patients with traumatic osteomyelitis of the lower jaw

Indicator	Stage of chronic endogenous intoxication	Level while hospitalization	On the 8th day after the operation with traditional treatment (comparison group)	On the 8th day after operation (main group)
Level of AMW (254 нм), standard units	Decompensated	0.543 ±	0.387 ±	0.256 ±
	Subcompensated	0.480 ±	0.347 ±	0.268 ±
	Compensated	0.358 ±	0.288 ±	0.247 ±
Level of AMW (280 нм), standard units	Decompensated	0.727 ±	0.429 ±	0.309 ±
	Subcompensated	0.577 ±	0.425 ±	0.329 ±
	Compensated	0.464 ±	0.393 ±	0.306 ±
Level of SCE, %	Decompensated	50.9 ±	39.7 ±	28.4 ±
	Subcompensated	45.3 ±	33.4 ±	26.0 ±
	Compensated	39.6 ±	30.9 ±	29.2 ±
Leukocyte intoxication index (LII), standard units	Decompensated	2.33 ±	1.67 ±	0.93 ±
	Subcompensated	2.17 ±	1.32 ±	0.74 ±
	Compensated	2.08 ±	1.36 ±	1.01 ±

Note. In the Tables 1 and 2 * - significant differences from the comparison group, $p < 0.05$.

compensated stage of chronic endogenous intoxication led to a significant reduction in the duration of inpatient treatment among patients of the main group (Table 2). Clinical recovery was achieved in 91.1% of patients in the main group, compared with 64.8% in the comparison group.

Conclusions. Thus, the results of the study showed that the definition of the sorption capacity of erythrocytes and the level of "medium molecular weight" should be recognized as the most informative methods for detecting the presence and subsequent dynamic monitoring of the level of endogenous intoxication. Integral leukocyte indices of intoxication can be used to identify patients at risk of a complicated course of the disease, who need an in-depth biochemical examination.

Carried out treatment according to the developed program made it possible to significantly improve the results of treatment of patients with decompensated and subcompensated stage of chronic endogenous intoxication, allowed to optimize the course of the postoperative period, to reduce the number of complications and relapses of the disease.

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Table 2

Postoperative bed-day among the patients with TOLJ with complicated course of the postoperative period

Stage of chronic endogenous intoxication	Traditional treatment of TOLJ (comparison group), days	Including the complex treatment of efferent therapy (main group), days.
Decompensated	25.6 ±	19.6 ±
Subcompensated	24.0 ±	17.6 ±
Compensated	19.6 ±	19.3 ±

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PATTERNS OF COMPLICATIONS IN THE PERIOPERATIVE PERIOD AND MORTALITY IN PATIENTS WITH ANEURYSMAL SUBARACHNOID HEMORRHAGE

ABSTRACT

The article presents the results of studying the patterns of complications and mortality from aneurysmal subarachnoid hemorrhage (aSAH) at the Anesthesiology, Reanimation and Intensive Care Unit (ARICU) of the Republic's Hospital No. 2 – Center for Emergency Medical Aid (ARICU RH No. 2 – CEMA) of the Sakha Republic (Yakutia) for the period of 2015-2017. During the study period, various complications were diagnosed in the preoperative period in 67.3% of the patients and in 64.7% of cases following surgery, and the mortality rate of this group of patients was 5.8% (9 patients).

The dominating pattern of the preoperative complications was cerebral vasospasm, with the specific gravity of 81.9%. Other complications of this period included ruptured aneurysms and cerebral edema with dislocation syndrome, 9.0% and 4.8% of the complications, respectively.

The complications during surgeries were of a technical nature and observed in 12.8% of the cases, leading to changes in surgical planning. These included ruptured aneurysm (85% of intraoperative complications), as well as pronounced cerebral edema and the impossibility of applying clips.

In the postoperative period, 64.7% of the patients had various intra- and extracerebral complications, which amounted to 61.38% and 38.6%, respectively, in the patterns of complications. Among the intracerebral complications, delayed cerebral ischemia (DCI) with 39.60% ranked first. This complication was more often observed in patients transported by air ambulance from district hospitals (32.1%) than among patients from the city of Yakutsk (19.2%). Among the extracranial complications, nosocomial pneumonia (NP) and severe cerebrocardiac syndrome (CCS) were more often diagnosed, making 20.79% and 12.87% in the patterns of postoperative complications.

Of the total number of treated patients, 62.2% of the patients were discharged with full recovery, 21.1% - with mild neurological deficit, 10.3% - with moderate neurological deficit, and 0.6% - in the vegetative state.

The data presented indicate the relevance of the issues related to treating patients with aSAH in the region, as well as the importance of measures for further improvement of the treatment, diagnostic and organizational-tactical approaches aimed at reducing complications and mortality in this group of patients.

Keywords: aneurysmal subarachnoid hemorrhage, intracerebral complications, extracerebral complications, cerebral vasospasm, nosocomial pneumonia.

Introduction. Currently, aSAH is diagnosed in over 75-85% of all hemorrhages in the subarachnoid space, posing a real threat to the lives of patients and remaining one of the topical issues in the neurological stage of reanimatology [13].

The recent studies show that the annual aSAH frequency in the world varies from 2-22.5 cases per 100,000 of population depending on a region, is more common in people over 50 years of age and develops mostly in women [9, 10, 13]. According to statistics from the Ministry of Health of the Russian Federation, the frequency of newly diagnosed subarachnoid hemorrhages (SAH) among adults in recent years has averaged 11.44 per 100,000 of population (in 2015 -13.69; in 2016 - 9.37; 2017 - 11.25 per 100,000 of population). In the Sakha Republic (Yakutia), the frequency of newly registered SAH among the adult population for the same period was 13.60, 11.31 and 12.86 per 100,000 of the population, respectively [3].

The median aSAH mortality rate in developed countries is as follows: the United States – 32%, England – 18%, European countries – 44%, Japan – 27% [13]. In Russia, the SAH mortality, given the latest management protocols, is at the level of 14.5% [6]. According to Chugunova S.A. and co-authors, in 2015, the Sakha Republic had the share of hemorrhagic strokes at 26.2% [8]. Our previous studies revealed that at the Center for Emergency Medical Aid of the Sakha Republic (Yakutia) in the period 2011-2015 ruptured aneurysms were observed in 50.75% of patients having been operated for non-traumatic SAH, and the mortality rate in this category of patients made 34.21% [1].

The modern approach to the treatment of aSAH involves active neurosurgical tactics and the use of various methods of intensive observation and therapy. Moreover, the right timing of surgery, objective neurological monitoring in the immediate postoperative period, monitoring the effectiveness of therapy, as well as prevention of complications are recognized as the main factors for the successful outcome of this severe pathology [7, 9]. It is proved that the main causes of disability and mortality of this group of patients are due not only to the direct effect of hemorrhage (55% of patients), or its recurrence (up to 17% of patients) [11], but also delayed cerebral ischemia, which is observed in 20-40% of patients [14, 15].

Cerebral vasospasm and ischemic cerebral damage should be attributed to the most common and severe compli-

cations during ruptured aneurysms. According to the Fisher grading scale, with grade 2 basal hemorrhage, cerebral vasospasm develops in 100% of cases, and cerebral ischemia occurs in over 50% of patients. Cerebral vasospasm, forming on days 3–4 from the onset of the disease and reaching the maximum by days 7–14, can lead to total obliteration of the vascular bed in 20% of cases. Cerebral infarction develops in more than 60% of patients with cerebral vasospasm [5, 7, 14, 15].

The next most frequent and severe complication is aSAH recurrence, developing in 17-26% of patients with aneurysm, in 5% of patients with arterio-venous malformation and very rarely with SAH of a different etiology. Most often, repeated hemorrhage occurs due to lysis of a blood clot at the ruptured aneurysm location, most often on day 1 (4%) and in the following 4 weeks (1–2% per day) [6, 9, 11].

Extracerebral complications such as pulmonary edema, myocardial ischemia, cardiac arrhythmias, hyperthermia of noninfectious genesis, venous thrombosis with complications, hyponatremia, which are observed in 10–20% of patients [6, 9, 11, 15], should be also taken into consideration.

Thus, the treatment of patients with SAH, and with aSAH in particular remains a topical issue in practical health care. From this point of view, a study of treatment results, an analysis of the frequency of development and patterns of complications, and mortality of aSAH patients in the specialized center of the Sakha Republic (Yakutia) is relevant.

The research objective is to study the patterns of intra- and extracerebral complications and mortality in aSAH patients having been operated at the specialized center of the Sakha Republic (Yakutia) in the period 2015-2017.

Materials and Methods. We conducted a retrospective analysis of the perioperative complications in 156 patients having been operated for aSAH and treated at the Anesthesiology, Reanimation and Intensive Care Unit (ARICU) of the Republic's Hospital No. 2 – Center for Emergency Medical Aid in the period 2015- 2017.

The age of the patients ranged from 19 to 79 years (mean age 51.4 ± 10.7 years); there were 52 men (33.3%) and 104 women (66.7%). All the patients were admitted for emergency reasons, with 78 (50.0%) patients having been transported by air ambulance from district hospitals of the republic.

The diagnosis of aSAH was confirmed in the preoperative period by instrumental studies with the X-ray computed tomography (CT); the diagnostic measures were carried out in accordance with the guidelines for the management of patients with SAH [7, 9, 12].

The neurological status of the patients was assessed at admission and in dynamics by the Glasgow Coma Scale (GCS) and the Hunt-Hess scale, before discharge – by the Glasgow Outcome Scale [7, 9, 12].

All the patients underwent surgical treatment: craniotomy for resection, hematoma removal, and arterial aneurysm clipping. The clinical guidelines for the management of patients with aSAH [9] were used for determining indications and scale of a surgery, anesthesia administration and postoperative intensive care.

Results and Discussion. The assessment of the patients' condition by the conscious state (GCS) and the severity (Hunt-Hess scale) at admission showed the following. The conscious state by GCS was 15 points (full consciousness) in 107 (68.6%) patients, 14-11 points (stupor) – in 38 (24.4%), 10-9 points (semicoma) – in 7 (4.5%), 8-6 points (moderate coma) – in 3 (1.9%), 4-5 points (deep coma) – in 1 (0.6%) patient. There were no patients in the terminal coma (Table 1).

Assessing the severity of a patient's condition at the beginning of treatment by the Hunt-Hess scale is of significant predictive value in terms of survival. In the study group, at admission, the severity of state of most patients was assessed at 1 (66 patients, or 42.3%) and 2 points (55, or 35.3%). These were the patients with full consciousness, minimal neurological deficit and prediction of survival at 60-70%. The number of patients with 3 points was 25 (16.0%) (prediction of survival at 50%); with 4 points - 7 (4.5%) patients (prediction of survival at 20%). The distribution of the patients by the studied years showed that while the share of the patients with 1 and 2 points did not change significantly, the share of the patients with 3 and 4 points increased in 2016-2017, and there were 3 (1.9%) patients with 5 points. These were the patients in a state of deep coma, with the prediction of survival at 10% (Fig. 1).

During the study period, an increase in the number of patients transported by the Republic's Center for Disaster Medicine (RCDM) was observed: in 2015 - 14 (29.2%), in 2016 - 30 (50.0%), in 2017 - 34 (70.8%). However, the transportation time of these patients to the specialized

Table 1

Assessment of the patients' conscious state by GCS at admission

ШКГ (баллы)	Год			Итого
	2015	2016	2017	
15	33 (68,7)	42 (70,0)	32 (66,7)	107 (68,6)
14-11	13 (27,1)	15 (25,0)	10 (20,8)	38 (24,4)
10-9	2 (4,2)	1 (1,7)	4 (8,3)	7 (4,5)
8-6	-	1 (1,7)	2 (4,2)	3 (1,9)
5-4	-	1 (1,7)	-	1 (0,6)
3	-	-	-	-
Всего	48	60	48	156

center from the onset of the ruptured aneurysm showed a decreasing trend: 5.4 ± 3.4 days in 2015, 5.5 ± 3.8 in 2016 and 3.0 ± 2.4 in 2017.

The great majority of the patients (108, or 69.2%) were operated within the first 5 days from the onset of hemorrhagic stroke, with 45 (28.8%) patients undergoing surgery in the acute period (in the first 2 days). The remaining patients underwent delayed surgeries: on days 6-10 - 25 (16.0%) patients, on days 11-15 - 8 (5.1%) patients, and in 16 days or more - 16 (10.3%) patients. The delayed surgery tactics was applied to the patients in critical condition with initial scores by the Hunt-Hess scale at 4 and 5 points (without intracerebral hematomas requiring emergency surgery), as well as in the cases of progressing concomitant pathologies.

The studies of the nature and localization of aneurysms indicated that single aneurysms (78.2% of the cases) and aneurysms of the middle cerebral artery (MCA) (47.4%) prevailed. Aneurysms of the anterior cerebral artery (ACA) and the internal carotid artery (ICA) made 34.6% and 18.0%, respectively (Table 2).

In 21 (13.5%) patients, hemorrhage was accompanied by the formation of intracerebral hematomas with a volume of over 50 cm^3 , and 70 (44.9%) patients suf-

fered blood breakthrough into ventricles of cerebrum.

A study of the patterns of complications during the management of patients with aSAH revealed the following results. In the preoperative period, complications were noted in 105 (67.3%) patients. Cerebral vasospasm (from functional to severe) was most frequent in the preoperative period and was diagnosed in 86 (55.1%) patients, being verified by instrumental studies (transcranial Doppler study with calculating the linear blood flow velocity, angiography or CT in the angio-mode). Accounting for 81.9%, the specific gravity of this complication among other preoperative complications was significantly higher. According to the recent studies, the pathogenesis of vascular spasm and ischemic changes as-

sociated with it during aSAH is complex and diverse. Its most important elements are intracranial hypertension, increased intracellular Ca^{2+} in smooth muscle cells and neurons, disruption of cell energy supply, dysfunction of ion channels, and inflammatory changes due to the blood-brain barrier breakthrough. The severity of vasospasm depends on the scale of a hemorrhage [5, 11].

In addition, in the preoperative period, the risk of repeated ruptured aneurysms remained due to the tactics of delayed surgeries. Within different periods (from 1 to 10 days), 14 (9.0%) patients experienced repeated ruptured aneurysms (13.3% of the preoperative complications).

Before the surgery, 5 (3.0%) patients had pronounced cerebral edema with dislocation syndrome (4.8% of the preoperative complications).

The complications during surgery were observed in 20 (12.8%) cases; they were of a technical nature and led to changes in the surgical planning. These were cases of ruptured aneurysm in 17 patients (85% of the reasons for the change in operational tactics); thus, the final clipping was performed on the second stage, after the application of temporary clips on the artery in order to stop the blood flow. Due to pronounced cerebral edema and the impossibility of applying clips in 3 patients (15% of the changes in operational tactics), the scope of the surgery was limited to decompression trepanning. In these cases, two patients underwent successful embolization later, and one patient died of a repeated hemorrhage.

In the postoperative period, 101 (64.7%) patients experienced various intra- and extracerebral complications, which accounted for 61.38% and 38.6% in the patterns of complications, respectively (Table 3).

The patterns of intracerebral com-

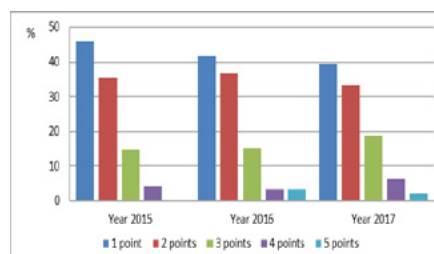


Fig. 1. Distribution of the patients by the Hunt-Hess scale at admission

Nature and localization of arterial aneurysms

Table 2

Nature and localization of aneurysms	Years						Total	
	2015		2016		2017			
	number	SG (%)	number	SG (%)	number	SG (%)	number	SG (%)
Nature of aneurysm								
Single	37	77.1	47	78.3	38	79.2	122	78.2
Multiple	11	22.9	13	16.7	10	20.8	34	21.8
Total	48	100	60	100	48	100	156	100
Localization of aneurysm								
ACA	20	41.7	10	16.7	24	50.0	54	34.6
MCA	19	39.6	36	60.0	19	39.6	74	47.4
ICA	9	18.7	14	23.3	5	10.4	28	18.0
Total	48	100	60	100	48	100	156	100

Table 3

The patterns of complications in aSAH patients in the postoperative period

Complications	Years			Total number, (%)
	2015	2016	2017	
Intracerebral complications	17 (16.83)	18 (17.82)	27 (26.73)	62 (61.38)
Delayed cerebral ischemia	8 (7.92)	10 (9.90)	22 (21.78)	40 (39.60)
Postoperative epi- and subdural hematomas	1 (0.99)	2 (1.98)	1 (0.99)	4 (3.96)
Repeated hemorrhage due to clip disposition	2 (1.98)	-	1 (0.99)	3 (2.97)
Occlusive hydrocephaly	2 (1.98)	-	-	2 (1.98)
Meningitis	1 (0.99)	-	2 (1.98)	3 (2.97)
Central diabetes insipidus	3 (2.97)	6 (5.94)	1 (0.99)	10 (9.90)
Extracerebral complications	10 (9.90)	17 (16.83)	12 (11.88)	39 (38.61)
Infectious complications, including:	6 (5.94)	10 (9.90)	8 (7.92)	24 (23.76)
- nosocomial pneumonia,	6 (5.94)	8 (7.92)	7 (6.93)	21 (20.79)
- sepsis	-	2 (1.98)	1 (0.99)	3 (2.97)
Pulmonary embolism	-	1 (0.99)	1 (0.99)	2 (1.98)
Severe cerebrocardial syndrome	4 (3.96)	6 (5.94)	3 (2.97)	13 (12.87)
TOTAL	27 (26.73)	35 (34.65)	39 (38.61)	101 (100)

plications of the postoperative period were dominated by DCI – 39.60% of all the complications (40 patients). Moreover, this complication increased by more than 1.5 times in 2017 compared to the years 2015-2016. This can be explained by the increase in the share of the patients with 3 and 4 points on the Hunt-Hess scale, which is demonstrated in the diagram above (Fig. 1). In addition, the analysis of each DCI case showed that this complication was more often observed in the patients transported by air ambulance from district hospitals than among patients from the city of Yakutsk — 32.1% and 19.2%, respectively. This fact indicates the importance of adequate prevention and treatment of cerebral ischemia during the management of patients in district hospitals, as well as their transportation, taking into account all aspects of its pathogenesis (vascular spasm, intracranial pressure, energy supply of neurons, etc.).

Another serious complication occurred in 10 (9.90%) cases of central diabetes insipidus (DI). Polyuria, characteristic of this syndrome, leads to pronounced water-electrolyte imbalance, requiring large-volume infusions, the introduction of potassium solutions, antidiuretic drugs, and lengthening the duration of ICU treatment of these patients. In our study, we observed a female patient with polyuria up to 34 liters a day. Previously, we published a clinical case of DI with severe polyuria (maximum daily diuresis of 22.7 liters) for 12 days in a female patient

with aSAH [4].

Being diagnosed in 21 patients and making 20.79% in the patterns of postoperative complications, NP stands out in the extracranial complications. This pathology was confirmed by clinical, instrumental (plain radiography and CT of the chest) and microbiological studies. These data indicates that the problem of NP for ICU patients remains relevant. Thus, in a study conducted at the ARICU CEMA in 2015 on patients with acute impairment of cerebral circulation, it was found that NP complicated the course of the disease in 36% of cases, and ventilator-associated pneumonia was found in 27% of the patients [2]. Gram-negative microorganisms were the causative agents of the hospital pneumonia: *Pseudomonas aeruginosa* (MBL) – 56%, *Klebsiella pneumonia* (BLRS) – 82%, *Escherichia coli* (BLRS) – 51% of the cases, and gram-positive microorganisms: *Staphylococcus aureus* (MRSA) – 10. 5% of the cases.

Severe CCS complicated the course of disease in 13 patients and amounted to 12.87% in the patterns of complications. This group included the patients without concomitant coronary heart disease (CHD), and they had to undergo targeted pharmacological correction due to CCS. These cases were combined with an extensive hemorrhage, severe brain damage and occurred in all the patients with the unfavorable outcome.

The mortality of aSAH patients over the study period was 5.8% (9 patients died): in 2015 – 4.2% (2 patients), in

2016 – 6.7% (4 patients) and in 2017 – 6.3% (3 patients). The analysis of the mortality confirmed the adequacy of the Hunt-Hess scale, used for assessing the severity of patients in the acute period of SAH (Fig. 2).

As can be seen in the diagram, the highest mortality was observed in the patients with 4 and 5 points by the Hunt-Hess scale: 2 patients died in each group, making 28.6% and 66.7%, respectively.

The analysis of mortality showed that intracranial complications were the direct cause of death in 6 (3.9%) patients: large-scale hemorrhage with cerebral edema and dislocation syndrome (3 patients) and repeated hemorrhage (3 patients). Severe extracranial complications caused the deaths of 3 (2.9%) patients: NP complicated by sepsis (1 patient), PE (1 patient), and pseudomembranous colitis complicated by peritonitis and abdominal sepsis (1 patient). Comorbidity contributed a lot to the outcome of treatment. First, these were diseases of the cardiovascular system, which in fact caused hemorrhages (CHD, hypertension, etc.) and were present in majority (98.7%) of the patients. Among other concomitant pathologies in the patients, there were diseases of the digestive (12.8%), endocrine (7.1%), and respiratory (5.8%) systems.

The patients stayed in the ARICU for 6.3 ± 6.0 bed-days, and as in-patients in hospital – for 28.5 ± 11.1 bed-days.

Of the total number of the patients who received treatment, 62.2% of the patients

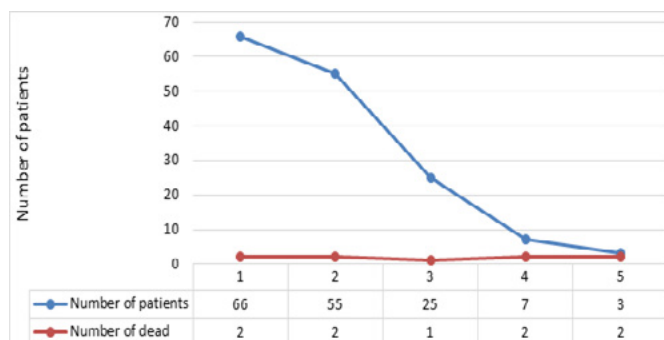


Fig. 2. ASAH mortality depending on the initial severity by the Hunt-Hess scale

were discharged with full recovery. 21.1% and 10.3% of the patients were discharged with mild and moderate neurological disability, respectively. One (0.6%) patient was discharged in the vegetative state (Table 4).

Conclusion

Thus, the study of the patterns of complications and mortality of aSAH at the ARICU, RH No. 2-CEMA of the Sakha Republic (Yakutia) in the period 2015-2017 showed that complications of a different nature were diagnosed in the preoperative period in 67.3% of the patients and in 64.7% of the cases following surgeries, and the mortality rate for this group of patients was 5.8% (9 patients).

In the patterns of the complications of the preoperative period, the dominant one was cerebral vasospasm, with the specific gravity of 81.9%. Other complications of this period included ruptured aneurysms and large-scale cerebral edema with dislocation syndrome, 9.0% and 4.8% of the complications, respectively.

During surgical treatment of the patients, in 12.8% of the cases there were changes in the surgical planning due to a ruptured aneurysm (85% of the reasons for changing the operational tactics), as

well as pronounced cerebral edema and the impossibility of applying clips.

In the postoperative period, 101 (64.7%) patients had various intra- and extra-cerebral complications, which accounted for 61.38% and 38.6% in the patterns of complications, respectively.

Among the intracerebral complications, DCI with 39.60% ranked first. Moreover, this complication was more often observed in the patients transported by air ambulance from district hospitals (32.1%) than among patients from the city of Yakutsk (19.2%). Of extracranial complications, NP and severe CCS were most common, comprising 20.79% and 12.87% in the patterns of the postoperative complications.

Of the total number of the treated patients, 62.2% of the patients were discharged with full recovery, 21.1% with a mild neurological disability, 10.3% with a moderate neurological disability, and 0.6% in the persistent vegetative state.

The data presented indicate the relevance of the issues related to treating patients with aSAH in the region, as well as the importance of measures for improved treatment, diagnostic and organizational-tactical approaches aimed at reducing complications and mortality in this group of patients.

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Table 4

The conscious state of the in-patients at discharge by the Glasgow Outcome Scale)

Glasgow Outcome Scale (points)	Years			Total number, (%)
	2015	2016	2017	
5 points Full recovery	29 (60.4)	40 (66.7)	28 (58.3)	97 (62.2)
4 points Light neurological disability	14 (29.2)	7 (11.7)	12 (25.0)	33 (21.1)
3 points Moderate neurological disability	3 (6.2)	8 (13.3)	5 (10.4)	16 (10.3)
2 points Persistent vegetative state	0	1 (1.7)	0	1 (0.6)
1 point Death	2 (4.2)	4 (6.6)	3 (6.3)	9 (5.8)
Total	48	60	48	156

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IMMUNOGENETIC MARKERS OF THE SIBERIA SOUTHERN REGIONS POPULATION UNDER THE EXPOSURE OF TECHNOGENOUS FACTORS

ABSTRACT

Peculiarities of the population health, characteristic for the newly emerging endemic provinces in Russia, are formed by the anthropogenic pollution conditions of the environment and determine the need to identify the indicator of immunological and genetic indicators that reflect the population health of industrial regions.

The aim of the work is to analyze the population immune and genetic indicators in the conditions of the anthropogenic impact of the urban environment on the example of the Southern Siberia region.

Materials and methods. Laboratory immunological and genetic examination of the adult population living in a combined influence of a chemical factors number of habitat zone is carried out. The content of specific antibodies to benzo(a)pyrene, aluminium, formaldehyde was detected by allergosorbent testing with an enzyme label. Cell populations were determined by CD markers on a flow cytometer. Biochemical markers were studied by enzyme immunoassay. Genetic features were detected by real-time polymerase chain reaction and allele discrimination, based on the diagnosis of single-nucleotide polymorphisms.

Results. There was a significant decrease in the number of CD3⁺CD25⁺ lymphocytes relative to the reference interval, and there were lower concentrations of CD16⁺CD56⁺ -, CD3⁺ and CD4⁺-cells relative to the comparison group. The decrease in serum IgG and IgM levels was combined with an increase in the level of IgG to aluminium and benzo(a)pyrene, IgE to formaldehyde relative to the values in the comparison group. There was a significant (p=0.02) increase in the frequency of occurrence of the minor allele of the enzyme eNOS rs1799983 gene associated with a decrease in serum levels of nitric oxide, which indicates the formation of additional risk factors under technogenic exposure.

Findings. The established changes in immune reactivity and genetic polymorphism indicate their population peculiarities of the technogenic chemical province of the Southern Siberia region, which can be used as formation of pathological health disorders markers associated with oxygen-associated processes in the vascular endothelium, the implementation of which can contribute to the identified imbalance of cellular and humoral immunity (CD3⁺CD25⁺ lymphocyte deficiency and IgG hyperproduction to aluminum and benzo(a)pyrene, IgE to formaldehyde).

Keywords: immune regulation, genetic polymorphism, eNOS gene rs1799983, technogenous factors.

Newly emerging Russian endemic provinces are evolving under the conditions of technogenic environmental pollution and immunological health of the population who live there, especially taking into account individual genetic variability, is subject to study due to necessity to solve treatment and preventive tasks under technogenic transformation of the external environment in the areas under active industrial influence [5, 6, 8, 9].

Chemical environmental pollution might cause the toxic effect on the functions of immune cells, as well as have both immunoactivating and inhibitory effects, leading to the development of immune-mediated diseases which are either allergic or autoimmune ones [1, 10, 14, 15]. It should be noted that the nature and specificity of the resulting changes are usually associated with the exposure features, exposure duration, exposure sources and properties of the factor itself or their combination. Therefore, it is particularly important to study the immunogenetic features of the population, with regard to the combined multi-factor environment, and to determine the indicators of pathogenetic trends related to health disorders [2, 3, 12].

The research aims at analyzing the immune and genetic indicators of the population under technogenic impact exerted by the urban environment and exemplified by Southern Siberia region.

Materials and methods. The population living in the industrial center located in the Irkutsk region was examined. The observation group included 50 people living in the zone of technogenic pollution factors (mean age amounts to 34.06 ± 0.84 years). The comparison group consisted of 31 people living on a relatively clean area outside the zone under industrial impacts, remote from the region of technogenic chemical province (mean age is 41.29 ± 2.22 years).

Immunoglobulin concentration (IgG, IgM, IgA) in serum was estimated using radial immunodiffusion (Mancini method). Specific response to the factors related to the chemical burdens was determined with reverse enzyme allergosorbent test according to the level of specific IgG antibodies to aluminum and benzo(a)pyrene, specific IgE antibodies to formaldehyde. The levels of nitrogen oxide and superoxide dismutase in serum were measured with enzyme immunoassay using commercial test systems ("BenderMedSystems", Austria, "RnD Systems", USA). The ratio of lymphocyte populations was determined as per membrane CD markers using panels of monoclonal antibodies

to CD receptors ("Becton Dickinson", USA) on FACSCalibur flow cytometer ("Becton Dickinson", USA), taking into account at least 10,000 events.

The data were processed using program Statistica 6.0 (Statsoft, USA), the results were presented as an arithmetic mean and standard error of mean ($M \pm m$). Statistical significance was assessed at $p < 0.05$ using Student's t-test.

The biological material from the mucous membrane of the oropharynx was obtained for genetic analysis. DNA was extracted by the sorbent method via cells destruction. Genotyping of polymorphisms was carried out using sets of "SNP-screen" ("Synthol", Russia). Genotypes were determined via polymerase chain reaction on CFX96 thermal cycler ("Bio-Rad", USA), using the real-time mode and the allele discrimination method to separate groups as per genotypes. Genotyping data were processed using "Gene Expert" program, genotype frequencies were calculated as per Hardy-Weinberg equilibrium based on the diagnosis of single-nucleotide polymorphisms (SNP). The statistical intergroup significance in the genotype and allele frequency distribution of studied traits was determined by χ^2 criterion, using co-dominant and multiplicative inheritance models. The data in terms of allele frequencies were analyzed with the calculation

of odds ratio (OR, 95%CI).

Results and discussion. The population research showed functional changes in immune indicators in the observation group (table 1). Thus, there was a significant decrease in the number of CD3⁺CD25⁺-lymphocytes relative to the reference interval in 75.9% of the examined ($p < 0.05$). As for the comparison group, a lower concentration of CD16⁺CD56⁺-lymphocytes on the average of 1.8-2.3 times, CD3⁺- and CD4⁺-lymphocytes at 1.2 times according to the absolute level of marker expression was revealed ($p < 0.05$).

At the same time, we may observe a significant change in humoral immunity. The levels of IgG and IgM were reduced by 1.2 and 1.5 times, respectively relative to the values in the comparison group ($p < 0.05$).

In the meantime, an increase in the level of specific antibodies was observed when compared with the reference range for IgG marker to aluminum in 64.6% of the examined ($p < 0.05$). Besides, the level of IgG antibodies to aluminum increased 2.8 times, IgG to benzo(a)pyrene 5.1 times, IgE to formaldehyde 3.0 times compared to the comparison group ($p < 0.05$).

Thus, we revealed the changes in the immune reactivity indicators in the examined population under technogenic influ-

Table 1

Indicators of immune regulation in the population under technogenic exposure

Index	Reference interval	Observation group	Comparison group
CD16 ⁺ CD56 ⁺ -lymphocytes. 109/dm ³	0.09-0.59	$0.148 \pm 0.033^*$	0.348 ± 0.098
CD16 ⁺ CD56 ⁺ -lymphocytes. %	5-27	$7.675 \pm 1.469^*$	13.737 ± 2.644
CD19 ⁺ -lymphocytes. 109/dm ³	0.09-0.66	0.203 ± 0.045	0.269 ± 0.054
CD19 ⁺ -lymphocytes. %	6-25	9.85 ± 1.102	10.842 ± 1.492
CD3 ⁺ -lymphocytes. 109/dm ³	0.69-2.54	$1.426 \pm 0.145^*$	1.762 ± 0.235
CD3 ⁺ -lymphocytes. %	55-84	76.325 ± 2.284	71.789 ± 2.543
CD3 ⁺ CD4 ⁺ -lymphocytes. 109/dm ³	0.41-1.59	$0.858 \pm 0.086^*$	1.036 ± 0.133
CD3 ⁺ CD4 ⁺ -lymphocytes. %	31-60	45.175 ± 2.411	42.684 ± 2.945
CD3 ⁺ CD8 ⁺ -lymphocytes. 109/dm ³	0.19-1.14	0.535 ± 0.063	0.639 ± 0.116
CD3 ⁺ CD8 ⁺ -lymphocytes. %	13-41	28.35 ± 2.341	25.579 ± 2.938
CD3 ⁺ CD25 ⁺ -lymphocytes. 109/dm ³	0.19-0.56	0.173 ± 0.045	0.129 ± 0.043
CD3 ⁺ CD25 ⁺ -lymphocytes. %	13-24	$9.448 \pm 2.479^{**}$	5.158 ± 1.457
IgG. g/cm ³	10-18	$11.994 \pm 0.583^*$	15.825 ± 1.035
IgM. g/cm ³	1.1-2.5	$1.558 \pm 0.101^*$	2.318 ± 0.431
IgA. g/cm ³	1.1-3.0	2.21 ± 0.15	2.392 ± 0.303
IgE to formaldehyde. IU/cm ³	0-1.5	$0.305 \pm 0.099^*$	0.103 ± 0.061
IgG to aluminum. cu	0-0.1	$0.216 \pm 0.053^{**}$	0.078 ± 0.03
IgG to benzo(a)pyrene. cu	0-0.3	$0.248 \pm 0.08^*$	0.049 ± 0.032

Note: * - the difference is significant relative to the comparison group; ** - the difference is significant relative to the reference interval ($p < 0.05$).

ence, which are associated with a quantitative imbalance in the main populations of immunocompetent cells, a decrease in the functional activity of humoral immunity with hypersensitivity development to the chemical influence factors regarding the level of specific antibodies to aluminum, formaldehyde, benz(a)pyrene.

The development of predisposition to allergic conditions in the population living on the territories where active technogenic development takes place is determined by the excessive allergenic load of multi-factor industrial pollution. As a result, there is an excessive activation of immune cells, which often leads to the strengthening of oxidative reactions and the development of oxidative stress and pathophysiological states [13, 16].

When performing genetic study of the population living on the observation area, we determined the features of individual genetic variability in the genes of inflammation and antioxidant protection of endothelial nitrogen oxide synthase eNOS (rs1799983) and superoxide dismutase SOD2 (rs2758330) (table 2). The ratio analysis of the genotype and allele frequencies in the examined groups revealed a significant increase in the prevalence of mutant allele T of the eNOS gene in the observation group at the level of 19.7% and at 6.5% in the comparison group ($p < 0.05$). At the same time, there were no significant differences in the frequency of occurrence of minor genotypes and alleles in the SOD2 gene. It might be assumed that the presence of the mutant allele T of the eNOS gene acts as an additional risk factor in the population with a high level of allergization under technogenic influence when developing inflammatory processes and oxidative stress ($OR = 3.566$, $95\%CI = 1.18-11.375$), since it is due to a decrease in the basal production of nitrogen oxide responsible for regulatory functions, including those associated with antioxidant activity [4, 7, 11].

Study of biochemical indicators in the population of the observation group (table 3), associated with these genes, confirms the importance of the interaction that oc-

Table 2
Features of genetic polymorphism in the population under technogenic exposure

Gene (polymorphism)	Genotype, allele	Observation group, %	Comparison group, %	χ^2	p
eNOS (rs1799983)	GG	65.8	87.1	4.68	0.1
	GT	28.9	12.9		
	TT	5.3	0		
	G	80.3	93.5	5.08	0.02
	T	19.7	6.5		
SOD2 (rs2758330)	CC	60.5	67.7	0.42	0.81
	CA	28.9	22.6		
	AA	10.5	9.7		
	C	75	79	0.31	0.58
	A	25	21		

curs between environmental factors and features of genetic polymorphism when it comes to resulting phenotypic manifestations. Thus, the population covered showed reduced concentrations of nitrogen oxide in serum in 66.7% of cases relative to the values of the comparison group, on average of 1.2 times ($p < 0.05$). The level of superoxide dismutase in the examined groups did not differ significantly.

Summing up what has been said, genetic analysis revealed a significant ($p = 0.02$) increase in the frequency of occurrence of the minor allele of eNOS rs1799983 gene associated with a decrease in serum levels of nitrogen oxide, which proves the formation of additional risk factors under technogenic influence.

Conclusions. When studying the population living in the Southern Siberia regions under intensive technogenic impact, significant changes in immune regulatory indicators were observed. What is more, there was a ratio violation of the main populations of immunocompetent cells with a decrease in the fraction of CD16⁺CD56⁺, CD3⁺ and CD4⁺ cells, the expression of the activation marker CD25, a decrease in the production of serum immunoglobulins IgG and IgM combined with the development of sensitization with an increase in the production of specific IgG antibodies to aluminum, benz(a)pyrene, IgE to formaldehyde. When sen-

sitivity of the population increased, the features of genetic polymorphism of the eNOS gene associated with a decrease in serum levels of nitrogen oxide were revealed, which indicates additional risk factors associated with the development of inflammatory and oxidative reactions, disorders in formation of the optimal adaptive oxygen-dependent processes in the body that provide detoxification and protection of endothelial cells.

The revealed features of the indicator immunogenetic indicators in the population on the surveyed area are proposed to be used as markers of pathological health disorders for finding solutions to treatment and preventive tasks in emerging technogenic geochemical provinces.

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Table 3
The biochemical markers in the population under technogenic exposure

Index	Reference interval	Observation group	Comparison group
Nitric oxide, $\mu\text{mol}/\text{dm}^3$	70.4-208.6	108.69 \pm 16.103*	134.39 \pm 17.304
Superoxide dismutase, ng/cm^3	30.1-88.1	61.067 \pm 11.316	65.679 \pm 11.201

Note: * - the significance of differences relative to the comparison group ($p < 0.05$).

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COMPARATIVE EXPERIMENTAL STUDY OF THE PERFORMANCE OF BACTERIOSCOPIC METHODS IN DETECTING ACID-FAST BACILLI: ZIEHL-NEELSEN MICROSCOPY, CONVENTIONAL FLUORESCENCE, AND LED FLUORESCENCE MICROSCOPY

ABSTRACT

Performance of bacterioscopic methods was comparatively studied in Bacteriologic Laboratory of the Phthisiatry Research-Practice Center, to assess the detection of acid-fast bacilli (AFB) by Ziehl-Neelsen (ZN) microscopy, conventional fluorescence microscopy (FM), and LED fluorescence microscopy (LED-FM). A total of 400 positive smears detected by FM were re-observed by ZN microscopy; additionally, we analyzed diagnostic material from 648 patients of the Pulmonology Department of the Yakutsk City Clinical Hospital, in whom the hospital laboratory did not detect

presence of AFB in smears after triple ZN microscopy of direct sputum. To compare the performance of FM and LED-FM microscopy in detecting AFB, diagnostic material from 1082 new pulmonary tuberculosis cases was analyzed.

Keywords: tuberculosis, diagnosis, acid-fast bacilli, Ziehl-Neelsen microscopy, fluorescence microscopy, LED fluorescence microscopy, fluorochrome.

Introduction. Despite the introduction to clinical practice of advanced microbiological and molecular-genetic methods for diagnosis of tuberculosis (TB), microscopic methods are still the key methods used in primary examination of individuals with suspicion for TB. The value of these methods is in their availability, simplicity, and opportunities to possibly fast detection of those patients who present epidemiological risk [1, 6, 9].

Ziehl-Neelsen (ZN) stain microscopy is one of essential methods used to confirm the diagnosis of pulmonary TB, based on detection of acid-fast bacilli in patient's sputum [2, 6].

ZN microscopy is relatively simple to perform, but its sensitivity can be decreased due to a number of factors. It is obviously more so in laboratories with intense daily load of microscopic procedures performed, that can lead to reduced quality of specimen preparation and smear staining technique, while the lab staff might simply not have enough time to observe all incoming fields of view (FOV) due to high workload [7, 9, 10, 11].

Fluorescence microscopy (FM) is currently a method of choice, with significant advantages over ZN microscopy. The method's sensitivity is 10-15% higher than that of ZN microscopy, on average [10, 11, 12]. Compared to transmitted-light microscopy, FM has a number of advantages: high contrast of luminous objects against dark field; considerably larger visible area due to less magnification needed to observe the object; saving of time, and more. [3].

Use of LED (light emitting diode) technologies has been the latest advancement made in the field of FM, which dramatically increased performance of microscopy [8]. Estimation by WHO confirmed diagnostic accuracy of LED-microscopy, comparable to conventional FM, and superior performance of LED fluorescence microscopy (LED-FM) over ZN microscopy [4]. Despite the positive feedback on the utility of LED-FM, just one study on the use of LED-FM could be retrieved from available Russian-language literature [8].

Aim: Comparative assessment of the performance of different microscopy methods in detecting acid-fast mycobacteria.

Material and methods. In performing routine microbiological examinations were complying with the procedure de-

scriptions provided in Appendices (10, 11) to the Order no.109 (issued 21.03.2003) "On improving anti-tuberculosis measures in the Russian Federation", and Order no.951 (issued 29.12.2014), of the Russian Federation Ministry of Health [5].

For ZN test, smears were treated with carbol fuchsin, decolorized with 3% hydrochloric acid-ethanol, and stained with 0.25% methylene blue.

ZN microscopy was performed using binocular microscope (Primo Star, Carl Zeiss, Germany) with 100x immersion lens, 10x eyepiece, and at 1000x magnification. Reading of results was done in minimums of 300 fields (negative results) and 100 fields (positive results).

For FM, sediment pH levels (sediments were obtained from the material prepared as described above) were adjusted to 6.8-7.0. Using a pipette, 1-2 drops of sediment were placed on the slide, and spread as a thin layer in the center of a slide, over an area of 2x1 sm. Then, smears were dried in biosafety hood for 15-20 min. at room temperature. Smears were fixed in dry-air sterilizer at 65-75°C for 2 hours. After staining with auramine OO and rhodamine C, specimens were examined using LED fluorescence microscope (Primo Star, Carl Zeiss, Germany) and conventional fluorescence microscope (Mikmed 2, Russia), at 400x magnification (40x lens, 10x/18 eyepiece).

Once the diagnostic material was processed with fluorescent dyes, and they started binding to waxy parts of microbial cell and penetrating to cytoplasm, followed by exposure to excitation light source, mycobacterial cells glowing orange or bright-yellow against black or dark-green background could be observed.

Statistical processing was performed using commonly employed software (Microsoft Excel, StatSoft Statistica 6), mean values ($M \pm m$), and significance values for statistical difference assessment (P).

Results and discussion. During the year 2016, we microscopically examined the sediments from various diagnostic samples, incoming to the lab, all collected from patients suspected for TB, or hospitalized patients on treatment. Overall, 9480 smears were subjected to FM, of them 1439 were AFB+. Detectability rate for AFB detected by FM method was 15.2%.

Of these 1439 AFB+ specimens, 400

smears were randomly selected for comparative examination by ZN microscopy, with the following categories of positivity: 100 smears (scanty); 100 "1+" smears (solitary AFB); 100 "2+" (moderate count of AFB); 100 "3+" (large count of AFB). All 400 positive smears were confirmed by culture tests for *M.tuberculosis* complex mycobacteria on liquid and solid media.

After observation by FM method, the smears were stained for ZN microscopy. Stained smears were then observed consecutively by 3 bacteriologists, who were unaware of the preceding results. In case of discrepancies in readings, the result received in most of the readings was considered final.

Results of comparative microscopic smear examinations are presented in Table 1.

As is seen in Table 1, out of 400 FM-positive smears, re-observation by ZN method showed the presence of AFB in 312 (78%) smears, while in 88 (22%) smears the presence of AFB could not be shown.

Among 100 smears classified as scanty, ZN microscopy was positive in 22 smears, and negative in 78 smears.

Out of 100 smears classified as "1+", 90 were proved positive by ZN, although only 34 were classified exactly as "1+", and 56 smears were shown to have scanty.

Smears classified as "2+" or "3+", were confirmed by ZN method in 100%. Positivity category "2+" matched in 52 smears; 44 smears were classified as "1+" and 4 smears as scanty. For category "3+", match was observed in 62 smears, while 28 smears were interpreted as "2+" and 11 smears as "1+."

Comparative study results supported better performance of FM over ZN microscopy, especially in scanty specimens, only 22% of which could be confirmed as positive by ZN method.

Hence, FM was shown to have a 22% higher sensitivity compared to ZN method, which is in agreement with literature data.

Our next step in comparative studies was to assess detectability of AFB by FM, using diagnostic material from 648 patients of the Pulmonology Department of the Yakutsk City Clinical Hospital, who had AFB-negative results of triple ZN microscopy of direct sputum performed at hospital laboratory. Based on indications, all patients were referred for further ex-

Table 1

Re-observation results for AFB+ fluorescence microscopic smears, by Ziehl-Neelsen microscopy (n, %)

Indicators:	Scores: FM+ smears			
	Scanty	1+	2+	3+
Total: AFB+ smears (FM) (n = 400)	100	100	100	100
Subjected to re-observation by Z-N microscopy (n = 400)	100	100	100	100
Of them, AFB+ n = 312 (78 %)	22	90	100	100
Of them, AFB- n = 88 (22 %)	78	10	-	-
Detection rate, %	22	90	100	100
Scoring AFB+ results (ZN): Scanty	22	56	4	-
1+	-	34	44	10
2+	-	-	52	28
3+	-	-	-	62

Table 2

Detection rates for direct sputum Ziehl-Neelsen test for AFB in clinical diagnostic laboratories of the Yakutsk City Clinical Hospital, 2014-2016

Years	Number of tests		Number of patients tested		Multiplicity, %
	Total	Of them, AFB+ n, %	Total	Of them, AFB+n, %	
2014	4378	19 (0.4)	2265	18 (0.8)	1.9
2015	4291	24 (0.5)	2216	23 (1.0)	1.9
2016	4971	25 (0.5)	2580	21 (0.8)	1.9

Table 3

Detection rates: FM for AFB in sediments from diagnostic materials collected from patients of Yakutsk City Clinical Hospital

Total tested	Of them, AFB+ n, %	Microscopy result scoring (n, %)			
		Scanty	1+	2+	3+
n= 648	22 (3.4)	10 (45.5)	3 (13.6)	7 (31.8)	2 (9.1)

Table 4

Results of FM and LED-M for sediments of diagnostic materials from newly identified patients with pulmonary tuberculosis

Microscopy method	Total new patients n= 1082	Of them, w/o cavities n, %	Of them, with cavities n, %	Test results		
				Positive sputum n, %	Positive sputum and cavities n, %	Positive sputum, no cavities n, %
FM	518	337 65.1	181 34.9	180 34.7	131 72.4	49 14.5
LED	564	392 69.5	172 30.5	251 44.5	143 83.1	108 27.5

amination to City Tuberculosis Treatment and Prevention Clinic.

As is seen from Table 2, over the period from 2014 to 2016, an annual number of ZN microscopies for TB performed at Yakutsk City Clinical Hospital ranged between 4291 (2015) and 4971 (2016), while the number of patients examined annually ranged from 2216 (2015) to 2580 (2016). AFB detectability rate (WHO standard is 1%) ranged between 0.8% (2014) and 1.0% (2015). Number of tests performed (WHO recommends 3.0) was stably 1.9 during the study period. Thus, reference values (detectability and number of tests) recommended by WHO were not met by primary level laboratory.

Examination of samples from 648 patients using FM method showed presence of AFB in 22 cases. AFB detectability rate was 3.4%, which was reliably higher (4.2% higher ($p < 0.05$)) than the detectability demonstrated by ZN microscopy performed at Yakutsk City Clinical Hospital laboratory (0.8% in 2016). Furthermore, positive results were classified as scanty in 10 cases, as 1+ in 3 cases, as 2+ in 7 cases, and 3+ in 2 cases, i.e. 9 patients (40.9%) were shown to have excessive bacterial load, undetected by ZN microscopy (Table 3).

The next step was to comparatively analyze performance of FM and LED microscopy in detecting AFB in sediments from diagnostic material collected from newly diagnosed pulmonary TB patients. Material from a total of 1082 patients was examined, of them, 518 were subjected to FM, and 564 to LED-FM.

Results of comparative analysis are shown in Table 4.

As is seen, using FM method, 34.7% (180/518) of patients had AFB-positive results, while 65.3% (338/518) were negative. Using LED-FM, 44.5% (251/564) of patients were positive for AFB, and 55.5% (313/564) were negative. Detectability of AFB by LED-FM was 44.5%, which was reliably higher (9.8% higher ($p < 0.001$)) than the detectability by FM (34.7%).

Using LED-FM, detection of smear-positive results (M+) among patients with lung destructions was 83.1% (143) and 27.5% (108) among patients without lung destructions, which was higher, compared to percent detected by FM (72.4% (131) and 14.5% (49), respectively).

Hence, performance of LED-FM was confirmed to be higher (by 9.8%, in our study), compared to conventional FM.

Conclusion. As the results of comparative study demonstrated, fluorescence

microscopes with mercury lamp or LED light source should be advised for use as more comprehensive compared to ZN microscopy, to achieve early detection of the presence of bacteria in diagnostic material and early diagnosis of TB infection at laboratories with high (>20 smears) daily workload.

As far as LED fluorescence microscopes are less demanding in terms of high-skilled maintenance and offer longer lamp life-span compared to conventional fluorescence microscopes, use of LED-technologies is economically reasonable and LED fluorescence microscopy should be recommended for extensive application in the diagnosis of TB.

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CORRECTION OF DISORDERS OF VITAMIN D METABOLISM IN PATIENTS WITH PATHOLOGY OF DIGESTIVE ORGANS AND OSTEOPENIA

ABSTRACT

The article presents the results of a clinical study on the metabolism of vitamin D in patients with gastroenterological pathology and osteopenia. We have developed a comprehensive non-drug method of treatment with fishbone flour and mineral water "Abalakhskaya" that has a positive effect on the functional state of the digestive organs, impaired metabolism of vitamin D and mineral density of bone tissue. 10 women aged 53 to 69 years old of the Yakut nationality are included in the study on a voluntary basis. The average age is 62.9 ± 4.9 years. All of them are in the dispensary control for chronic acalculous cholecystitis and focal atrophic gastritis.

The clinical study included drinking of the Abalakhskaya mineral water (AMB) twice a day in the amount of 400-600 ml / day and fishbone flour at 18 g / day every day for 45 days with two 1.5 monthly intervals. The duration of treatment was 6 months.

The clinical study demonstrated a positive therapeutic effect of the combined use of fish bone flour and mineral water "Abalakhskaya" in elderly patients with gastroenterological pathology and metabolic disorders of vitamin D for the clinical course of diseases, bone mineral density, paraclinical indicators. Developed by us the non-drug method will allow the introducing of personalized medical technologies into practical healthcare.

Keywords: vitamin D, disorders of calcium-phosphorus metabolism, bone mineral density, fish bone flour, mineral water "Abalakhskaya", non-drug treatment.

Introduction. The gastrointestinal tract is one of the main body systems responsible for the absorption and metabolism of vitamin D and its metabolites. In any diseases of the stomach, intestines, liver, gallbladder, pancreas, accompanied by malabsorption syndrome, various expressiveness of exchange osteopathy may occur [1]. The range of metabolic osteopathies in diseases of the gastrointestinal tract can range from a subjective impression of a decrease in bone density according to radiographs to marked osteoporosis with characteristic clinical, radiological and biochemical symptoms [2, 3]. Factors contributing to the disturbance of mineral and bone metabolism are the use of products with low vitamin D content, living in regions with extreme climatic conditions with a long winter period, insufficient solar insolation, negatively affecting all types of metabolism: proteins, fats, carbohydrates, macro- and micronutrients.

Objective: to study the metabolism of vitamin D in patients with pathology of the gastrointestinal tract and osteopenia.

Materials and research methods. The study was conducted at "Educational and research laboratory the Medical Technologies in Gastroenterology" at the "Hospital Therapy, professional Diseases and Clinical Pharmacology" Department of the Medical Institute MK Ammosov NEFU and approved at the meeting of the Local Com in the February 15, 2017, decision No. 1).

10 women aged 53 to 69 years old of the Yakut nationality are included in the study on a voluntary basis. The average

age is 62.9 ± 4.9 years. All of them are in the dispensary control for chronic acalculous cholecystitis and focal atrophic gastritis.

Monitoring of calcium and phosphorus metabolism (levels of ionized calcium in the blood and daily urine, 25 (OH) D - calcidiol and phosphorus in the blood), X-ray densitometry on GE Lunar iDXA, in 3 standard projections (lumbar spine, femoral neck bones, radial bone of the forearm), office measurement of blood pressure, ultrasound (US) of the abdominal organs, esophagogastroduodenoscopy (EFGDS) were held. When interpreting the indicators of bone mineral density (BMD), the densitometric classification of WHO was used (1994). Statistical processing of the material was carried out using the program STATISTICA V6.0 for Windows.

We have developed a comprehensive non-drug method of using Abalakhskaya mineral water and fish bone flour to correct metabolic disorders of vitamin D and mineral metabolism in patients with gastroenterological pathology. The regimen of the Abalakhskaya mineral water drinking was prescribed individually, taking into account the functional state of the stomach and biliary tract.

The clinical study included drinking of the Abalakhskaya mineral water (AMB) twice a day in the amount of 400-600 ml / day and fishbone flour at 18 g / day every day for 45 days with two 1.5 monthly intervals. The duration of treatment was 6 months.

Results and discussion. Patients before the beginning of the course of treat-

ment complained of bitter taste in the mouth, the feeling of lump in the chest, belching with bitterness, bloating, pain in the right hypochondrium and epigastric pain, unstable stools when taking fat, fried food. Also they were disturbed with pain in the knee, hip joints, in the lumbar spine when prolonged static stress, brittle nails, muscle cramps in the limbs, weakness and fatigue. Half of the patients had non-intensive pains in the right hypochondrium and one had moderate-intensity pain syndrome in the right hypochondrium and epigastric area.

After the course of complex therapy, patients noted improvement in overall health, relief of abdominal pain, normalization of stool, improvement of appetite, reduction of pain in joints, lumbar spine, increased physical activity, improvement of the skin, nail plates and hair, which were noted not only by the patients themselves, but also by professionals - masters of a beauty salon.

The intensity of the pain syndrome gradually decreased from the 2nd-3d days and during completely stopped for 5-8 days.

The patients noted the decrease and disappearance the symptoms of gastric dyspepsia at different periods of treatment, depending on the degree of their manifestation, on average after 10 days.

The initially observed expressed flatulence in the patients was neutralized on the 8th day of treatment.

When taking fish bone flour and mineral water "Abalakhskaya" in the observed group, no adverse reactions were recorded, patients were happy to receive treat-

ment.

During treatment, reduction in body weight has been achieved. The average value of body mass index (BMI) before the course of treatment was $28.5 \pm 1.6 \text{ kg} / \text{m}^2$; after treatment - $27.8 \pm 1.5 \text{ kg} / \text{m}^2$.

Endoscopic examination of the stomach in all patients revealed changes in the mucous membrane characteristic of gastritis, which was morphologically confirmed. The atrophic form of gastritis with signs of unexpressed inflammation was mostly met. After the course of treatment, positive dynamics in the form of a decrease in the inflammatory process in the gastroduodenal mucosa, epithelialization of acute erosions in the antrum of the stomach and a decrease in the severity of duodenogastric reflux was observed.

Ultrasound examination of the abdominal cavity, conducted in dynamics, testified the normalization of the contractile function of the gallbladder and intestines.

After the course of complex treatment there is a tendency to decrease in the level of ionized blood calcium from 1.23 ± 0.05 to $1.16 \pm 0.02 \text{ mmol/l}$ and the daily excretion of calcium in the urine from 5.65 ± 2.62 to $4.76 \pm 2.20 \text{ mmol/day}$, which is associated with improved absorption of calcium in the intestine, input of it to the bone tissue and slowing down of bone resorption. Baseline serum calcidiol ranged from 13 to 34 ng / ml. The average index of vitamin D was $23.7 \pm 5.29 \text{ ng} / \text{ml}$, which corresponds to a slight deficiency of vitamin D in the blood serum.

After the course of treatment, increase in the average level of calcidiol in the blood to $28.01 \pm 5.29 \text{ ng} / \text{ml}$ with a range of fluctuations from 15 to 38 ng / ml was

registered.

At the same time, the minimum concentration of vitamin D was noted in the patient who had not previously consumed fresh fish, and the maximum concentration was noted in the patient who is actively engaged in physical exercise and regularly consumes fresh fish and fish products.

According to x-ray densitometry after 6 months of observation, the increase in BMD in the observed group averaged 3.36% ($0.03 \text{ g} / \text{cm}^2$), the increase in T and Z criteria - by 0.3 SD. The increase in bone mineralization in the axial skeleton was observed in the segments, where the initial BMD corresponded to osteopenia.

Conclusion. The clinical study demonstrated a positive therapeutic effect of the combined use of fish bone flour and mineral water "Abalakhskaya" in elderly patients with gastroenterological pathology and metabolic disorders of vitamin D for the clinical course of diseases, bone mineral density, paraclinical indicators. Developed by us the non-drug method will allow the introducing of personalized medical technologies into practical healthcare.

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ORGANIZATION OF HEALTH, MEDICAL SCIENCE AND EDUCATION

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THE CURRENT STATE OF THE FUNCTIONAL DIAGNOSTICS DOCTORS STAFFING IN THE RUSSIAN FEDERATION AND ITS SUBJECTS (2012-2017)

Abstract. Staffing issues are one of the main health problems. The *aim* of the study was to analyze the current situation in the provision of functional diagnostics by doctors in the Russian Federation and its subjects. *Material and methods:* the method of descriptive statistics was used to analyze the data of Federal statistical observation №30 "Data on medical organization" in the context of the subjects of the Federation for the period from 2012 to 2017. *Results* of the study: during the analyzed period, the availability of functional diagnostics by doctors providing outpatient care, despite the almost stable value of the indicator (on average 0.36 per 10,000 population), had some tendency to increase. Ranking of subjects of the country by the level of security showed that both at the beginning and at the end of the analyzed period the top ten were the republics of Chuvashia and Mordovia, St. Petersburg, Khanty-Mansiysk Autonomous Okrug, Orenburg region, Trans-Baikal and Altai territories. *Conclusion:* in the whole country and its constituent entities of the Federation there is a low provision of outpatient departments with doctors of functional diagnostics, although in most of them there is a positive dynamics of the indicator.

Keywords: doctors of functional diagnostics, staffing, medical organizations, indicators, trends.

Introduction. One of the main priorities of health care and the Government as a whole is to ensure the quality and accessibility of health care in order to maintain and improve the health of the population [2-4]. In this regard, the provision of medical organizations with personnel and the rational cost of working time of medical specialists is the relevance of the problem [5, 6, 8, 9]. However, it is not always possible to implement new labor standards due to the lack of financial capacity of medical organizations [1, 7, 10, 11].

Aim of research: analysis of the current situation on the provision of doctors with functional diagnostics in the Russian Federation and its subjects.

Material and methods. The method of descriptive statistics was used to analyze the data of the Federal statistical observation №30 "Information about the medical organization" in the context of the subjects of the Federation for the period from 2012 to 2017.

Results and discussion. Functional diagnostics in the practice of any special-

ist doctor is important for diagnosis verification. In this regard, the availability of specialists in this field is one of the urgent problems of practical health care. To assess the rationality of the use of human resources and their activities, we analyzed the data of the official statistical observation on the availability of functional diagnostics by doctors for the period from 2012 to 2017.

The results of the study showed that during the analyzed period of time, the provision of functional diagnostics doctors providing medical care in outpatient settings in the Russian Federation, despite the almost stable value of the indicator (on average 0.36 per 10 000 population), had some tendency to increase (+2.7% for 2015-2017) (Table).

While year-to-year growth rate of doctors of functional diagnostics was in the interval of 0.28% to 0.45%. The analysis of the provision of doctors with functional diagnostics in the context of the subjects of the Russian Federation indicates a higher increase in the provision of specialists in such subjects as the Penza region (300.0%), Jewish Autonomous district (233.3%), the Republic of Tyva and Altai (200.0%), Magadan (130.8%) and Tambov (117.4%) regions. Negative growth was observed in 13 regions of the country, especially in the Republics of Adygea (-44.4%), Chuvashia (-24.1%), Nizhny Novgorod region (-16.7%) and Moscow (-15.3%).

Our ranking of subjects of the country according to the level of provision of functional diagnostics by doctors for

2012 and 2017, showed that both at the beginning and at the end of the analyzed period, the top ten were the republics of Chuvashia and Mordovia, St. Petersburg, Khanty-Mansi Autonomous district, Orenburg region, TRANS-Baikal and Altai territories. In the first place in 2012 was the Republic of Chuvashia, in 2017 – the Republic of Karelia. The Republic of Adygea, the Chechen Republic and the Kurgan region have the lowest availability of specialists.

Functional studies are important in all areas of health care. In some cases, without the necessary functional studies it is impossible to establish the correct diagnosis. However, not all medical organizations have consistently high availability of these specialists. In this regard, the analysis of the availability of functional diagnostics by doctors is one of the urgent problems of practical health care. This is necessary for planning both the Program of state guarantees, as well as improving the quality and timeliness of medical care. The results of this study indicate a shortage of personnel in the field of functional diagnostics, which requires organizational decisions on rational training.

Conclusion. In general, in the Russian Federation and its regions there is a low staffing by functional diagnostics doctors providing medical services on an outpatient basis, although in most of them there is a positive dynamics of the indicator. However, in 15.3% of the subjects, against the background of low availability of medical specialists, there is a negative increase in the indicator.

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Staffing of outpatient departments of medical organizations with doctors of functional diagnostics in the Russian Federation and in its Federal districts for the period 2012-2017 (per 10 000 population, the rate of increase/decrease in %)

Russian Federation subject	2012	2013	2014	2015	2016	2017	2017/2012
Russian Federation	0,34	0,35	0,37	0,37	0,38	0,38	10,6
Central federal district	0,39	0,4	0,4	0,39	0,39	0,4	2,3
North-West Federal district	0,37	0,39	0,42	0,44	0,45	0,46	24,1
Southern Federal district	0,36	0,36	0,4	0,41	0,41	0,41	13,3
North Caucasus Federal district	0,31	0,3	0,38	0,39	0,38	0,37	19,7
Volga federal district	0,29	0,3	0,35	0,35	0,37	0,38	31,6
Ural Federal district	0,31	0,33	0,34	0,34	0,35	0,34	9,5
Siberian Federal district	0,28	0,29	0,28	0,3	0,31	0,32	12,9
Eastern federal district	0,24	0,24	0,27	0,24	0,28	0,27	12,6

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HYGIENE, SANITATION, EPIDEMIOLOGY AND MEDICAL ECOLOGY

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POLYMORPHISM OF GENES LOCALIZED ON THE X-CHROMOSOME AS A MARKER OF PREDISPOSITION TO INFECTIOUS PROCESS CHRONICITY AT HEPATITIS C IN THE ETHNIC GROUP OF MALE YAKUTS

ABSTRACT

The work studied variable sites of six genes localized on the X-chromosome in the Yakut ethnic group - residents of the Republic of Sakha (Yakutia). The candidate TLR7 rs179009 gene was found, the C-allele of which is associated with the chronic course of hepatitis C. The minor C allele is more than 2 times more common in patients with chronic hepatitis C than in the group with spontaneous recovery. It was found that the chances of hepatitis transition to a chronic course are 2.7 times higher in carriers of the C-allele than in carriers of the T-allele rs179009 TLR7. The obtained data confirm the possible significance of the rs179009 polymorphism of the TLR7 gene as a genetic marker of predisposition to the chronicity of the infectious process while viral hepatitis C in the ethnic group of male Yakuts.

Keywords: hepatitis C, single nucleotide polymorphisms, toll-like receptors, X chromosome, chronic infection process, Yakuts, male.

Introduction. In the Republic of Sakha (Yakutia), there is a high incidence of viral hepatitis C (52.4 per 100 thousand of population), which is 1.5 times higher than the average Russian index [2]. The fact that representatives of Yakut men are more involved in the epidemic process than women stands out. In men, liver cirrhosis and hepatocellular carcinoma are more frequent and develop faster [4]. However, it is known that in some patients after hepatitis C virus (HCV) infection spontaneous recovery is possible [14, 21]. Predisposition to the chronic course of hepatitis after acute or latent period is genetically determined and varies significantly among members of different ethnic groups [1, 11, 12, 22]. Thus, according to D.L. Thomas et al., (2009), spontaneous recovery occurs in 36.4% of Caucasians and only in 9.3% of African Americans [12]. However, molecular genetic mechanisms that determine the ethnic and gender features of natural course and outcome of hepatitis C (HC) have not been discovered yet. In this direction, the role of single nucleotide polymorphisms of genes (SNPs) encoding the synthesis of cytokines, interferons and adapter molecules of innate immunity has been actively studied recently [3, 9, 19]. When analyzing gender characteristics of HC and its outcomes, it is necessary to take into account that in men, the genes located on the X chromosome are most susceptible to the influence of SNPs on the functions of antiviral immunity and oncological control due to the absence of the second allele. In the Yakut ethnic group, such studies have not yet

been conducted.

Research objective: to improve the personalized prognosis of the course of viral hepatitis C, identify associative links between alleles of single nucleotide polymorphisms of genes localized on the X-chromosome and a predisposition to chronic HCV infection in the male Yakuts ethnic group.

Materials and methods. Presented studies were performed in 2017-2018 on the territory of the Republic of Sakha (Yakutia). The material was collected in the Yakutsk City Clinical Hospital, department for the treatment of patients with viral hepatitis, Gornaya Central District Hospital, Namsk Central District Hospital, Hangalasskaya Central District Hospital in accordance with the ethical principles of the Declaration of Helsinki of the World Medical Association.

In total, molecular genetic studies were performed in 96 Yakut men, including 48 patients with chronic hepatitis C (CHC) and 48 patients with a confirmed spontaneous clearance of the virus. The average age of patients with HC was 53.4 ± 12.5 years, the average body mass index - 26.7. All the examined patients lived on the territory of the Republic of Sakha (Yakutia), including 19 (39.6%) people from the city of Yakutsk and 29 (60.4%) from other uluses (Gornyy, Namsk, Hangalassk). Out of the 48 patients with CHC, 1b - 75.0% (36), prevailed in the structure of genotypes, genotype 2 accounted for 4.2% (2), genotype-3 - 20.8% (10). The control group of persons with spontaneous clearance of HCV (SC) had no significant differences with the experimental

one in gender, age and body mass index. All patients have given informed consent to perform a genetic study.

The diagnosis of CHC was made on the basis of medical history, clinical examination, determination of hepatic transaminases activity, detection of anti-HCV IgG and HCV RNA. SC was proved according to the criteria regulated by the sanitary and epidemiological rules of the SP 3.1.3112-13 "Prevention of viral hepatitis C" (decree of October 22, 2013 N 58, registered in the Ministry of Justice of Russia on 19.03.2014 N 31646). Patients with the presence of anti-HCV in the blood were on follow-up monitoring for at least two years, and with repeated negative results of HCV RNA, they were proved to have a spontaneous recovery, if there was no antiviral therapy in the history. Exclusion criteria were patients with cirrhosis, hepatocellular carcinoma, as well as having a combined pathology or co-infection of the liver of a different etiology.

In these patient samples genetic studies of SNP of the following genes were performed: *TLR7* (rs179008); *TLR7* (rs179009); *TLR8* (rs3764879); *IRAK1* (rs3027898); *TAB3* (rs1000129516); *MECP2* (rs1734791). When selecting genes, the authors considered polymorphisms at the X chromosome loci that affect the structure or function of receptors and adapter molecules involved in transmission of intracellular signals — activators of antiviral factors of innate immunity. Molecular genetic studies were performed using an amplifier for real-time PCR Rotor-Gene Q (Qiagen Hilden, Ger-

many). Amplification of certain regions of the genes was carried out using primers and probes of one's own design, synthesized at Sintol Research and Production Company and ZAO Evrogen (table 1).

When analyzing the results of genetic studies, we compared allele occurrence rates. The odds ratio (Odds Ratio, OR) was calculated at a confidence interval level of 95% (Confidence Interval, 95% CI). The significance of differences was assessed after adjusting for multiple comparisons using the average proportion of false deviations of the hypotheses (corrected p-value) [6]. The level of statistical significance was taken at $p \leq 0.05$.

Results and discussion. More than 200 genes are involved in the transmission of the intracellular signal from the pattern recognition receptor to the NFkB transcription factor and its translocation into the nucleus, 13 of which are located on the X-chromosome [25]. This puts the male representatives in unequal conditions, since the absence of the second allele manifests any changes in the variation sites of the genes involved in the innate immune response. According to the literature, males dominate among carriers of HCV antibodies [5, 16]. Perhaps the predominance of males among patients with chronic hepatitis C is associated not only with differences in risk factors for infection, but also due to genetic characteristics of innate immunity reactions. In addition, the predisposition of men

to develop HCC in the outcome of HCV is well known. The ratio of females and males in patients with HCC varies from 1: 1.7 in Turkey to 1: 4.1 in Korea [20].

The analysis revealed that out of six SNP only TLR7 rs179009 significantly differed in the frequency of alleles in the group of patients with spontaneous clearance and CHC (table 2). The minor C-allele is more than 2 times more common in patients with chronic hepatitis C than in the group with spontaneous clearance. At the same time, it was established that the chances of HV transition to the chronic course are 2.7 times higher in C-allele carriers than in rs179009 TLR7 T-allele carriers. Despite the long chain of transmission of the intracellular signal, it is Toll-like receptors (TLR) that play a key role in the pathogenesis of HC, since they represent the first viral recognition line that induces the primary "alarm" signal [19]. The recognition of viral RNA initiates signaling along two parallel duplicate paths: from TLR7 / 8 through the MyD88 molecular adapter to the cell nucleus and from TLR3 through the TRIF adapter molecule to the nucleus (the so-called MyD88 independent pathway) [15, 18]. The functional purpose of both signals is the same: ensuring the synthesis of α - and β -interferon and cytokines, which ensure the destruction of the virus and the degradation of viral RNA in the early stage of infection. "Breakdown" of one of the pathways is associated with a

violation of the signal transmission rate in the cell and a change in the level of innate immunity genes expression.

Presently, experimental studies of the role of several SNPs of the TLR3 gene localized on the fourth pair of chromosomes have been described [9]. In Caucasians, human macrophages, carriers of the rs13126816 TLR3 G-allele, when in contact with viral antigens, have the ability of rapid and potent interferon- β production [17]. Perhaps for this reason, the G-allele rs13126816 TLR3 is associated with a high incidence of the 1st HCV genotype SC in the Caucasians of North America, African Americans and Latin Americans [17]. The same SNP is associated with the individual's innate resistance to the herpes virus [24]. Unlike the locus described above, another SNR rs3775291 (A/G) TLR3 is in the exon zone. Replacing leucine with phenylalanine in TLR3 protein leads to a loss of receptor activity [23]. The alleles and genotypes of TLR3 SNPs associated with the NF-kB expression level and, as a result, with a decrease in the production of type I interferons have been described [23].

There is significantly less information concerning SNPs of the TLR7 gene. In the present study, no significant differences were found between SNPs in the rs179008 TLR7 variable site and the nature of the HC course. However, other studies established the significance of this SNP in the induction of innate immu-

Table 1

Variable sites of genes and primers for identifying them in real-time PCR

Gene	SNP	Localization, the nature of the replacement	5'→3' primers and probes for real-time PCR
TLR7	rs179008	Chromosome X; exon, not synonymous, Gln-11Leu	F GGTGTTTCCAATGTGGACACTG R ACATCCAGAGTGCATCACAGG 5'(FAM)- TTATGTTAAAAAGGATAAGAATT(A-LNA)G(T-LNA)C- (RTQ1) 5'(R6G)- TTATGTTAAAAAGGATAAGAATT(T-LNA)G(T-LNA)C- (BHQ2)
	rs179009	Chromosome X; intron 2	F TTTGCTAAAGAGCTAAGATGCTAA R TTCAGCTGTCTAAACAGCATCC 5'(FAM)- GTAAGTACAAATACA(G-LNA)TC(T-LNA)TGG - (RTQ1) 5'(R6G)- GTAAGTACAAATACA (T-LNA)C(G-LNA)TGG - (BHQ2)
TLR8	rs3764879	Chromosome X; above reading frame	R TCVTCATTGTTCTGGGACCT F AGATGAARACCTGAAACAACGT 5' - (FAM)- GACTACGGAATGT(G-LNA)AAGT(A-LNA)C-RTQ 5' - (R6G)- GACTACGGAATGTG(A-LNA)AGT(C-LNA)C-BHQ2
IRAK1	rs3027898	Chromosome X; below reading frame	F 5' - AGATGAARACCTGAAACAACGT R 5' - TCVTCATTGTTCTGGGACCT 5' - (FAM)- GACTACGGAATGT(G-LNA)AAGT(A-LNA)C-RTQ 5' - (R6G)- GACTACGGAATGTG(A-LNA)AGT(C-LNA)C-BHQ2
TAB3	rs1000129516	Chromosome X; intron	F 5'-AGGTTGGTTTGGGTC R 5'-AGAGCACAGTAGTAGG 5'-FAM-TCACAGAAGTGAAGG(T-LNA)A-RTQ1 5'-R6G-TCACAGAAGTGAAGG(C-LNA)A-BHQ2
MECP2	rs1734791	Chromosome X; intron	F 5'-ACAGAATAGTCATAAAATC R 5'- AAGTGCTGGGCCACCA 5'-FAM-AAACAGATGA(T-LNA)AAAAG(A-LNA)AA-RTQ1 5'-R6G-AAACAGATGA(T-LNA)AAAAG(T-LNA)AA-BHQ2

nity reactions [8, 10]. By its nature, this SNP is non-synonymous and is characterized by the replacement of glutamine (Gln) with leucine (Leu) in the encoded protein. As a result, the signal peptide of the TLR7 receptor manifests a functional deficiency [13]. In response to synthetic inducers, low expression of IFNL1 mRNA, IL-10R β and IL-28R α is observed in dendritic cells and hepatocytes of carriers of the minor T-allele [7].

Conclusion. The described immunological phenomena explain the potential significance of genes localized on the X chromosome while HC in the context of ethnic groups and the gender of an individual. The discovered association of TLR7 rs179009 with predisposition to chronicity of HC in male Yakuts complements the idea about the toll-like receptors role in the antiviral defense of the body, which will further let us develop personalized approaches to prognosing the course and outcome of the HCV infection natural course

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Table 2

Associations of gene alleles mapped on the X chromosome with the SC of the hepatitis C virus in the ethnic group of Yakut residents of the RS (Ya)

Gene, variable site	The allele	Group Characteristic		OR (95% CI)	p
		spontaneous clearance (N=48) п(%)	chronic hepatitis C (N=48) п(%)		
TLR7 rs179008	A	35(72,9)	40(83,3)	1,0	0,2
	T	13(27,1)	8(16,7)	0,54 (0,20-1,45)	
TLR7 rs179009	T	40(83,4)	31(64,6)	1,0	0,036
	C	8(16,6)	17(35,4)	2,7 (1,05-7,18)	
TLR8 rs3764879	C	36(75,0)	38(79,1)	1,0	0,6
	T	12(25,0)	10(20,8)	0,79 (0,30-2,05)	
IRAK1 rs3027898	A	40(83,3)	40(83,3)	1,0	1,0
	C	8(16,7)	8(16,7)	1,0 (0,34-2,93)	
TAB3 rs1000129516	A	29(60,4)	30(62,5)	1,0	0,92
	G	19(39,6)	18(37,5)	0,92 (0,40-2,08)	
MECP2 rs1734791	A	37(77,1)	38(79,1)	1,0	0,89
	T	11(22,9)	10(20,8)	0,80 (0,34-2,33)	

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VECTOR OF DISTRIBUTION, DYNAMICS OF THE NUMBER OF IXODIC TICKS IN THE TERRITORY OF YAKUTIA AND THE BACKGROUND OF THE EXPLOSION OF LOIMOPOTENTIAL OF TICK INFECTIONS IN HUMANS

ABSTRACT

The authors report the data of medical and entomological monitoring.

The **purpose** of the study was to determine vectors of distribution and dynamics of the number of ixodic ticks in the territory of Yakutia and the background of the explosion of loimopotential of tick infections in humans.

According to the data of medical and entomological monitoring, an administrative-zonal (cartographic) format has been compiled; vectors of ectoparasite distribution are determined, including laboratory-indicative indicators, their contamination by designated infectious agents (causative agents of tick-borne encephalitis (TBE), ixodic tick-borne borreliosis (ITBB) and human granulocytic anaplasmosis (HGA)).

Sporadic and group cases of people's diseases, including a mixt-infection, detected against the background of general infection among the population indicate certain clinical, epidemiological, cause-and-effect risk factors of their loimopotential.

Findings:

1. The intense south-north vector of ixodic tick propagation and transmissivity is stated.
2. It has been established that ticks are contaminated with tick-borne encephalitis, borreliosis, and there is an increased risk potential for human morbidity.
3. From the standpoint of autochthonousness in "silent" foci latent infection among the population is revealed.

The area of the taiga tick (*Ixodes persulcatus* Schulze), the main custodian and carrier of the causative agent of tick-borne encephalitis (TBE), is almost completely located on the territory of the Russian Federation and has expanded in the last decade to the north and east [2-5, 11, 12], forming the loimopotential [5] of epidemiological risks for other tick-borne natural focal infections (ITBB, HGA).

Earlier on the topic, including the number of registrations of the attack of ticks on a person, quite informative materials were published [1, 3, 9, 13].

At present, cases of ixodic tick attacks on the territory of Yakutia have been noted in all administrative areas of southern,

southwestern and central Yakutia (Fig. 1).

Every year the largest number of cases is registered in the Aldan and Neryungri districts - over 43% of the total number of attacks in the Republic. Lensky and Olekminsky districts are in second place - up to 20%. In Central Yakutia, the highest incidence of ixodide attacks is noted in the Khangalassky district, Yakutsk and in the Namsky district, with over 10 cases recorded annually in the first two. In the districts over the Lena River, the population of Megino-Kangalassky and Amginsky districts is most often in contact with ticks. In most of the remaining territories, isolated cases of tick suction are recorded, up to a maximum of 7 (Suntarsky district). The most northern points where tick victims were found are the environs of Sangar and Kobyai (63 degrees north latitude, Kobyai district), and Kaskil (Tomponsky district) in the eastern zone of Yakutia.

This report provides additional data [1, 9, 10] from 2007 to 2018. Since the number of ticks at the limit of the range is extremely low, we estimate the situa-

tion on an indirect basis - the dynamics of the number of people affected by bites - the parasite suckers (Fig. 2).

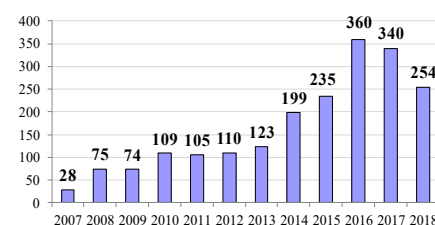


Fig.2. Dynamics of the number of tick attacks on people.

Over the past 14 years, there has been a sharp increase in the number of registered individuals affected by tick attacks. In general, if from 1975 to 1996, 182 victims were registered, then for 2000–2009 their number was 363, in the next 5 years (2010 – 2014) - 644, and for 2015–2017 - 933. It should be noted that as in August 2018 only 254 cases were recorded, then in total for the last 5 years (2014–2018) the growth trend persists - 1388 cases.

The mosaic character of the spread of foci is confined to anthropogenically altered sections of taiga and river valleys [6], as well as in areas adjacent to AYAM railway line (the highest proportion of bites-suckers of ticks was observed in Neryungri - 28.4% and Aldan districts - 23.3%).

The territory of the Republic Sakha

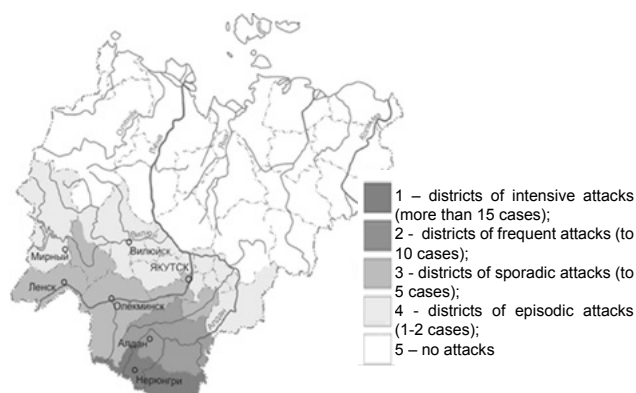


Fig. 1. Frequency of taiga ticks' (area of *I. persulcatus*) attacks on people in Yakutia.

(Yakutia) officially is not endemic for tick-borne encephalitis, since the tick virus activity and the morbidity of people here previously had a sporadic character [6], which assumed the character of intensity. In 2013 out of 105 specimens of the studied ticks, taken from people in 6 cases, positive results of their infection were obtained (5.7%). Contacts with virus-borne mites occurred in the Churapchinsky, Khangalassky, Namsky, Lensky, Neryungri areas and Yakutsk. In 2014, in a laboratory study of 183 specimens of ticks taken from people, 18 were already infectious (9.8%), and positive results were determined in studies of blood suckers from Aldan, Megino-Kangalassky, Namsky, Neryungri, Nyurba, Olekminsky, Suntarsky, Churapchinsky districts and Yakutsk (Fig. 3).

For 2012-2017 1332 studies of ixodid ticks taken from humans and animals by epidemiological indications using the

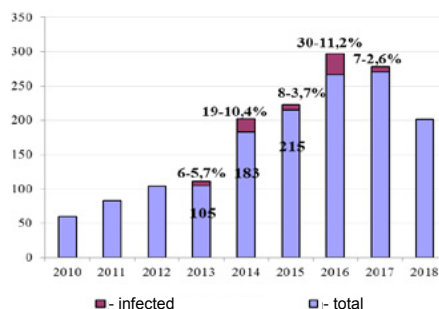


Fig. 3. The number of examined ticks and their infection in the period 2010-2018.

ELISA method were carried out. The TBE virus antigen was found in 70 specimens of ixodid ticks (5.2%).

In 2015 a modern technique (PCR) of tick NA detection for tick-borne encephalitis virus (TBE), tick-borne borreliosis pathogen (TCB), human granulocytic anaplasmosis (HGA) and human monocytic ehrlichiosis (HME) pathogens was introduced.

For 2016-2017 at performing PCR using multiplex tests on TBE, ITBB, HGA, HME, in the tested 528 specimens positive findings made 2%, in 10 specimens of ixodid ticks *Borrelia burgdorferi* RNA were found (Aldansky - 5; Yakutsk - 3; Namsky - 1; Neryungri - 1). In 2018 at conducting 201 laboratory studies of parasites, no positive results were found on TBE. However, in pool studies, HGA RNA was detected: out of 35 - 1 (2.8%), out of 28 - 1 (3.5%) and in 4 (11.4%) DNA of the ITBB pathogen was found.

Thus, one can confirm that in the territory of Yakutia there is not only an expansion in the area, but also an increase in

the activity and infection of ixodid ticks by various pathogens [14].

New positive results of tick-borne encephalitis causative agent in 11 and borreliosis in 5 districts of the Republic were obtained, which complicates the epidemiological situation of these transmissible infections, manifestations of the mixt-forms of the disease in humans are not excluded.

The potential of autochthonous risk of infection by tick-borne encephalitis is aggravated by the transport of up to 5.4% of victims who arrived from the territory of other Russian subjects, as well as from near and far abroad. Interterritorial cases of diseases were diagnosed in Yakutia from Primorye, Eastern Siberia, the Baltic states and the Czech Republic.

Borreliosis, the local cases of which were found in the Neryungri, Lensky districts and in the village Zhaatai, imported ones – in Mirny and Yakutsk, requires special attention.

In August 2018, 2 residents of the village Tokko Olekminsky district were diagnosed with tick-borne encephalitis (TBE) (patient A-nov, born in 1971) and mixt infection (TBE + ITBB) (patient D, born in 1973). The situation deserves clinical, epidemiological and prognostic assessment. Clinical and epidemiological studies have been confirmed by the results of indicative, virus-immunological parameters, pathological changes in the cerebrospinal fluid and the determination of specific antibodies aVTBE Ig M, aVTBE IgG and ITBB IgG against tick-borne encephalitis and borreliosis pathogens, the value of which is taken as evidence-based tests.

Epidemiological echo [6-8] testifies that the first case of tick-borne encephalitis, diagnosed in 1964 (isolation of the TBE virus from the cerebrospinal fluid) has its hidden "silent" and real-combined manifestation in the present.

Findings:

1. The intense south-north vector of ixodid tick propagation and transmissivity is stated.

2. It has been established that ticks are contaminated with tick-borne encephalitis, borreliosis, and there is an increased risk potential for human morbidity.

3. From the standpoint of autochthonousness in "silent" foci latent infection among the population is revealed.

4. The incidence of people is episodic, acquires group manifestations, including mixt-infections.

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ARCTIC MEDICINE

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MAJOR DEMOGRAPHIC TENDENCIES OF THE ARCTIC AND SUB-ARCTIC ZONE OF RUSSIA

ABSTRACT

The **aim** of the research: was the description of the general evolution of basic demographic indicators of the territories of the Arctic zone of the Russian Federation for the period 1993-2017.

Methods. A description of the main demographic indicators for the period of 1993-2017 in the Krasnoyarsk Area, the Arkhangelsk, Murmansk regions, the Komi Republics, the Sakha (Yakutia), the Nenets, the Yamalo-Nenets and the Chukotka Autonomous Districts in comparison with the national indicators.

The data of the Central Statistical Database of the Federal State Statistics Service, the Russian database on fertility and mortality were used.

The analysis used indicators: standardized total mortality rates, life expectancy at birth, infant mortality, total fertility rate, demographic burnout.

Conclusions. Despite the general positive demographic trends, the territories of the Arctic zone of Russia remain areas of a tense demographic situation, manifested in supermortality, insufficient fertility for the reproduction of the population, migration outflow of the population, which leads to continued depopulation of these regions.

Keywords: Arctic, fertility, mortality, migration.

Introduction. The modern territorial concept of the Arctic zone was formed by a Presidential Decree of May 2, 2014, which determined the boundaries of the

land areas of the zone [4]. Moreover, only a part of large territorial entities is included in this zone. In this regard, we have analyzed the enlarged territories, namely

the regions, districts, territories, taking as a basis the assumption about the similarity of the trends in them in general and in their individual territories in particular.

Table 1

Chain growth rates (losses) of the average population of the Arctic zone (1993 - 2017)

	Krasno-yarsk Area	Arkhan-gelsk Region	NAO	Mur-mansk Region	YaNAO	ChAO	Komi Republic	Sakha (Yakutia)
1993	-0.4	-1.2	-3.8	-3.0	-1.0	-13.4	-1.2	-1.6
1994	-0.7	-1.3	-3.9	-3.0	1.5	-12.1	-2.1	-2.0
1995	-0.6	-1.4	-3.4	-2.9	2.1	-13.0	-2.5	-2.1
1996	-0.5	-1.5	-2.3	-2.6	1.4	-9.9	-1.8	-1.3
1997	-0.5	-1.4	-1.8	-2.4	1.1	-7.5	-1.6	-1.2
1998	-0.6	-1.4	-1.2	-2.4	0.7	-7.3	-1.7	-1.6
1999	-0.7	-1.5	-0.7	-2.4	-0.2	-7.6	-1.7	-1.6
2000	-0.8	-1.6	-0.7	-2.2	-0.1	-7.4	-1.6	-1.0
2001	-0.7	-1.4	-0.3	-1.9	0.7	-5.3	-1.3	-0.6
2002	-0.7	-1.3	0.9	-1.8	1.0	-3.9	-1.3	-0.5
2003	-0.8	-1.3	1.2	-1.8	0.8	-3.1	-1.5	-0.1
2004	-1.0	-1.3	0.2	-1.9	0.6	-1.3	-1.6	0.2
2005	-1.1	-1.3	0.0	-1.9	0.6	0.4	-1.9	0.2
2006	-1.0	-1.3	-0.1	-1.9	0.7	1.1	-2.0	0.2
2007	-0.6	-1.0	0.0	-1.5	0.6	0.4	-1.5	0.2
2008	-0.2	-0.8	0.0	-1.1	0.1	-0.7	-1.2	0.1
2009	-0.1	-0.8	0.3	-0.9	0.0	-1.6	-1.2	0.0
2010	-0.1	-0.9	0.3	-0.7	0.2	-1.7	-1.3	0.0
2011	0.1	-1.0	0.4	-0.7	1.2	-0.2	-1.2	-0.1
2012	0.3	-0.9	0.8	-0.9	1.6	0.4	-1.0	-0.1
2013	0.3	-0.9	0.7	-1.1	0.3	-0.4	-1.0	-0.1
2014	0.2	-0.8	0.7	-0.9	-0.2	-0.2	-0.9	0.1
2015	0.2	-0.7	0.9	-0.6	-0.5	-0.4	-0.9	0.3
2016	0.3	-0.7	0.6	-0.6	-0.4	-0.7	-0.8	0.3
2017	0.2	-0.8	0.2	-0.6	0.4	-0.8	-0.9	0.2

Source of data: authors' calculations based on Rosstat data.

Study objective: to describe the general evolution of basic demographic indicators of the territories of the Arctic zone of the Russian Federation.

Materials and methods. The analysis was carried out for the Krasnoyarsk Area, the Arkhangelsk, Murmansk regions, the Komi Republics, Sakha (Yakutia), Nenets (NAO), the Yamalo-Nenets (YNAO), and the Chukotka (ChAO) autonomous districts in comparison with the national indicators.

The period of analysis: 1993-2017.

The data of the Central Statistical Database of the Federal State Statistics Service [6], the Russian database on fertility and mortality [2] are used.

Results and discussion. In the territories under consideration, a decline

in the population prevails in general, despite the positive growth trends in the whole country. Sustainable growth in the last decade is demonstrated only by the Krasnoyarsk Area and the Nenets Autonomous District. These trends have continued since the early 1990s (Table 1). The leaders in population decline over the past five years are the Komi Republic (-3.5%), the Murmansk and Arkhangelsk regions (-3.1%). Of those territories that demonstrate a positive population dynamics, significant steady growth is observed only in the Sakha Republic (Yakutia), while in the Krasnoyarsk Area the growth is compensatory, when the growth rates by 2016 only reached the level of 2012, and in 2017 dropped again. In the NAO in 2016 they returned to the level of

2014 in order to decline again in 2017. The decrease in population is ensured by both the natural movement of the population and the migration outflow. In all regions, with the exception of the Krasnoyarsk Area, over the past five years, there has been a negative migration inflow. Most regions show either a slowdown or a decrease in natural population growth. The exceptions are NAO and Chukotka, where natural population growth has a steady upward trend over the past five years.

The population of the Arctic regions is subject to aging, as well as in the whole country, which is associated with a recession of fertility and mortality in the working age. The process of demographic aging of the population leads to an increase

Table 2

Demographic burden per 1000 of the working age population (15-59 yrs), 2017

Age	RF	Krasno-yarsk Area	Arkhan-gelsk Region	NAO	Mur-mansk Region	YaNAO	ChAO	Komi Republic	Sakha (Yakutia)
0-14	287	301	299	377	274	328	319	306	372
60+	348	305	370	235	279	111	158	288	210
Общая	635	606	669	612	553	439	477	594	583

Source of data: authors' calculations based on Rosstat data.

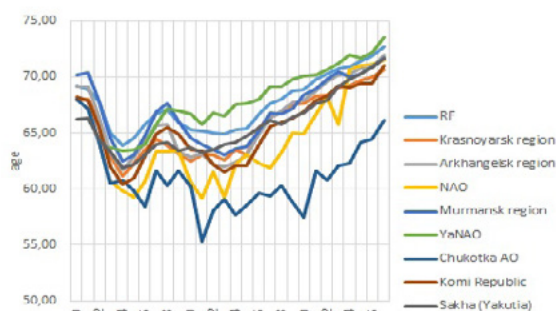


Fig. 1. Life expectancy at birth, total population, both sexes, years, 1990-2017

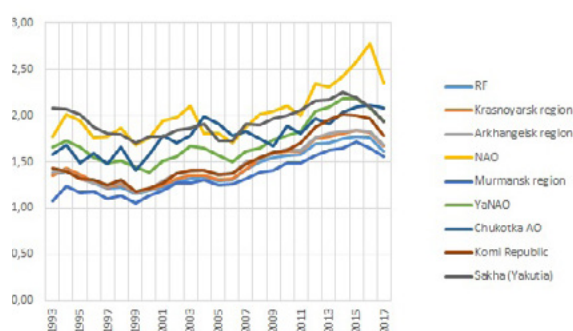


Fig. 2. Total fertility rate, 1993-2017

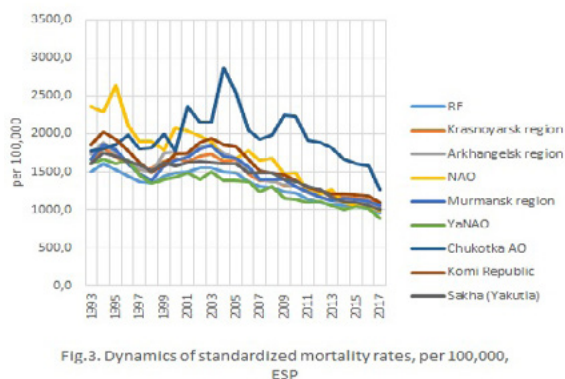


Fig. 3. Dynamics of standardized mortality rates, per 100,000, ESP

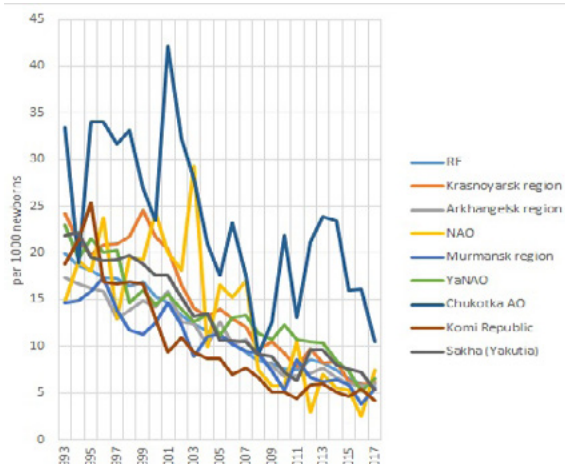


Fig. 4. Dynamics of infant mortality, per 1000 newborns

in the demographic burden on the working population (Table 2). By the end of the second decade of the 21st century, various trends in demographic burden indicators are observed in the studied regions. So, in the Arkhangelsk region, as well as in the whole country, there is a negative picture, when the burden of the older age groups prevails over the burden of children. In the NAO, the demographic burden of older ages is much lower comparing with Arkhangelsk region. In the Murmansk region rendered by younger and older age groups are practically in parity.

The dynamics of life expectancy at birth (LE) in the studied regions was congruent to the all-Russian, differing in level (Fig. 1). In general, most regions show lower indicators of LE in comparison with all-Russian ones. The lowest rates of life expectancy for the entire population, in comparison with the all-Russian, were observed in the NAO and ChAO, where throughout the analyzed period, the gap with the national indicators reached 9 - 12 years. Moreover, if the difference in the life expectancy of the population of the NAO and the country tends to reduce, the gap with the indicators of ChAO has increased, reaching a historical maximum in 2010 (16.5 years for men and 15.1 years for women), after which some positive trend began and by 2017, the difference reached 9.1 years. Separately, the YNAO stands out, where LEs exceeded all-Russian indicators since the late 1990s for the entire population, and in the male population since the mid-1990s, reaching a maximum by the middle of the first decade of the new century. This trend was absent in the female population, where there was a gradual reduction in the gap until the early 2000s, then a decline and then a new reduction. As a result, the life expectancy of the female population of the YNAO by 2016 is almost equal to the life expectancy of women in the whole country. In all regions, as well as in the whole country, there is a reduction in the life span of men and women.

The lowest values of the total fertility rate in the studied regions, as well as in the whole country, were noted in 1999 (Fig. 2). Then there was a period of its increase,

followed by local declines, which lasted, in general, until 2015, when the indicator was equal to approximately the values of the early 1990s, reaching in some regions the level necessary for simple reproduction of the population (2.1). However, by 2017, the regions showed a decrease in the indicator. It should be noted that in general, in the studied regions in 2015, a slowdown in the growth rate of the total birth rate was noted, and from 2016 its full stop and turn to decrease. As a result, in 2017 all regions showed the largest decline. In particular, the NAO stands out, where the decline in the total fertility rate for the year was 15.3%.

Similar to the dynamics of life expectancy, the dynamics of overall mortality was identical to the fluctuations in mortality in the country (Fig. 3). It should be noted that in all the studied regions, in addition to the YNAO, the mortality rate, with a similar dynamics, was distinguished by a high level throughout the study period. The maximum gap with the all-Russian indicators was demonstrated by the NAO, ChAO and Komi Republic. On average, over the past quarter century, the mortality rate in the ChAO was higher than the national one by 26.5%. Moreover, the gap between the death rates in this region and those for the whole country tends to increase until 2015. The reduction in mortality in its duration is unprecedented. As a result, by the middle of the second decade of the new century, the mortality rate in the studied regions reached the levels of the early 1990s and less. However, the rate of this decrease gradually decreases and by 2014-2015 it almost stopped, slowing to a minimum, and in some territories, for example, in the YNAO and NAO, the death rate even increased compared with previous years.

The infant mortality rate, as well as LEs, is an integral indicator reflecting, among other things, the quality of life of the population (Fig. 4). The infant mortality rate in the regions, as well as in the whole country, had a steady downward trend with the exception of short-term upturns of the early 1990s and 2000s. Most of the regions, with identical dynamics, showed higher rates of infant mortality than in the

whole country. As in the case of the general mortality rate, the leader in excess was ChAO, where the infant mortality rate in 2015 exceeded the national one by 2.9 times, and the average over the past 25 years was 95.8% higher than the country level.

In all regions, the distribution of the leading classes of causes of death was traditional for the country. Cardiovascular diseases remain the leading class of causes of death, followed by neoplasms, and then external causes, injuries and poisonings, the level of which exceeds the national level.

The analysis of basic demographic processes taking place in the Arctic and subarctic belt of the Russian Federation shows that against the background of general positive changes in the demographic situation, negative trends remain. A significant migration outflow of the population, noted in most of the studied regions, is one of the main reasons for the depopulation of the Russian Arctic [5]. Nevertheless, in a number of regions, rooting of the visiting population can be observed, since the in them is higher than that of the migrants. These regions include the NAO rate of natural increase, the Yamal-Nenets Autonomous Okrug, the Republic of Sakha (Yakutia). In contrast, the Arkhangelsk and Murmansk regions, the Republic of Komi, ChAO, demonstrate a fairly steady downward trend in population. In these regions, even in conditions of a positive balance of natural movement of the population, the migration outflow is so great that it completely eliminates the existing successes associated with an increase in the birth rate and a decrease in mortality. This circumstance indicates the continuing, noted earlier socio-economic inequality of regions completely or partially related to the Arctic [1, 3]. In general, the main factors hindering natural population growth and stimulating migration outflows are the low standard of living of the population, severe climatic conditions, poor quality of public goods, alcoholism [3, 7, 9, 10]. It should also be noted that in regions with harsh climatic conditions, rotational work methods are widespread, not involving a change of permanent residence. In addition, since 2011, the methodology for calculating internal migration has been changed, making it difficult to compare data before and after this year. The rise in infant mortality in the early 1990s and 2000s is associated with improving the quality of accounting and the transition to new standards for determining live birth [8].

Conclusions. Despite the general positive demographic trends, the territories of the Arctic zone of Russia remain areas of a tense demographic situation, manifested in supermortality, insufficient fertility for the reproduction of the population, migration outflow of the population, which leads to continued depopulation of these regions. It is impossible to fully ensure geopolitical interests, sovereignty, security of economic activities in the Arctic without the due attention to the negative demographic processes occurring in the Arctic and subarctic belt of Russia.

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THE ANALYSIS OF NUTRITION OF CHILDREN OF ANABARSKY DISTRICT OF THE SAKHA REPUBLIC (YAKUTIA)

ABSTRACT

The article presents the results of a study of the diets of students living in the village of Saskylakh, Anabarsky district of the Sakha Republic (Yakutia). The authors assessed the nutrition and health status of 103 children of schoolchildren from 6 to 10 grade. The analysis of the diet of school-age children in Saskylakh has been carried out using a questionnaire method.

As a result of the analysis of the obtained data, it was established that children eat meat (94.1%) or fish (50.4%) with pasta (64%) every day or several times a day. One of the characteristics of children in the Arctic region is that children eat more often than children from the central regions of the RS (Ya) region raw foods (meat and fish). This is fresh meat or fish caught by frost and not losing juice. It is planned with thin long shavings and is called planed. Of the meat products, game birds predominate - polar quails, ducks, geese, and eggs of migratory birds (the same ducks and geese) - complete the grocery range of subarctic cuisine. It has been revealed that schoolchildren do not consume enough milk and dairy products, since many in the Arctic region do not keep a household and do not contain cows. Eggs, vegetables (mainly potatoes) and fruits are consumed in small quantities, as they are of short storage and are delivered only by flight to the northern regions. As for the use of salt by schoolchildren, it was clearly excessive. Most schoolchildren prefer to eat: salty (50.4% of respondents), not salty (23.3%), spicy (26.3%) foods. This fact is aggravated by the fact that, as shown by survey data, many schoolchildren often eat sweets, carbonated drinks and excessive amounts of salt.

As part of this study, we also examined children and identified the morbidity structure of the child population in Saskylakh.

In the first place, endocrine pathology was detected in 62.1%, which is most likely due to the endemicity of the territory due to its low iodine content.

In second place, dental pathology was found in 58.2%. Dental pathology in the Anabarsky district is worsening, which in winter people use ice, where fluoride concentration is even lower than in the water itself.

In the third place is the disease of the musculoskeletal system (32%). In the Anabarsky region, a short and cold summer is complemented by strong winds; in winter there is a blizzard, which always becomes an obstacle to any movement. Lack of nutrients and extreme climatic conditions, lifestyle affect the development of the musculoskeletal system in children in the Anabarsky district.

The results revealed that the nutrition of schoolchildren living in the Arctic conditions has its own characteristics.

Based on the obtained results, conclusions and recommendations on optimizing the nutrition of school-age children were made.

Keywords: nutrition, schoolchildren, Republic Sakha (Yakutia).

Introduction. Extreme conditions of living in the North demand higher standards of man's health, and providing effective life activity of population of this region, especially balanced nutrition, gets main social and medical significance. Epidemiological surveys, having been held in different regions of Russia, suggest about significant nutritional disorders and pupils' health. These disorders include irrational proportion of main nutrient materials, subnormal content of saturated aliphatic acids, vitamins, macronutrients and minerals (calcium, ferrum, iodine and others), dietary fibers. Overconsumption of bakery products, salt and added sugar is being noted everywhere. Health indicators and anthropometric characteristics of children and adolescents are declined due to violation of dietary intake's standards [6-10].

Aim of research: Analysis of the diet of school-age children in Saskylakh village of Anabarsky district, the Republic of Sakha (Yakutia).

Materials and methods. In order to consider the attitude of schoolchildren to a rational diet, we conducted a questionnaire. We have included in the structure of a continuous sample of schoolchildren from 6 to 10 forms of Saskylakhsky

secondary school in the amount of 103 pupils.

Results. As a result of the analysis of the obtained data, it was established that children eat meat (94.1%) or fish (50.4%) with pasta (64%) every day or several times a day (See the table 1). Mostly boiled, also children eat raw foods (meat and fish). This is fresh meat or fish caught by frost and not losing juice. It is planned with thin long corrugated slices and it is called *stroganina*. Sometimes the game birds - polar partridges, ducks, geese and eggs of migratory birds (the same ducks and geese) - complete the product range of subarctic cuisine. Local children eat fish (chir, muksun, etc.). Raw fish from chyr and muksun, salted, dried in the sun and wind, frozen is served. An independent dish is fish roe.

The questionnaire of children shows that they often eat the roe of northern fish. It is lightly salted, add onions or garlic, black pepper, filled with vegetable oil. Milk and dairy products are sufficiently consumed, who has a private household (they have a cow).

It was found out that schoolchildren drink milk and dairy products in insufficient quantities - in the overwhelming majority of cases (75.7%) children drank

only 1-2 glasses several times a week, mostly only 1-2 times a week. At the same time, eating of sweets, chocolates by schoolchildren was clearly redundant - among the answers the most frequently mentioned options were 3-4 pieces and a lot of sweets, which significantly exceeds the recommended amount (Table 2). An egg, vegetables (mainly potatoes) and fruits are consumed in small quantities, as they are of short storage and are delivered only by flight to the northern districts. The data presented in the table shows that from the surveyed schoolchildren (70%) they consumed only 1-2 eggs 2 times a week, daily - 11.6% and several times a day - 11.6%, in general, they eat an egg only 23.2% of respondents. Vegetables, mainly potatoes, are consumed daily only by 11.6%; no one eats fruits every day. Only 23.3% of them eat twice a week. As for the use of salt by schoolchildren, it was clearly excessive.

Most schoolchildren prefer to eat: salty (50.4% of respondents), not salty (23.3%), spicy (26.3%) foods. This thing is compounded by the fact that, as shown by the survey data, many schoolchildren often eat sweets, carbonated drinks and an excessive amount of salt.

As part of this study, we also exam-

Table 1

Food ration of schoolchildren of Anabarsky district. Saskylakh village

Food products	Proportion of school children in %				
	Several times a day	Daily	Several times a week	Several times a month	Less than 1 time per month
Meat products		90.3	5.8	0	0
Milk and dairy products	2.9	8.7	75.7	7.7	4.8
Vegetables	0	11.6	49.5	23.3	14.2
Fish and fish products	11.6	38.8	31	14.5	3.8
Eggs	11.6	11.6	28	29	19.4
Fruits	0	0	23.3	37.8	38.8
Butter	36.8	39.8	17.4	0	5.8
Pasta	23.3	40.7	26.2	4.8	4.8
Cereals	3.8	11.6	40.7	23.3	20.3
Sausage products	1.9	17.4	64	13.5	2.9
Sweets, chocolates	17.4	35.9	34.9	11.6	0
Carbonated drinks	3.8	14.6	29.1	37.8	14.6
Natural juices in tetrapacks	5.8	14.5	28.1	39.8	11.6
Roast	17.4	17.4	54.3	16.5	2.9
Farinaceous dish	4.8	9.7	66.9	11.6	6.7

Table 2

Distribution of surveyed schoolchildren in accordance with the amount of food consumed(%)

Food products	1,2 pieces	3,4 pieces	Many	Not eat
Sweets	30.1	23.3	46.6	0
Chocolate	34.9	41.7	23.3	0
Egg	70	25.2	4.9	0
Bread	33	38.9	28.1	0
Biscuit	28.1	38.8	28.1	0
Sugar	65	11.7	23.3	0
Pancakes, meat patties	29.1	21.4	49.5	0

Table 3

Pathology profile of the child population of Saskylakh, Anabarsky district

Disease	Number of pupils	
	abs.	%
Endocrine Diseases	69	66.9
Respiratory diseases	17	16.5
Diseases of the digestive organs	18	17.4
Diseases of the musculoskeletal system and connective tissue	33	32
Diseases of the nervous system	15	14.5
Eye disease	27	26.2
Diseases of the cardiovascular system	16	15.5
Dentistry	60	58.2

ined children and identified the morbidity structure of the child population of Saskylakh, Anabarsky district of the Sakha Republic (Table 3).

Endocrine pathology is mainly represented by endemic goiter 1-2 degrees in 62.1%. This is due to the endemicity of the territory of the Republic of Sakha according to the iodine content and the presence of endemic goiter [3]. Thyroid endemia is most widespread in the Urals, the North Caucasus, Altai, in the Far East and Siberia, the Upper and Middle Volga region, as well as in the Central region of the European part of the country [4, 5]. There is a number of epidemiological studies on the prevalence of endemic goiter in Yakutia, however, these studies were completed in the period up to 2000. [1,2,3].

Dental pathology was found in second place in 58.2% and was mainly represented by multiple caries in 33.9% of those examined.

It is known that one of the factors for the development of caries is a low concentration of fluoride in drinking water.

In winter, the population consumes ice, where the concentration of fluoride is even lower than in the water itself. It was also determined excessive consumption of sweets and candies by many children.

In the third place is the disease of the musculoskeletal system (32%), mainly represented by a violation of posture in 28.1%. The Republic of Sakha (Yakutia) belongs to the regions of the Russian Federation that has unfavorable children's health indicators. It is connected with extreme climatic conditions, and with the peculiarities of nutrition and lifestyle of the population [10].

Conclusion. Nutrition of children and adolescents in Anabarsky District of the Republic of Sakha (Yakutia) has its own regional characteristics, which are characterized by the presence of a deficiency in the main components of food, an imbalance in the nutrient composition. Rations do not have a variety of foods and dishes, characterized by inadequate consumption of basic ones, such as dairy products, eggs, vegetables, fruits. According to the results of the questionnaire of schoolchildren, it was revealed that dairy products, egg, vegetables and fruits consume less than half of the surveyed schoolchildren daily. It should also be noted that the daily consumption of fruits and vegetables does not work for many of the respondents.

Thus, a questionnaire conducted by

schoolchildren has made it possible to establish that the rare use of some products is related to the lack of products for sale, the high cost and the rare import of some products due to the transport infrastructure of the Arctic regions of the Republic of Sakha (Yakutia).

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ETHNICITY-DEPENDENT EVALUATION OF EXCESSIVE BODY MASS AND OBESITY IN THE NATIVE POPULATION OF NORTHERN YAKUTIA

ABSTRACT

In the expeditionary conditions in the North of Yakutia, representatives of the indigenous population (Evenks, Dolgans, Evens, Yukagirs, Chukchi, Yakuts) were examined in order to identify overweight and obesity. Overweight in terms of BMI ranged from 27.1% in Dolgans to 37.8% in Yakuts, and there were no significant differences, more often it was observed in men. Obesity was significantly more common in the Evenks compared with the Evens, the Yukagirs and the Chukchi, the Yakuts compared with the Evens and the Chukchi, and the Dolgans compared with the Chukchi. Women suffered most often.

The mean values of systolic blood pressure in Evenks and Yakuts were higher compared to other ethnic groups. There was a high frequency of hypertension in all ethnic groups. A strong positive correlation of BMI with the level of systolic blood pressure was revealed.

Keywords: overweight, obesity, arterial hypertension, indigenous people, arctic zone, Yakutia.

Introduction. Excessive body mass and obesity had large-scale implications over the past few decades, contributing to mortality, affecting it directly and indirectly. Among the main causes of death in people with obesity are cardiovascular diseases (CVD). There is an increase in overweight and obese population in many developed countries. We analyzed medical examination data of 20,607 people aged 25–65 years in 12 regions of the Russian Federation, the prevalence of hypertension equaled to 41.6%. In the north of Russia, in particular in the Tyumen region, a high frequency of arterial hypertension (AH) (49%) and obesity (40.3%) was noted as part of a multicenter observational study of ESSE-RF. Previously, numerous studies have been conducted using the definition of body mass index (BMI) in the indigenous population of Yakutia, in particular Yakuts, where a relatively low incidence of increased body mass and obesity was noted compared with the non-native population. But in recent years, many researchers have noted their growth among the Yakuts, as well as among certain groups of indigenous minorities of Yakutia, particularly the Evenks, Evens and the Dolgans. Changes in the traditional lifestyle of the indig-

nous people of the Arctic zone of Yakutia led to "diseases of civilization", such as hypertension, diabetes, obesity, etc.

Objective: to assess the frequency of ethnicity-dependent overweightness and obesity among the indigenous population of Northern Yakutia.

Materials and research methods.

The collection of study material was carried out in the expeditionary conditions in the north of Yakutia, including the places of compact residence of the indigenous peoples. For a comparative analysis, 6 groups of 529 people, representatives of the indigenous population (Yakuts, Evenks, Evens, Dolgans, Chukchi, Yukagirs) were formed: 1st - Evenks (n = 67), of whom 13 were men, 54 were women; 2nd - Dolgans (n = 85), of whom 26 were men, 59 were women; The 3rd is the Evens (n = 141), of whom 51 were men, 90 were women; The 4th is the Yukagir (n = 77), of whom 34 were men, 43 were women; The 5th is the Chukchi (n = 40), of whom 20 were men, 20 were women; The 6th group is the Yakuts (n = 119), of which 30 were men and 89 were women. The average age of the respondents was 45.59 ± 0.55 years.

Exclusion criteria: representatives of non-indigenous nationalities.

The research program included following sections: a survey to assess the general state of the respondent; the informed consent of the respondent to conduct research (according to the protocol of the Ethics Committee of the YSC CMP); anthropometric examination with height and weight measurement. Growth was measured in the standing position without shoes using a stadiometer with an accuracy of up to 0.5 cm. To measure body weight, we used mechanical physician scales that passed metrological control. The weight was recorded with an accuracy of up to 100 g. For further analysis, the traditional indicator was used - body mass index (BMI) or Quelet index, which was calculated by the following formula [Khaltaeva ED, Khaltaev NG, 1982, Pyorala K. et al., 1994]: $BMI (kg / m^2) = \text{body weight (kg)} / \text{height (m}^2\text{)}$. Overweight was considered to be a $BMI \geq 25$ and $<30 kg/m^2$, obesity was determined at a BMI of $\geq 30 kg/m^2$ [according to European recommendations of the III revision, 2003]. Blood pressure was measured on the right arm in a sitting position after 5 minutes of rest with an OMRON M2 Basic tonometer. The level of blood pressure was measured twice with an interval of about 2-3 min-

utes. The analysis took into account the average of two measurements. AH was determined at a systolic blood pressure level (SBP) of ≥ 140 mm Hg. and/or diastolic blood pressure (DBP) ≥ 90 mm Hg, or if the patient received antihypertensive drugs (recommendations developed by RMSAH (Russian Medical Society for Arterial Hypertension) and RSC (Russian Society of Cardiology) Committee of Experts, 2008).

Statistical data processing was carried out by means of standard methods of mathematical statistics, using the software package of SPSS (version 19.0). Data are submitted as $M \pm m$ where M – average value of the sign size, and m – an average error of the sign size. Intergroup differences were estimated by means of the variance analysis or nonparametric criteria. The differences were considered as statistically significant at $p < 0.05$.

The research was conducted within research projects of YSC CMP "A contribution of a metabolic syndrome to development of atherosclerosis of coronary arteries in residents of Yakutia", "Development of new technologies of treatment and risk prediction of hypertension and insult in the Republic of Sakha (Yakutia)" (Government contract No. 1133).

Research results and discussion.

To assess overweightness and obesity, we conducted a study of average body mass index (BMI) (Table 1). It is shown that the average values of BMI are higher than the reference (BMI < 25) for all ethnic groups from 26.4 ± 0.66 for the Chukchi to 30.79 ± 0.72 for the Evenks. Comparing the average BMI between ethnic groups, it was found that the Evenks had a BMI significantly higher compared to others, with the exception of the Yakuts. The Yakuts also had statistically significant differences compared to the Evens, the Yukagirs and the Chukchi.

Overweightness (OW) in terms of BMI among ethnic groups varied from 27.1% among Dolgans to 37.8% among Yakuts and did not have significant differences between them (Fig. 1). When analyzing the gender affiliation, it should be noted that OW is most often observed in men than in women, with the exception of Dolgans. Statistically significant differences between men and women were observed in the Evenk and Yakut populations.

As for obesity by the criterion of BMI (Fig. 2), it was significantly more common in Evenks compared to Evens, Yukagirs and Chukchi, also in Yakuts compared to Evens and Chukchi, and among Dolgans compared to Chukchi. The main contribution to the frequency of obesity, in con-

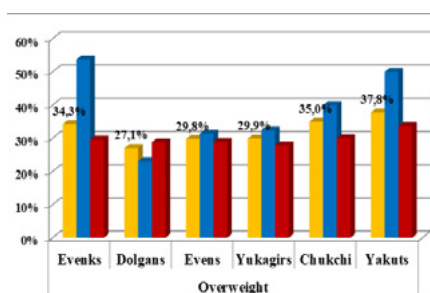


Fig. 1. The frequency of overweight on the value of BMI, depending on ethnic and gender identity

*- $p < 0.05$.

trast to OW, was made by women.

A comparative analysis of the average values of SBP among respondents was conducted, and it ranged from 132.0 to 145.63 (Table 2). Statistically significant differences in the level of SBP were observed in the Evenks and Yakuts compared to the Chukchi and Dolgans, between the Yakuts and Yukagirs. The mean values of both BMI and SBP, among Evenks and Yakuts were higher compared to other ethnic groups. Comparing the SBP by gender, large values of SBP were observed in women, there were no significant differences. This is confirmed by many studies conducted in

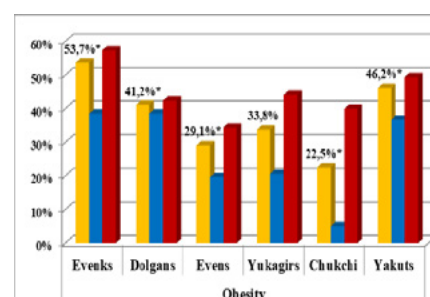


Fig. 2. The frequency of obesity by the value of BMI, depending on ethnic and gender identity. *- $p < 0.05$

Russia based on ESSE-RF studies [3, 6, 8, 9].

The prevalence of AH among the indigenous population of the Arctic zone of Yakutia was determined. Thus, there was a high frequency of AH in all ethnic groups and it averaged 53.7%. There were significant differences in the frequency of AH among the Chukchi compared to the Evenks (37.5 and 64.2%, respectively, $p = 0.008$) and Yakuts (63%, $p = 0.006$).

We also found a correlation between body mass index and AH level. Among all respondents, there was a strong positive association of BMI with the level of SBP ($r = 0.418$, $p = 0.000$).

Table 1

Comparative analysis of body mass index depending on ethnicity and gender

	Evenks	Dolgans	Evens	Yukagirs	Chukchi	Yakuts
	1	2	3	4	5	6
BMI	30.79±0.72	28.6±0.68	26.74±0.47	27.58±0.68	26.4±0.66	29.52±0.51
p	$p_{1-2}=0.031$ $p_{1-3}=0.000$ $p_{1-4}=0.002$ $p_{1-5}=0.000$	$p_{2-3}=0.024$ $p_{2-5}=0.047$	$p_{3-6}=0.000$	$p_{4-6}=0.022$	$p_{5-6}=0.001$	
men	29.0±1.20	27.35±0.88	25.29±0.63	25.74±0.71	24.8±0.55	28.0±0.65
women	31.22±0.84	29.15±0.90	27.57±0.63	29.05±1.03	28.0±1.10	30.03±0.63
P_{m-w}	>0.05	>0.05	<0.05	<0.05	<0.05	>0.05

Table 2

Comparative analysis of mean systolic blood pressure depending on ethnic and gender affiliation

	Evenks	Dolgans	Evens	Yukagirs	Chukchi	Yakuts
	1	2	3	4	5	6
SBP	144.48	132.0	140.0	137.14	132.0	145.63
p	$p_{1-5}=0.012$ $p_{1-2}=0.002$	$p_{2-6}=0.002$		$p_{4-6}=0.019$	$p_{5-6}=0.002$	
men	137.69	131.54	138.24	133.82	131.0	141.67
women	146.11	132.20	141.0	139.77	133.0	146.97
P_{m-w}	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05

Conclusion. The conducted research revealed a high incidence of arterial hypertension, overweightness and obesity among the indigenous population of the Yakutian North. The highest frequency of all indicators was observed in the Evenks and Yakuts, in comparison to other ethnic groups. This is not only a medical, but also a social problem of our community. The change in the traditional way of life, eating habits (mainly due to the carbohydrate/fat component), as well as low physical activity changed the perception of a low incidence of hypertension and obesity among the indigenous population of the North.

Our study confirmed the opinion of scientists all over the world that body mass index is closely associated with AH [14]. Thus, by correcting obesity, we can influence blood pressure.

The current situation requires an integrated approach from regional authorities towards the state's policies in healthcare to: control population values of body weight, starting from childhood, providing conditions for sports in walking distance, promote healthy eating, and healthy lifestyle.

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SEASONAL FUNCTIONAL ORGANIZATION OF THE EXTERNAL RESPIRATION SYSTEM IN CHILDREN OF SENIOR SCHOOL AGE, RESIDENTS OF THE ARCTIC REGION

Abstract

The aim of the work is to reveal the peculiarities of the seasonal functional organization of the external respiration system in children of senior school age living in the Arctic region.

Methods.

35 boys (16.3 ± 0.13 years) and 35 girls (16.6 ± 0.2 years old), residents of Arkhangelsk were examined in different season (winter, spring, summer, autumn). The following parameters were evaluated by spirometry: the lungs volumes and capacity, patency of airways, gas analysis of the expired air.

Results and discussion.

The parameters of external respiration system and character of its connection are changing during the year. In the group of boys moderate positive correlation were revealed between minute respiratory volume (V) and oxygen consumption (VO_2) in spring ($r=0.531$; $p<0.01$), in summer ($r=0.592$; $p<0.05$), and in autumn ($r=0.664$; $p<0.01$), but from spring to autumn it is getting stronger, and in winter it getting weaker and become statistically insignificant. In winter there is strong positive correlation between tidal volume (TV) and VO_2 ($r=0.786$; $p<0.01$), which in the other season were moderate or weak. The negative connection between V and oxygen utilization coefficient (UCO_2) in winter and autumn were revealed. In the group of girls moderate positive correlation between V and VO_2 were revealed in spring ($r=0.676$; $p<0.01$), and strong ($r=0.765$; $p<0.01$) in summer, but in winter and autumn it getting weaker and become statistically insignificant. At the same time in winter in the group of girls also were revealed moderate positive correlation between TV and VO_2 ($r=0.663$; $p<0.01$). In the other seasons this connection statistically insignificant. In spring strong positive correlation between VO_2 and UCO_2 ($r=0.797$; $p<0.01$) was revealed.

Conclusions. During the summer and transitional seasons of the year (spring and autumn), the change in the oxygen demand of the organism is provided by a changes in the V, and in winter - by optimizing the gas exchange conditions and changes in the ratio of static lungs volumes (TV and ERV).

Keywords: Arctic region, children of senior school age, external breathing, seasonal changes, functional organization of respiration.

Introduction. Senior school age is the final stage of the body formation when the structural and functional maturity of many systems occurs, puberty occurs, and environmental factors have a significant impact on these processes. The Arctic territories are characterized by extreme climatic conditions that cause stress on all functional systems of the human body, especially in children [6, 8, 9]. Among the environmental factors of high latitudes emit a whole group of pulmonotropic, which have a direct effect on the respiratory system [4, 10]. Therefore, regular changes occur in the respiratory system during the year due to seasonal dynamics of climatic factors. At the same time, the direction and severity of functional changes depend on the severity of the climate in the place of residence of the person [3, 5]. It should be emphasized that within the framework of these

changes, the external respiration system should perform its main function - to ensure the necessary level of oxygen consumption and carbon dioxide excretion for the organism [6, 11, 12].

Currently, there are information about the functional intersystem organization of external respiration in healthy men living in territories with a continental climate (Western Siberia) [3,10], as well as seasonal changes in the external respiration system in residents of a temperate continental climate (Komi Republic) [2]. Publications devoted to the analysis of the seasonal functional organization of the respiratory system in children are practically absent, which prompted the present study.

Objective of the study is to identify the features of the seasonal functional organization of the external respiration system in children of senior school age living

in the Arctic region.

Research materials and methods.

The study of the functional parameters of the respiratory system dynamics were carried out in practically healthy children of senior school age who were born and permanently reside in an area with a moderate maritime climate in the city of Arkhangelsk, which belongs to the Arctic zone of the Russian Federation (AZ RF) [7]. Examination of the same students was conducted four times in year - in winter (January), in spring (April), in summer (June) and autumn (September) with observance of ethical norms.

The method of spirometry (microprocessor portable spirometer SMP-21/01 - "RD") examined 35 boys (16.3 ± 0.13 years) and 35 girls (16.6 ± 0.2 years). We did not include children with chronic respiratory diseases, acute illnesses and complaints on the day of the survey.

The study was conducted in the morning in 1.5 - 2 hours after breakfast, with maximum physical, mental rest and temperature comfort, in conditions close to the main exchange. All parameters were recorded in a sitting position.

The subjects assessed pulmonary volumes and capacities: tidal volume (TV), reserve inspiratory reserve volume (IRV), expiratory reserve volume (ERV), vital capacity (VC); indices of pulmonary ventilation: respiratory rate (RR) and minute respiratory volume (V); airway patency: forced expiratory volume in the first 1 second (FEV₁). The percentage content of oxygen (FeO₂) and carbon dioxide (FeCO₂) in exhaled air was determined by gas analyzer PGA-200. The value of oxygen consumption (VO₂) and oxygen utilization coefficient (UCO₂) were calculated.

The obtained data were subjected to statistical processing using the SPSS 21.0 package. The normal distribution of the obtained variables was determined using the Shapiro – Wilk test (n≤50). The distribution of data differed from the normal one; therefore, Friedman analysis of variance was used; for pairwise comparisons, the Wilcoxon criterion for dependent samples using the Bonferroni correction. The results of non-parametric data processing methods were presented as a median (Me), first (Q1) and third (Q3) quartile. A correlation analysis was conducted with the determination of the non-parametric Spearman rank correlation coefficient. The critical level of significance (p) for all tested statistical hypotheses was taken as 0.05.

Results and discussion. A seasonal survey of children of senior school age, natives of AZ RF, made it possible to identify the peculiarities of compensatory-adaptive reactions of the respiratory system and evaluate their functional significance. It was established that during the year not only the values of the external respiration system activity indicators, but also the nature of the connections between them changes. Thus, in the group of boys moderate positive correlation were found between the parameters of V and VO₂ in spring, summer and autumn, while from spring to autumn the correlation is getting stronger, and in winter it is getting weaker and becomes statistically insignificant (Table 1).

At the same time, in the winter there is strong positive correlation between TV and VO₂, which in the other seasons of the year was moderate and weak or statistically insignificant. Instead of the missing links between TV and VO₂, there is

a moderate positive correlation between VO₂ with UCO₂ in summer and autumn, which was weak and insignificant in winter and spring.

There is negative correlation between the volume of pulmonary ventilation and its efficiency (V - UCO₂) in the winter and during the transitional period of the year from warm to cold (autumn). Also in the fall, negative correlation which depends on the moderate force between the RR and TV in providing the V was revealed.

The value ERV has moderate positive correlation in all seasons of the year with the VC. The strength of the correlation of other lung volumes that make up the VC (TV - VC, ERV - TV) for boys does not statistically significantly change during the year. During the annual cycle in boys of senior school age, the strength of the correlation between bronchial patency (FEV₁) and RR and TV values do not change either. The correlation between VO₂ and RR is expressed in winter (p < 0.05) and spring (p < 0.05), in summer this correlation disappears.

In the group of girls moderate positive correlation was found in spring and strong in summer between V and VO₂, and in winter and autumn it correlation is getting weaker and becomes statistically insignificant (Table 2). At the same time, in winter, as well as in the group of boys, there is moderate positive correlation between the values of VO₂ and TV. In the rest of the seasons, the relationship be-

tween VO₂ and TV is statistically insignificant. In autumn, instead of the missing correlation between VO₂ and TV, there is a strong positive correlation between VO₂ and UCO₂. Negative correlation has been revealed between the volume of pulmonary ventilation (V) and its efficiency (UCO₂), which in winter has strong positive correlation.

In the summer and autumn a strong negative correlation was found between RR and TV in providing V. The strength of the correlations of other lung volumes that make up the VC (ERV - TV and TV - VC) does not practically change in the dynamics of the annual cycle in girls, except for TV - VC in summer, when moderate correlation (p < 0.05) is established. During the year, the strength of the correlation between the integral bronchial patency index (FEV₁) and TV does not change.

Thus, the study indicates change in the seasonal functional organization of the respiratory system in children of senior school age, residents of the Russian Federation's AZ. Attention is drawn to the fact that the correlation between V and VO₂ in both boys and girls groups in winter disappears. In addition, this correlation disappears in girls in autumn. A similar fact was discovered earlier in adult residents of Western Siberia [10]. It can be assumed that this situation of the functional organization of the external respiration system is caused by the

Table 1

The correlation coefficients (r) between the indices of external respiration in boys of senior school age, natives of the AZ RF, in different seasons of the year

Correlation	Winter	Spring	Summer	Autumn
V – VO ₂	0.343	0.531**	0.592*	0.664**
TV – VO ₂	0.786**	0.379	0.295	0.202
VO ₂ – UCO ₂	-0.211	0.204	0.607*	0.596*
TV – RR	0.162	-0.318	-0.639	-0.652**
VC – ERV	0.562*	0.646*	0.543*	0.413
VC – TV	-0.199	0.359	0.283	-0.169
TV – ERV	-0.268	0.098	0.315	0.136
RR – FEV ₁	0.041	-0.074	0.125	0.009
TV – FEV ₁	-0.229	0.500	0.261	-0.240
RR – VO ₂	0.521*	0.527*	-0.038	0.335
V – RR	0.638**	0.174	0.487	0.755**
V – TV	0.011	0.499	0.097	-0.113
V – ERV	-0.354	-0.011	0.130	0.309
V – UCO ₂	-0.225	0.315	0.018	-0.163
VO ₂ – ERV	-0.418	-0.379	-0.154	0.359

Note. In the Tables 1 and 2 significance at * - p < 0.05; ** - p < 0.01..

Table 2

The correlation coefficients (r) between the indices of external respiration in girls of senior school age, natives of the AZ RF, in different seasons of the year

Correlation	Winter	Spring	Summer	Autumn
V – VO ₂	0.542	0.676*	0.765**	0.379
TV – VO ₂	0.663*	-0.133	0.369	0.256
VO ₂ – UCO ₂	0.129	0.443	0.341	0.797**
TV – RR	-0.067	-0.510	-0.719**	-0.865**
VC – ERV	0.693**	0.505	0.322	-0.055
VC – TV	-0.113	-0.337	0.660*	0.221
TV – ERV	-0.386	-0.061	0.273	-0.333
RR – FEV ₁	-0.056	-0.625**	-0.177	-0.469
TV – FEV ₁	0.325	0.407	0.198	0.339
RR – VO ₂	0.136	0.589*	-0.041	-0.372
V – RR	0.518	0.725**	0.208	-0.314
V – TV	0.718**	0.080	0.311	0.636*
V – ERV	-0.289	0.742**	-0.047	-0.104
V – UCO ₂	-0.703**	-0.910	-0.212	0.110
VO ₂ – ERV	0.204	0.753**	0.173	0.720**

action of the cold factors. Probably, the cold limits the number of functioning acini due to the fact that part of the cooled acini overlaps. However, the stable maintenance of the required level of VO₂ in this case is possible only with an increase in the efficiency of gas exchange in the respiratory regions of the lungs, as indicated by the UCO₂ value.

The correlation between TV and VO₂, which appeared in winter in both boys and girls, indirectly indicates an increase in the airiness of the lungs, i.e. those acini which continue functioning. Increasing the airiness of the acini leads to stretching of the interalveolar septa, reducing the thickness of the alveolar-capillary membrane and increasing the area of the respiratory surface [13, 14]. All this increases the diffusion capacity of the lungs, accelerates the transfer of oxygen from alveolar gas into the blood of the pulmonary capillaries, increasing the efficiency of pulmonary ventilation in winter.

The change in V in winter in boys and in spring in girls is consistently based on the respiratory rate, since a positive correlation was found between these pa-

rameters: moderate in winter and strong in spring. It can be concluded that in these seasons the restructuring of the V is carried out by increasing the RR, which leads to more intense work of the respiratory muscles.

Being the second component of the VC and the first component of the functional residual capacity of the lungs, the magnitude of the ERV has moderate positive correlation in all seasons of the year with the VC in the boys and in winter in the girls. It should be noted that ERV has an important role in the mechanisms of regulation and accumulation of metabolic CO₂, since, in functional terms, the reserve expiratory volume is a buffer capacity of conducting airways that reduces the possibility of unhindered release of metabolic CO₂ through the lungs to the outside [1]. Therefore, the reserve expiratory volume acts as a kind of locking mechanism, allowing to gradually reduce the oxygen tension in the inhaled air to the level of the alveolar and, conversely, prevent a sharp decrease in the partial pressure of CO₂ in the lungs to the level of atmospheric pressure.

Conclusion. Thus, in senior school age children, residents of the Arctic region, during the summer and transitional seasons of the year (spring, autumn), the change in the oxygen demand of the body (VO₂) is provided by a change in pulmonary ventilation (V), and in winter, by optimizing the gas exchange conditions as a result of a change in static pulmonary volumes (TV and ERV), leading to the fact that backup acini is included in ventilation and gas exchange, increasing, respectively, the respiratory surface and improving the conditions of oxygen diffusion in the lungs.

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MICROELEMENTAL COMPOSITION OF BLOOD AMONG ABORIGINAL INHABITANTS OF THE ARCTIC

ABSTRACT

The level of microelement status indicators in the blood of aboriginal inhabitants of the Arctic is determined, on the basis of which it is possible to conduct future comparisons under conditions of industrial development of territories. The study included 107 indigenous inhabitants of the North, belonging to the ethnic group of Dolgan, living in Yuryung-Khaya of the Anabar district of Yakutia. The content of 20 microelements in the blood serum was studied.

The content of many elements, including manganese, cobalt, strontium, nickel and iron in blood is higher than reference values, which can influence the development of diseases of the cardiovascular system, nephropathy and oncological diseases.

Keywords: trace elements, indigenous peoples of the North, Arctic.

Introduction. The stability of the chemical composition of the body is one of the most important and necessary conditions for its normal functioning. Accordingly, deviations in the content of chemical elements caused by environmental, occupational, climatogeographic factors or diseases lead to a violation in the state of health [6]. The Northern territories are extremely different from the Central regions of Russia by climatic, biogeochemical, dietary and adaptive characteristics.

Alluvial diamond deposits are being developed in the valley of River Ebelyah, which is the left tributary of the Anabar River in Yakutia. During the development of the natural landscape structure and environmental conditions have undergone

significant changes. A special danger in the development of the Deposit is the contamination of the surface layer of soil with chemical elements with toxic and radioactive properties contained in the ore. Filtration effluents of the downstream of the wellhead dam of the concentrator form a clear technogenic hydrochemical anomaly of manganese, chromium, Nickel, copper, lead and molybdenum [4, 9].

Toxic elements, migrating to streams and rivers in the form of mineral particles, accumulate in the bottom sediments and gradually decomposing, for a long time, fall into large watercourses, on the banks of which are located settlements. The local population drinks this water, uses it for economic purposes, eats fish that

lives in this water and feeds on microorganisms that inhabit these watercourses, thereby accumulating toxic elements in their bodies. The danger of area pollution of the environment with toxic radioactive elements and heavy metals is associated with wind drift of mineral particles from the quarry and from the dumps of off-balance ores [4, 9]. Area dispersion of mineral particles with toxic elements accumulates in plants, primarily in the moss, where it enters the body of animals and birds. When consumed in food, a person also accumulates toxic elements in his body. Poisoning of the body as a result of these factors, the process is hidden and "stretched" in time, depends on the individual characteristics of the human body

and lifestyle, eating behavior, as a result, it is impossible to accurately determine the cause of a disease.

In this regard, we conducted this study in order to establish a regional baseline indicators of the elemental status of the body of indigenous inhabitants of the Arctic, on the basis of which future research will be conducted.

Materials and methods of research.

In the present study involved 107 native peoples of the North, on a nationality the Dolgans. The surveyed population lives in isolation in the tundra on the bank of the Anabar River, the village of Yuryung-Khaya. It is Anabar district of the Republic of Sakha (Yakutia). Prior to inclusion in the study, written informed consent was obtained from residents. The survey was conducted in accordance with the principles and ethical standards established by the Helsinki Declaration.

Blood sampling from the ulnar vein is done in the morning on an empty stomach using a test tube "Vacutest". The obtained blood was centrifuged with the aim of obtaining serum for 10 minutes at 1800 R/min. Serum was separated and frozen endorph at a temperature of -27°C for storage and transport. By atomic emission and mass spectrometry with ionization in inductively coupled argon plasma on the instrument the mass spectrometer ICP-MS Elan 9000 (Canada) we examined the serum of blood of the next 20 microelements: phosphorus (P), scandium (Sc), titanium (Ti), vanadium (V), chromium (Cr), manganese (Mn), iron (Fe), cobalt (Co), Nickel (Ni), copper (Cu), zinc (Zn), arsenic (As), rubidium (Rb), strontium (Sr), yttrium (Y), niobium (Nb), cadmium (Cd), cesium (Cs), thallium (Tl), lead (Pb). The content of the studied chemical elements in blood serum was expressed in micrograms per liter ($\mu\text{g/l}$).

Statistical processing of the obtained results was carried out with the help of SPSS 19 application software package. A descriptive analysis of the numerical characteristics of the signs (Me (Q25-Q75) median (interquartile range 25 and 75). At comparing the differences in the groups, nonparametric evaluation criteria (Mann-Whitney U – test) were used. Statistically, the significance of the differences was considered significant at $p < 0.05$.

The results and discussion. In the study were men 35 (32.7 %) and women – 72 (67.3 %). The age of the subjects was from 20 to 77 years. The average age of men was 51 (42-60) years, women – 45.5 (34-54) years, without statistically significant differences ($p=0.094$). Median

concentrations were calculated to determine the content of trace elements in blood serum.

The contents of one of the main "structural" elements of the person, and phosphorus (P), most Dolgan high 148,02 (124,01-171,60) mg/l , more than 3-4 times the data of residents of other regions of Russia (25,08-44,91 mg/l) [2, 3], which is probably due to traditional fish food. Phosphorus plays a fundamental role in many basic cellular processes, such as bioenergy, intracellular signaling and mineralization of bones and teeth, it is a part of nucleic acids, cell membranes [1].

According to our data, the content of scandium (Sc), chromium (Cr), lead (Pb) in the blood corresponded to the data of literary sources.

Chromium (Cr) – is important for the normal course of carbohydrate metabolism in the human body. The main role of chromium is to reduce blood glucose levels.

The need for chromium increases in people as a result of various stresses, fatigue, injuries, diabetes and diseases of the cardiovascular system [6].

The content of copper (Cu), zinc (Zn), rubidium (Rb) was above the upper limit of reference values (Table 1).

Copper (Cu) – one of the essential elements necessary for the normal functioning and development of the body. The source of copper is food. Being a part of 16 different metalloproteins, copper is an essential element for the cells of the body. It is also important in iron metabolism. Copper is rapidly absorbed from the stomach and upper intestine, deposited in the liver and in various copper-containing cell proteins in plasma [11].

Biological functions of zinc (Zn) are determined by the fact that it is part of metalloenzymes, RNA and DNA polymerases, carboxypeptidase and alcohol-dehydrogenase. Zinc absorption occurs mainly in the duodenum and proximal intestine. Especially rich in zinc, prostate, semen, liver, kidney, retina, bone and muscle. The concentration of zinc in red blood cells is 10 times higher than Rubidium (Rb) – little-known trace element, often in the body acts as a potassium synergist. The role of rubidium in the body is poorly understood. The daily requirement of a healthy adult in rubidium is about 1-2 mg, which exceeds the rate of consumption of many other trace elements. Most of the rubidium (about 40%) enters the body with drinks such as drinking water, tea and coffee. Some rubidium is found in the liver and muscles of marine fish

[6]. There is a study that the level of potassium and rubidium was significantly reduced in the blood of patients with Alzheimer's disease compared to the healthy group, but the content of cerebrospinal fluid was within normal limits [10]. Experiments on animals have shown that the lack of rubidium causes a delay in fetal development, abortion and premature birth, a reduction in life expectancy [8].

In this study, the serum Nickel (Ni) content was a median of 57.08 $\mu\text{g/l}$ and strontium (Sr) – 146.55 $\mu\text{g/l}$, which exceeded the norm by 2 - 3 times.

Strontium (Sr) is found in all organs and tissues, affects the processes of bone formation, the activity of enzymes of catalase, carbonic anhydrase and alkaline phosphatase. In addition, strontium ions are so close in characteristics to calcium ions that they are included in the exchange with it, but, having a greater intensity of metabolism and significantly different in size, gradually disrupt the functioning of calcium-dependent metabolic processes [8].

The content of iron (Fe) in blood serum was 5219.43 $\mu\text{g/l}$, which is 4-5 times higher than the accepted standards [11]. High iron content is associated with an increased risk of cardiovascular disease and some cancers.

The manganese (Mn) content was 130.86 $\mu\text{g/l}$, which is much higher than normal. According to the literature, there are cases of acute intoxication with manganese dust in the workplace. Excess manganese leads to increased fatigue, memory loss, depression, encephalopathy, and neurological disorders [5]. Perhaps this factor leads to mental disorders with suicidal attempts, this problem requires further study.

Microelements with a very low concentration in the studied sera were isolated into a separate group (table. 2).

Cobalt (Co) and cesium (Cs) were detected in almost all subjects, yttrium (Y) and cadmium (Cd) in half of the cases and in less than 1/5 of the cases niobium (Nb), arsenic (As), vanadium (V), thallium (Tl). The content of cobalt (Co) in Dolgans exceeded the known values many times, which requires additional in-depth study.

The analysis of the content of elements separately in men and women. At comparing by gender the median of all investigated trace elements in addition to rubidium (Rb), significant differences were not revealed. According to our data, the rubidium median (Rb) in men was significantly higher ($p=0.005$) and amounted to 322.95 (286.62-372.46) $\mu\text{g/l}$ than in

Table 1

The content of trace elements in blood serum Dolgan, µg / l

Trace element	n	Me (Q25-Q75)	Reference values (literature data)*
Scandium (Sc)	105	13.97 (9.13-19.57)	10-40
	2	<0.001	
Titanium (Ti)	104	153.05 (83.98-265.82)	
	2	<0.001	
Chromium (Cr)	106	276.67 (246.69-324.70)	165-305
Manganese (Mn)	100	130.86 (63.88-173.25)	0-10
	5	<0.001	
Iron (Fe)	98	5219.43 (3123.30-9197.05)	600-1800
	5	<0.001	
Nickel (Ni)	83	57.08 (23.38-146.07)	1-28
	23	<0.001	
Copper (Cu)	81	1323.60 (953.07-1902.63)	750-1300
	21	<0.001	
Zinc (Zn)	93	1076.11 (677.48-1686.24)	543-1130
	12	<0.001	
Rubidium (Rb)	105	299.45 (264.35-346.34)	230-270
	2	<0.001	
Strontium (Sr)	87	146.55 (77.99-234.11)	44-64
	18	<0.001	
Lead (Pb)	70	9.48 (3.61-23.75)	< 25
	33	<0.001	

Note. In the Tables 1 and 2 n - number of observations
Me (Q25-Q75) - median (interquartile range 25 and 75)

*AMAP Assessment 2002: Human Health in the Arctic // Arctic Monitoring and Assessment Programme (AMAP) - Oslo, Norway, 2003

women - 292.92 (256.21-332.60) µg/l.

The subjects were divided into three groups by age: the first group of young people – from 20-44 years, the second group of middle age – from 45-59 years and the third group of elderly people over 60 years.

The phosphorus content in the age groups in men and women did not differ significantly, despite an increase in the average age in both sexes.

According to the literature, serum iron should be higher in men. In this study, the iron content in women was higher, although statistically insignificant, while increasing with age. In 12 young men, the median iron was 4.4 mg / l, the average age of 13 subjects-5, 6 mg/ l, 8 elderly-3, 3 mg/ l, on the contrary, in 31 young women-4.8 mg/ l, in the middle group of 28 subjects-6.1 mg/l and the highest rates of iron in the group of 7 women over 60 years – 9.9 mg / l (compared with the same group of men p=0.049). These indicators require extensive research.

Considered significantly high in men Dolgan element rubidium (Rb) by age groups. For all three groups in men, the

serum rubidium content was expected to be higher and amounted to 13 young-321.5 µg / l, in the middle group of 13 people - 343.2 µg / l, in 9 men over 60 years-321.6 µg/l. the rubidium content was in women in the respective groups: 295.8 µg/l, 293.4 µg/l and 248.7 µg/l.

In our study 26 people had an increase in atherogenic cholesterol associated with increased levels of iron, cobalt and rubidium. According to the study, cardiovascular disease (CVD) amounted to 691 per 1000 population. It indicating a high incidence of CVD to Dolgan. At the same time, the lipid spectrum with a high coefficient of atherogenicity was observed in 1/3 of the examined patients.

Conclusion. Thus, the study revealed an increased content of many elements, including manganese, strontium, cobalt and iron in the blood, which can affect the development of diseases of the cardiovascular system and other diseases in the indigenous inhabitants of the Arctic.

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Table 2

The content of ultramicroelements in blood serum Dolgan, µg / l

Trace element	n	Me (Q25-Q75)	Референсные значения (литературные данные)*
Vanadium (V)	18	4.78 (1.42-17.03)	
	88	<0.001	
Cobalt (Co)	73	4.09 (1.54-9.25)	0.05-0.1
	30	<0.001	
Arseni (As)	26	4.94 (2.88-19.58)	2 - 62
	78	<0.001	
Yttrium (Y)	58	0.80 (0.27-1.73)	
	44	<0.001	
Niobium (Nb)	35	10.07 (4.13-16.68)	
	69	<0.001	
Cadmium (Cd)	56	0.38 (0.16-0.78)	0.01-2
	48	< 0.001	
Cesium (Cs)	103	1.05 (0.69-1.39)	
	3	<0.001	
Thallium (Tl)	13	2.64 (0.29-7.14)	
	92	<0.001	

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ACTUAL TOPIC

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REGIONAL FEATURES OF MORBIDITY AND MORTALITY FROM MALIGNANT NEOPLASMS IN THE REPUBLIC SAKHA (YAKUTIA)

Abstract

We have completed an analysis of the dynamics of morbidity and mortality from malignant neoplasms (C00-97) among the population of the Sakha (Yakutia) Republic for the period of 2008-2017. In these dynamics, there is an increase in standardized indicators (world standard) of incidence from 203 to 213 per 100,000 population (average growth rate of 0.6). At the same time, mortality rates continue to decline with an average decline rate of -1.7. Regional features of cancer pathology are high – compared with the average in the Russian Federation – morbidity rates (3.6 times) and mortality (3.8 times) of the population of both sexes from malignant neoplasms of the liver and intrahepatic ducts (C 22) and of the female population from malignant tumors of the trachea, bronchi, and lung (1.9 times higher than in the Russian Federation).

Keywords: malignant neoplasms, morbidity, mortality, ratio of mortality and morbidity, Sakha (Yakutia) Republic, regional characteristics.

Introduction. Malignant neoplasms (MNP) are one of the leading causes of death in the world. The increase in incidence is associated with the aging of the population, and methods of treatment, despite the achievements of modern medicine, are not always effective or fully developed. In the Russian Federation, along with the trend of increasing morbidity, a high mortality rate from cancer still remains. The main reason for this is the late diagnosis of the disease. At the same time, morbidity and mortality rates in the regions of the Russian Federation have significant differences, including those concerning main localizations of malignant tumors.

The Sakha (Yakutia) Republic is the largest subject of the Russian Federation with a population (as of January 1st, 2017) of 962.8 thousand people living in an area of 3.1 million square km [7]. The vast territory determines the remoteness of many settlements from the center, the differences in transport accessibility, socio-economic level, including access to diagnostic and therapeutic assistance. The harsh climate and the features of demographic processes also change the structure of morbidity and mortality of the population. Thus, life expectancy in 2017 in the Republic was below the national average by 1 year. At the same time, Yakutia is one of the few regions of the Russian Federation with a positive natural population growth, which affects the average age of the population (34.1 years) [7].

Aim of the study was to analyze the dynamics and structure of morbidity and mortality from malignant neoplasms

(MNP) in the population of the Sakha (Yakutia) Republic for the period of 2008-2017.

Materials and Methods. We have carried out a retrospective epidemiological analysis of morbidity and mortality of the population of the Sakha (Yakutia) Republic from malignant neoplasms for the period of 2008-2017 using statistical data from Territorial Body of the Federal State Statistics Service for the Sakha (Yakutia) Republic and the Moscow P.A.

Herzen Oncologic Research Institute [3, 7]. For comparative analysis, we used indicators standardized according to the world standard for the age structure of the population [10]. When analyzing the dynamics of incidence, we determined the average existing growth rate.

Results and Discussion. The incidence of MNP in the Sakha (Yakutia) Republic in 2017 was 208.3 per 100,000 population (Table 1). The age-standardized (AS) incidence rate among

Table 1

Dynamics of morbidity and mortality from malignant neoplasms per 100,000 population (codes C00-97) for 2008-2017 [2]

Year	Sakha (Yakutia) Republic					Russian Federation				
	Morbidity		Mortality		K	Morbidity		Mortality		C
	esti- mate	AS	esti- mate	AS		esti- mate	AS	esti- mate	AS	
Men										
2008	210.6	242.9	137.7	167.7	0.65	347.4	271.7	233.9	180.4	0.67
2009	224.6	256.4	147.8	173.4	0.66	358.2	277.7	237.1	182.2	0.66
2010	216.5	250.1	134.0	159.0	0.62	362.6	279.6	236.2	180.2	0.65
2011	219.9	255.8	146.4	175.4	0.67	363.2	273.5	234.3	173.9	0.65
2012	226.1	249.0	147.3	164.1	0.65	363.6	270.7	231.3	169.3	0.64
2013	213.9	228.6	139.9	150	0.65	369.0	271.3	231.3	167.5	0.63
2014	234.3	248.9	138.4	151.7	0.59	383.3	277.6	229.3	164.2	0.60
2015	257.9	270.9	143.0	152.4	0.55	398.1	284.0	233.0	164.0	0.59
2016	242.5	245.3	154.2	160.0	0.64	402.5	283.1	234.3	162.1	0.58
2017	256.5	255.2	151.5	153.2	0.59	414.1	286.7	228.8	155.6	0.55
Women										
2008	206.1	177.4	113.7	100.7	0.55	344.2	200.3	174.3	91.4	0.51
2009	221.2	185.8	116.5	100.1	0.53	353.9	204.1	177.1	92.2	0.50
2010	211.3	179.6	107.5	90.6	0.51	365.6	208.9	177.2	91.4	0.48
2011	225.7	186.5	105.3	88.0	0.47	367.4	207.9	175.2	88.9	0.48
2012	224.7	183.8	109.1	88.6	0.49	370.5	208.5	174.8	87.5	0.47
2013	238.7	187.1	111.9	88.1	0.47	377.3	210.7	175.2	87.0	0.46
2014	238.1	185.8	116.1	87.7	0.49	392.1	216.9	173.7	85.4	0.44
2015	269.3	207.1	114.0	84.7	0.42	406.4	223.0	176.2	85.7	0.43
2016	247.9	184.7	112.9	82.9	0.46	413.9	225.6	173.4	83.6	0.42
2017	262.0	191.8	118.1	82.8	0.45	425.7	229.6	171.3	81.2	0.40

Note. In the Tables 1, 3 AS – age-standardized indicator (world standard); C – the ratio of “estimate” mortality and morbidity.

the male population was 25% higher than among the female population (255.2 and 191.8 0/0000, respectively). Over the 10-year period (2008-2017), there has been an increase in the AS indicator of the incidence of MNP from 203 to 213 0/0000 (with average growth rate of 0.6). In all analyzed years, the incidence of MNP in the Sakha (Yakutia) Republic among both sexes was slightly lower than in the Russian Federation.

In 2017, in the Sakha (Yakutia) Republic, 1,294 people have died (including 708 men and 586 women) from malignant neoplasms. The mortality rate from MNP (estimate) for the entire population of the republic was 134.3 0/0000 (SP 109.7 0/0000), the proportion of mortality from MNP in the structure of total mortality of the population is 16.5%. Mortality rate among the male population of the Republic was 1.9 times higher than that of the female population. In the course of 10 years, both in the Russian Federation as a whole and in the Sakha Republic, we have observed a decrease in mortality rates (the average rate of decline was -1.4 for the Russian Federation and -1.7 for the Sakha Republic).

Ratio of mortality and morbidity can indicate both the aggressiveness of the MNP and the accessibility and quality of diagnosis and treatment of patients [11]. For the analyzed period, the indicator dropped from 0.60 to 0.52 (in the Russian Federation from 0.58 to 0.47). At the same time, in all the years it was higher than in the Russian Federation as a whole (for both sexes).

In the structure of the incidence among male population in 2017, the main locations of MNP were the tracheal, bronchus, lung, stomach, prostate, liver, intrahepatic ducts, and skin. Among the female population, respectively, MNP were forming in the breasts, cervix, trachea, bronchi, lung, colon, and kidneys. The incidence rate among male population of MNP in the liver and intrahepatic ducts in the republic is 3.8, and the mortality rate is 3.4 times higher than in the Russian Federation as a whole (Table 2). The incidence of MNP in the esophagus, stomach, pancreas, bones and articular cartilage is slightly higher, against the background of higher mortality rates from esophageal MNP.

If we look at similar indicators among the female population (Table 2), then in the Republic there is a significantly higher AS of the incidence of women with MNP in the liver and intrahepatic ducts (7 and 2⁰/₀₀₀₀ respectively), trachea, bronchi, lung (15 and 8⁰/₀₀₀₀ respectively), cervix (20 and 16⁰/₀₀₀₀ respectively), esophagus (2.5 and 0.8⁰/₀₀₀₀ respectively), larynx (1.4 and 0.4⁰/₀₀₀₀ respectively). AS of mortality from MNP of the liver and intrahepatic ducts is 2.7 times higher than the average in the Russian Federation (6.2 and 2.3⁰/₀₀₀₀ respectively), similar differences are observed with esophageal MNP (1.5 and 0.8⁰/₀₀₀₀ respectively), trachea, bronchi, and lung (13 and 6⁰/₀₀₀₀ respectively).

To answer the question of whether the revealed differences in the incidence are regional features of cancer pathology, or are associated with changes in diagnostic capabilities in 2017, we conducted a study of indicators for the period of 2008-2017 (Table 3). Analysis of the dynamics showed that in the Republic there are stably high – compared with the Russian Federation – morbidity and mortality rates of both sexes from liver and intrahepatic

ducts MNP and among female population from MNP of the trachea, bronchi, and lung.

Significant differences in the incidence rates of liver and intrahepatic ducts MNP suggest the presence of a risk factor in the region that does not depend on gender. One of the possible factors is the prevalence of chronic viral hepatitis B and C in the region, as well as the carrier state of the hepatitis B virus [1, 4, 5, 8, 9]. According to the Sakha Republic's Rospotrebnadzor, the incidence of chronic viral hepatitis B and C in the Republic in recent decades has significantly exceeded similar figures for the Russian Federation as a whole (Table 4). Thus, the incidence of chronic viral hepatitis B in 2017 was 34.1 per 100,000 population (RF 9.6⁰/₀₀₀₀), chronic viral hepatitis C – 52 (RF 34.0⁰/₀₀₀₀), respectively [2]. At the same time, the rate of carriage of the hepatitis B virus is also significantly higher than in the Russian Federation as a whole. Researchers associate the high frequency and progression of chronic viral hepatitis among the population of Yakutia with a violation of the activity of

Table 2

Standardized morbidity and mortality rates of the population of the Sakha (Yakutia) Republic from certain types of malignant neoplasms in 2017 [2]

ICD code 10	Morbidity		Mortality	
	Republic	Russia	Republic	Russia
Men				
C00-97 Malignant neoplasms	255.2	286.7	153.2	155.6
C15 Esophagus	13.9	6.5	10.5	5.5
C16 Stomach	26.6	20.2	14	16.4
C18 Colon	13.4	17.9	9.3	9.5
C22 Liver and intrahepatic bile ducts	19.8	5.2	19.1	5.6
C33,34 Trachea, bronchi, lung	49.0	49.0	37.3	40.4
C44,46.0 Skin (without melanoma)	13.2	28.7	1.6	0.8
C61 Prostate gland	24.3	40.5	6.7	12
C64,65 Kidney	13.8	14	4.3	5.2
C81-96 Lymphatic and hematopoietic tissue	12.7	16.3	4.5	8.3
Women				
C00-97 Malignant neoplasms	191.8	229.6	82.8	81.2
C15 Esophagus	2.5	0.8	1.5	0.8
C16 Stomach	8.7	9.1	5.8	6.5
C17 Small intestine	0.6	0.5	0.1	0.3
C18 Colon	13.0	14.0	6.5	6.8
C22 Liver and intrahepatic bile ducts	7.1	2.2	6.2	2.3
C33,34 Trachea, bronchi, lung	15.0	8.1	13.3	5.6
C50 Breast	37.7	52.0	10.4	14.2
C53 Cervix	20.2	15.8	6.1	5.2
C64,65 Kidney	10.2	7.8	1.7	1.8
C81-96 Lymphatic and hematopoietic tissue	10.7	12.6	4.2	5.2

Table 3

Динамика показателей заболеваемости и смертности от некоторых форм ЗНО за 2008-2017 гг. в Республике Саха (Якутия) [2]

Year	Sakha (Yakutia) Republic					Russian Federation				
	Morbidity		Mortality		K	Morbidity		Mortality		C
	esti- mate	AS	esti- mate	AS		esti- mate	AS	esti- mate	AS	
Code C22 MNP of liver and intrahepatic ducts (both sexes)										
2008	14.4	15.2	12.9	13.9	0.9	4.6	2.8	5.9	3.6	1.28
2009	16.0	15.7	13.1	13.6	0.82	4.7	2.9	5.9	3.6	1.26
2010	13.6	13.6	11.7	11.8	0.86	4.6	2.8	5.9	3.6	1.28
2011	13.9	13.7	10.3	10.4	0.74	4.6	2.7	6.0	3.5	1.30
2012	14.7	13.7	12.5	11.9	0.85	4.4	2.6	6.0	3.5	1.36
2013	15.0	13.7	12.0	10.9	0.80	4.7	2.8	6.2	3.5	1.32
2014	15.0	13.8	12.1	11.0	0.81	5.0	2.9	6.4	3.6	1.28
2015	17.8	15.9	13.3	11.3	0.75	5.5	3.1	6.8	3.8	1.24
2016	15.2	13.2	13.9	12.1	0.91	5.7	3.2	6.7	3.7	1.18
2017	15.2	12.4	13.8	11.3	0.91	6.0	3.4	5.5	3.0	0.92
Code C33, 34 Tracheal, Bronchi, Lung MNP (female)										
2008	15.7	14.8	14.5	13.3	0.92	13.4	7.0	11.3	5.6	0.84
2009	22.5	18.1	18.6	16.0	0.83	13.6	7.0	11.4	5.6	0.84
2010	17.1	15.4	12.0	10.4	0.70	13.9	7.1	11.5	5.7	0.83
2011	20.5	16.7	14.4	11.6	0.70	13.8	7.0	11.3	5.5	0.82
2012	17.3	13.4	14.0	11.2	0.81	13.5	6.8	11.5	5.5	0.85
2013	18.9	13.8	13.0	10.3	0.69	14.2	7.2	11.6	5.7	0.82
2014	17.9	13.1	15.3	11.0	0.85	14.6	7.3	11.8	5.6	0.81
2015	20.1	14.2	12.7	9.4	0.63	15.5	7.7	12.0	5.6	0.77
2016	20.2	14.7	13.7	9.7	0.68	15.8	7.7	11.9	5.5	0.75
2017	21.4	15.0	19.8	13.3	0.93	16.7	8.1	12.2	5.6	0.73

Table 4

Incidence of chronic viral hepatitis B and C in the Sakha (Yakutia) Republic, 2001-2017 (per 100,000 population) [3]

Year	Chronic Hepatitis B				Chronic Hepatitis C	
	Morbidity		Mortality		Morbidity	
	Russia	Yakutia	Russia	Yakutia	Russia	Yakutia
2001	16.0	38.0	89.6	200.0	29.0	17.0
2002	15.0	46.1	74.1	190.0	30.0	29.0
2003	14.9	63.3	65.5	140.0	33.0	45.0
2004	15.5	57.9	61.9	131.0	34.0	35.0
2005	13.9	51.9	50.6	80.2	31.0	43.0
2006	14.0	43.9	47.7	82.2	35.0	39.0
2007	14.0	33.2	42.7	55.8	37.0	42.0
2008	14.2	34.7	36.3	51.0	39.0	42.0
2009	14.4	39.3	32.4	43.4	40.0	51.0
2010	13.3	35.7	25.6	39.5	40.0	51.0
2011	13.0	34.2	22.0	32.8	40.0	51.0
2012	12.6	30.4	21.1	24.3	39.0	40.0
2013	11.7	27.8	18.1	21.4	39.0	43.0
2014	11.3	27.8	15.9	23.3	39.0	39.0
2015	10.8	35.2	13.8	17.4	38.0	54.0
2016	10.1	37.1	11.7	16.9	36.0	51.0
2017	9.6	34.1	10.1	15.0	34.0	52.0

alcohol dehydrogenase and aldehyde dehydrogenase in the native inhabitants of the Republic [4, 5].

The reasons for the significant differences in the AS of the incidence among female population of Yakutia in tracheal, bronchus, and lung MNP also need additional research (incidence rate is 1.9 times higher than in the Russian Federation). Chronic respiratory diseases, tuberculosis (morbidity rates that exceed the average in Russia by 1.2 times), as well as smoking and environmental factors can be possible reasons contributing to the high incidence of women with tracheal, bronchus, and lung MNP.

Conclusion. Thus, the results of the study suggest that although the standardized incidence rates of MNP in the Sakha (Yakutia) Republic are slightly lower than in the Russian Federation as a whole, there are some regional characteristics, which include the high morbidity and mortality of both sexes from MNP of liver and intrahepatic ducts and among female population from the tracheal, bronchial, and lung MNP. More research is needed to clarify possible risk factors. Taking into account regional characteristics of morbidity and mortality can help determine the direction of measures to reduce them, helping to preserve lives and increase the life expectancy of the population.

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SCIENTIFIC REVIEWS AND LECTURES

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IMMUNOGENICITY INDICATORS OF VACCINES AGAINST THE HUMAN PAPILLOMA VIRUS IN FEMALES ACCORDING TO SCIENTIFIC DATA, PUBLISHED IN THE INTERNET SYSTEM

ABSTRACT

The article outlines the features of searching in the Internet system for scientific articles on the effectiveness of vaccination against human papillomavirus. Publications containing data on the immunogenicity of human papillomavirus vaccines in girls and young women in the long-term period are analyzed. The age of the patients, the principles of formation of comparison groups, materials and laboratory methods, the duration of the research, the name of the used vaccines were established.

In Internet the search for scientific publications on the vaccination efficacy against HPV is valid and based on matches of the user keywords with the article title words.

Internet provides equal opportunities for researchers the availability of sharing knowledge, regardless of the publisher's rating and the number of citations.

The vaccination efficacy against HPV includes an evaluation of the vaccines' immunogenicity. The HPV vaccine immunogenicity in girls and young women from 9 to 25 years old, in the long-term period from 3 to 7 years, is determined by the level of

antibodies against HPV vaccine and the frequency of immune system cells sensitized to HPV. Patients participating in the studies were vaccinated by various schedule with Cervarix (human papillomavirus bivalent vaccine) and Gardasil (human papillomavirus quadrivalent vaccine).

Keywords: HPV, human papillomavirus, vaccines, cancer, immunogenicity.

Introduction. Given the lot of scientific publications in the health sciences, for clinicians who, due to their work, are busy, it is difficult to "keep up" with constantly updated literature. Therefore, articles analyzing scientific research are an effective method of obtaining the

necessary information. In addition, such articles are a kind of tool that allows medical doctors to determine the relevance of their own unique experience and the opportunity to share it in the publications and participation in professional events.

We have been interested to establish

features of the search and preliminary analysis of scientific articles with open access to the Internet, devoted to the effectiveness of vaccination, including the immunogenicity of vaccines against human papillomavirus (HPV). The article authors plan to make future research with a similar focus among of the Republic of Sakha (Yakutia) residents.

Materials and methods. Publications were searched for on the first three pages of the Google Internet System (IS) on January 23-25, 2019, by keywords (KW) "hvp, efficacy, vaccine, protection, immunity, immunogenicity, cervix, cancer, infection," in various combinations. The location was Yakutsk. The inclusion criteria of selected publications (5 in total) are presented in Table 1.

In accordance with our interest for future research work, we set ourselves the initial tasks - to find scientific articles in the IS, using the KW, and for further search in scientific databases - to determine the most frequently used keywords by the selected articles authors (authKW); then find out the features of the IS's search, depending on the use of KW and authKW. To design our future project, it was decided to select articles containing original data assessing the vaccines immunogenicity in girls and young women over a long-term period (more than 2 years) and to determine the age of the participants, and to clarify the formation of comparison groups, the study periods, what materials and laboratory methods are used, Brand and generic names of vaccines.

Results and discussion. With the using of KW's six combinations, as well as the inclusion criteria, 22 articles were selected [5-26]. The search results are presented in Table 2. The largest amount - 7 articles, were issued using the option "hvp vaccine efficacy protection immunity" (5 words in total).

The article of D.M. Harper et al. [14] was found in larger amount, 5 times out of 6, the first two words in the title of which is matched with the first two words of the printed KW. Since the number of scientific articles returned by the IS did not depend on the number of KW used per one search, and the largest amount of articles were returned using five words, we also decided to identify the five authKW, most often included in the publication's separate line. We considered establishing au-

Table 1

The inclusion criteria of selected publications

The criteria	Characteristic
Publication's type	Scientific article
Access to full version	Open
Language	English
Publication's term	Since 2010 up to nowadays
doi	Yes

Table 2

Publications' search results depending on the keywords' use

Search option	Number of Reference	Publications' amount	(Ranking*)
hvp vaccine efficacy (words' total amount – 3)	[9, 11, 14, 20]	4	(4)
hvp vaccine efficacy protection (words' total amount – 4)	[9, 10, 14, 20, 25]	5	(3)
hvp vaccine efficacy protection immunity (words' total amount – 5)	[12, 15, 16, 19, 21, 22, 26]	7	(1)
hvp vaccine efficacy protection immunity cervix cancer (words' total amount – 7)	[13, 14, 15, 20, 21, 26]	6	(2)
hvp vaccine efficacy protection immunity cervix cancer cervical infection (words' total amount – 9)	[5, 8, 14, 18, 23]	5	(3)
hvp vaccine efficacy protection immunogenicity cervix cancer cervical infection (words' total amount – 9)	[6, 14, 17, 24, 26]	5	(3)

Note * - ranking was carried out in descending order of the selected publications' amount.

Table 3

Keywords and publications in which they are highlighted

Keyword	Number of Reference	Publications' amount
vaccine (vaccines)	[6, 9, 14, 16, 18, 19, 20, 26]	8
HPV	[5, 6, 14, 15, 16, 20, 24]	7
human	[9, 18, 19, 24, 26]	5
cancer	[5, 14, 17, 18, 19]	5
papillomavirus	[9, 15, 17, 18, 19]	5

Table 4

Publications' indicators where the immunogenicity of HPV vaccines in girls and young women over a long-term period studied

Number of Reference	Females' age	Main indicators of the comparison groups formation	Materials	Lab methods	The duration of long-term period	Vaccine's Brand name
[5]	10-23	1. The number of doses received vaccine (1.2 or 3) 2. the period between the 1st and next doses (60th, 180th day and later)	Plasma	Determination of the binding antibodies against the vaccine protein L1 of HPV 16, 18, 6 and 11 concentration of based on multiplex technology (Luminex)	From 48 months to 7 years	Gardasil
[12]	16-23	1. The number of months between the first dose of vaccine and the time of the laboratory test	Serum	1. Determination of the neutralizing antibodies against the vaccine protein L1 of HPV 16, 18, 6 and 11 concentration based on multiplex technology (Luminex) 2. Determination of the total antibodies against HPV vaccine virus particles 16, 18, 6 and 11 concentration based on multiplex technology (Luminex)	After 7, 24, 48, 108 months	Gardasil
[16]	14-17	1. The number of doses received vaccine (1.2 or 3)	Capillary blood	The definition of IgG against HPV - 16, 18, 31, 33, 45, 52, 58 based on multiplex technology (Luminex)	Up to 4.5 years from the first dose of vaccine	Cervarix
[24]	9-25	1. The number of doses received vaccine (1.2 or 3) 2. the term between the 1st and next doses (6 and 12 months)	Serum	1. Determination of the anti-HPV-16 and anti-HPV-18 antibodies concentration on the basis of ELISA 2. Determination of the neutralizing antibodies against HPV-16 and 18 concentration, based on PBNA	Up to 36 months from the first dose of vaccine	Cervarix
			Lymphocytes	1. Determination of CD4 + and CD8 + T cells specific for HPV-16/18/31/45 by intracellular cytokine staining 2. Determination of the B-memory cells to HPV-16/18/31/45 by the enzyme immunoassay (ELISPOT)		

thKW for the further search of scientific literature in special databases.

The authKW's analysis allowed us to single out five such words, these were "HPV, vaccine (vaccines), human, cancer, papillomavirus", presented in Table 3. Of the articles, the largest amount of authKW, 4 out of 5 often used, had P.

Basu's et al. article [19], which appeared in the pool of the most effective article search (Table 2). It should be noted that 10 articles (almost half of the 22 articles) were not included in the analysis, since autKW were not highlighted in them. If we compare the KW - "hvp, efficacy, vaccine, protection, immunity, immunogenicity,

cervix, cancer, cervical, infection", and five commonly used authKW - "HPV, vaccine (vaccines), human, cancer, papillomavirus", you might see that only 3 words matched.

Then we made an analysis of the matches of article title words with KW we determine that the larger amounts had

the words "hpv, vaccine, efficacy, cancer, immunogenicity". In general, the title of 21 articles out of 22 contained KW in various quantities and combinations. That is, the search in the IS is based on matches of the selected by the user words with the article title words.

The amount of the selected articles' citing was heterogeneous - the spread ranged from 0 in D. Gunawardane [13] to 187 in M. Stanley et al. [23]. Both are review articles, an article by M. Stanley et al., 2010, is in a journal published since 2006, includes the following branches of biomedical knowledge: Infectious Diseases, Epidemiology, Oncology, Cancer Research, the journal has a SiteScore 2017 of 2.21 [1]. D. Gunawardane's article had released in 2018, devoted to the safety and cost-effectiveness of HPV vaccination (the name of the article includes the word "effective" without economic definition), published in the journal, which has existed since 2011, includes one branch of medical knowledge: General Medicine, has the SiteScore 2017 - 0.17 [2]. That is confirmed - IS provides almost equal opportunities for authors for the availability of their scientific publications to users regardless of the publisher's rating. We would like to draw attention to that, authKW words are not highlighted in both articles.

Since we want to make research to evaluate efficacy of the girls and young women vaccination against HPV over a long-term period (more than 2 years), scientific papers from 22 articles returned by IS, which included similar indicators and assessed immunogenicity of vaccines based on original studies were selected. These articles' (total 4 articles) analysis is presented in Table 4.

The minimum age of females was 9 years, the maximum - 25 years, the maximum difference of age - 16 years [24]. The comparison groups were formed by several signs - by the number of vaccination doses - from one [5, 12] to three [5, 16, 24], by the term period between the first and others doses of vaccination - from 1 month to 12 months [24]. The minimum term period from the first dose vaccination to the time of taking the biomaterial (on the basis of more than 2 years) was 36 months [17], the maximum - 7 years [5].

The samples (materials) studied were plasma [5], serum [12, 24], venous blood leukocytes [24], and capillary blood [16]. In three of the four papers, laboratory assays were provided on the multiplex technology basis. They determined the concentration of binding (neutralizing)

antibodies against the vaccine protein L1 of HPV 16, 18, 6 and 11, total antibodies against the vaccine HPV, IgG against HPV - 16, 18, 31, 33, 45, 52, 58. L.M. Huang et al. determined the concentration of neutralizing antibodies by BNA, pseudovirion-based neutralization assay, anti-HPV-16 and -18 antibodies by ELISA, the cellular immunity was determined by the frequencies of sensitized to HPV CD4 + and CD8 + T cells and memory B cells [24].

Brand names for vaccines in selected studies are Cervarix and Gardasil. Cervarix's generic name is human papillomavirus bivalent vaccine. Gardasil is named human papillomavirus quadrivalent vaccine. Both vaccines are registered in the Russian Federation [3, 4].

Conclusion

In Internet the search for scientific publications on the vaccination efficacy against HPV is valid and based on matches of the user keywords with the article title words.

Internet provides equal opportunities for researchers the availability of sharing knowledge, regardless of the publisher's rating and the number of citations.

The vaccination efficacy against HPV includes an evaluation of the vaccines' immunogenicity. The HPV vaccine immunogenicity in girls and young women from 9 to 25 years old, in the long-term period from 3 to 7 years, is determined by the level of antibodies against HPV vaccine and the frequency of immune system cells sensitized to HPV. Patients participating in the studies were vaccinated by various schedule with Cervarix (human papillomavirus bivalent vaccine) and Gardasil (human papillomavirus quadrivalent vaccine).

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ATTITUDE OF THE POPULATION TOWARDS THE POST-MORTEM ORGAN DONATION IN FOREIGN COUNTRIES AND THE REGION OF RUSSIA AND THE SOURCES OF INFORMATION INVOLVED IN ITS SHAPING

ABSTRACT

This study focuses on the need to shape attitude of the Russian people to support the development of the post-mortem organ donation program. The **aim** of the work was to study the attitude of the population to the post-mortem organ donation and to determine the sources of information involved in its shaping, based on a study of the results of medical and sociological researches in foreign countries and analysis of survey data from a group of people in the region of Russia. The objectives of the study were: to study, according to data from sources of literature, the results of population surveys in countries around the world about attitudes towards participation in programs of post-mortem organ donation; explore the importance of different sources of information involved in the shaping of public opinion on this issue; to analyse the attitude of the group of the population of the region of Russia, in which transplant operations of human organs are performed, towards the possibility of participation in programs of post-mortem organ donation and sources of information that are important for its shaping. The study was based on the publications of the RSCI and PubMed and the results of a survey of 250 patients at the federal medical center where organ transplant operations are performed. The analysis of publications demonstrates the multi-stage process of shaping a position of support for the post-mortem organ donation among the population of the countries of the world - from understanding the humanity of this activity to concrete steps to support it. At the same time, propaganda of organ donation is important through the involvement of the media, educational system resources, and scientific professional communities. In Russia, it is necessary to start outreach with the population concerning organ donation from the first stage, to facilitate an understanding of the need for its development in order to save the lives of seriously ill people, and therefore systematic work is needed using opportunities primarily from television and Internet sources.

Keywords: post-mortem organ donation, sources of information for the public.

According to the concept of self-sufficiency in transplantation, adopted by WHO in Madrid in 2010, the shaping of a positive attitude towards organ donation and organ transplantation among the population is the most important task of each state striving to develop these high-tech medical assistance programs [14, 29]. In the Russian Federation, at present, human organ transplants, in addition to the specialized centers of the cities of Moscow and St. Petersburg, are performed only in every fourth region of the country, while the systems of interaction between the participants of transplant programs and organ donation in the subjects of the Russian Federation have individual features [3]. Accordingly, outreach with the population, aimed at promoting organ donation, should take into account both the ethnic and religious characteristics of the inhabitants, as well as the organization of this type of medical care in the region. One of the subjects of the Russian Federation that successfully develops organ donation and transplantation programs is the Nizhny Novgorod Region, where, on the basis of the Federal Budgetary Healthcare Institution "Volga District Medical Center" of the Federal Medical-Biological Agency, kidney, liver and pancreas transplants are performed. At the same time, the main problem limiting the growth in the number of operations is the shortage of donor organs, which is caused, among other things, by the high frequency of refusals of relatives of post-mortem donors from organ removal [5].

In connection with the above, we determined the following purpose of this work: on the basis of studying the results of medical and sociological researches in foreign countries and analysing data from a survey of a population in the region of Russia, study the attitude of the population towards post-mortem organ donation and determine the sources of information involved in its shaping. The objectives are:

- to study, according to data from sources of literature, the results of population surveys in countries around the world about attitudes towards participation in programs of post-mortem organ donation,
- explore the importance of different sources of information involved in the shaping of public opinion about the problems of organ donation,
- to analyse the attitude of the group of the population of the region of Russia, in which trans-

plant operations of human organs are performed, towards the possibility of participation in programs of post-mortem organ donation and sources of information that are important for its shaping.

Materials and methods. The study of literary sources was carried out on the information resources of the RSCI and PubMed. Own medical sociological research consisted of a questionnaire survey of 250 surgical patients of the surgical Federal Budgetary Healthcare Institutions of the Volga District Medical Center of the Federal Medical-Biological Agency (ФБУЗ ПИОМЦ ФМБА), Russia. The choice of the group of respondents was due to the fact that patients had personal experience of health problems, physical suffering, restrictions on the quality of life, which, in our opinion, made for them more relevant than for the general population discussion of problems associated with the treatment of serious diseases. Patients were asked to answer following questions:

- Do you think that post-mortem organ removal should be carried out (answer options: in the presence of the lifetime consent of the donor, with the consent of the donor or his relatives, regardless of the consent of the donor or his relatives);
- if you asked to agree to a posthumous organ donation, you would answer (answer options: agree, disagree, not sure);
- please select the sources of information from which you received information about organ transplantation (answer options: TV, Internet sources, newspapers, radio, etc., the opportunity to specify any other sources of information was provided).

A comparative analysis was carried out using the calculation of the Pearson's Chi-square test, pairwise comparisons with the Bonferroni adjustment.

As the results of the analysis of publications have shown, in many countries the opinion of the population or its groups is being studied on the issues of acceptance or objection of post-mortem organ donation. At the same time, as experts emphasize, a positive answer to the question of the questionnaire is by no means a guarantee of a person's actual registration of consent to the post-mortem removal of organs. Thus, 75% of the respondents in Turkey expressed their willingness to donate after death, while only 24% of the population actually ac-

cepts consent [13]. The same trend was noted in Iran, where according to the survey, 78% of the country's population favored organ donation issues, but only 25% issued a donor card [8], as well as in Italy, where 95% of respondents expressed support for post-mortem donation, but in reality only 22% of them have officially registered this consent [22]. In the UK, with a general understanding of the need for development of donor programs, only 57% of families agreed to a question about a possible donation and only 30% of the population registered on the official portal as possible donors [15, 23]. In China, 67% of those surveyed said they were willing to donate a kidney after their death, but only 53% said they agreed to register their consent in the registry [21]. In Nigeria, 47.3% of survey participants had a positive attitude towards post-mortem donation and only a quarter expressed readiness to become kidney donors after death [12].

According to medical and sociological research, there is also no correlation between willingness to donate and the indicator of donor activity: in Europe, 83% of residents of Sweden, 77% of Malta, 72% of Belgium and Finland, 70% of Denmark, expressed their willingness to agree to a post-mortem donation. 66% - France, 64% - Ireland and the Netherlands, 62% - Slovenia and Luxembourg, 61% - Great Britain and Spain, 60% - Portugal, 53% - Hungary, Poland and Croatia, 49% - Italy, 47% - Germany [Левада-центр Евробарометра 333a]. While Belgium and Malta lead in both of the analyzed indicators, Spain and Croatia, the leaders of Europe in donor activity, lost first place in a sociological study to Denmark and Sweden, where the indicator does not exceed 13-17 per 1 million people [4, 24, 25].

Among the means of shaping public opinion, experts all over the world primarily note the media work [1, 2, 4, 6, 11 23 26 28]. At the same time, the authors highlight mass media influence: for example, according to M. Boratinska, from 10 to 20% of the refusals from relatives of the post-mortem donor are caused by negative speech of some journalists. According to the results of the Levada-Center study in Russia, less than 10% of respondents encountered positive examples of transplantation development in the mass media; the percentage of respondents who had experience of facing with negative speech turned out to be three times higher [4].

Shaping a positive attitude to the development of donor programs can also

be carried out through Internet, including social networks [18]. Such approach has been recognized as very effective in Canada [28] Israel [2], USA [1]. Apart from the public awareness, social networks are very useful in sharing information between members of professional communities. The leading magazine for doctors interested in different aspects of transplantation and organ donation, Transplantation, actively uses Twitter to interact with authors, readers, scientists, coordinators, etc. Internet resources allowed the journal to implement new forms of work: upload videos, present the works of young scientists, analyze the readers interests. [10, 19].

There is in no way less important factor of informing the public about the importance of organ donation, that is the use of an educational resource in educating the public [6, 13, 21], and its particular professional groups such as nurses [16, 20, 22], police [27]. In this case, of course, the special direction is the training of doctors, starting with students [6, 7, 8, 22].

Family relationships are important in increasing the population supporting the efforts of promoting organ donation: the emergence of a potential organ recipient, the signing of donor card by one of the family members, as a rule, contribute to obtaining consent to post-mortem organ donation of other relatives [6, 7, 16, 21].

The results of our research based on a questionnaire survey in which 250 patients from a surgical hospital took part, people of different age groups (from 18 to 79 years old), showed that only $14.0 \pm 2.2\%$ of respondents support the presumption of consent to post-mortem organ removal, regulated by country's local legislation. $34.0 \pm 3.0\%$ believe that the necessary condition for post-mortem organ donation should be a person's lifetime consent, the majority ($52.0 \pm 3.2\%$) will accept the possibility of obtaining the donor's lifetime consent as well as post-mortem consent of his relatives. At the same time, $40.8 \pm 3.1\%$ stated that they would have signed a consent to the posthumous organ donation, if they had been approached with such a proposal, $54.8 \pm 3.2\%$ had refused, the rest were not sure. Among the possible factors that could influence their decision, $24.4 \pm 2.7\%$ noted the opinion of a representative of a religious denomination, $4.4 \pm 1.3\%$ - financial incentives and $45.6 \pm 3.2\%$ - information about a person, which they could save.

Analysis of the survey results allowed to determine the list of sources of informa-

tion involved in the shaping of the respondents' opinion on organ donation. We identified four groups of respondents: the first group, the most numerous, indicated the only source of information - television programs, percentage of this group was $42.4 \pm 3.1\%$, the second group ($20.8 \pm 2.6\%$) preferred also one source - Internet sites, a third group made up $12.0 \pm 2.1\%$ of respondents who indicated several sources of information as sources of information (television, radio, newspapers), the fourth - $13.2 \pm 2.1\%$ of respondents receive information from all of the above sources (television radio, newspapers, Internet). The percentage of the other groups of survey participants who received information from other sources, for example, from the medical literature, did not have statistical significance.

Comparative analysis did not allow to determine the dependence of the possibility of registration the consent of respondents on the post-mortem organ donation on the preferred source of information ($\chi^2 = 7.4$ at a critical value of 12.6). Conducted pairwise comparisons also did not allow to identify statistically significant results.

The understanding of the humanity and safety of organ donation by society is the key to the success of the implementation of these programs in national health care. The data of literary sources analyzed by us testify to the complexity and multi-stage nature of shaping the public opinion from a person's understanding of the problem of organ donation to concrete steps to promote it, while outreach should combine a wide variety of forms and use all available information sources for the population. In Russian society, according to sociological research, the majority of the population treats organ donation with distrust, which is certainly a consequence of the negative reflection of the situation in the media and the inadequacy of the work of the professional medical community in promoting the results of transplantation centers [1, 4, 5].

The results of the conducted survey, having general compliance, differ from the similar study by the Levada Center in the 2013, in which more than half of the respondents found it difficult to answer the question about the possibility of obtaining consent to a post-mortem organ donation, every fourth declared readiness to sign consent and 13% reported their refusal [4]. In our study we analyzed the opinion of hospital patients, that is, a group of people who have a greater interest in the problems associated with helping people who are suffering than the

general population. Accordingly, there were large groups with a clearly shaped attitude to consent or refusal of posthumous organ donation. At the same time, the leading factor that could influence the decision of the respondents was information about a person who can be saved by transplanting organs. The foregoing emphasizes once again the importance of public outreach. An analysis of respondents relevant sources of information on this topic showed, given the specific role of each of them, the priority importance of Internet sources and television. At the same time, the absence of any difference in relation to the post-mortem donation of people who receive information from different sources indicates the uniformity of their approach to the coverage of this problem.

Conclusion. The results of our study indicate the need for systematic advocacy with the population of our country, aimed at developing among Russians the understanding of the humanity of organ donation. Such activities should be carried out by using all possible sources of information, primarily television and Internet sites, also it should be systematic all over the country and coordinated by the professional medical community.

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BIOETHICAL PROBLEMS OF RENDERING MEDICAL AID TO PATIENTS WITH DEMENTIA

ABSTRACT

Currently, there is a steady increase in the number of elderly patients with cognitive impairment in need of specialized and high-tech medical care worldwide. We aim to outline the main bioethical problems of scientific research and medical care for patients with dementia in the Department of neurodegenerative diseases of the Hospital of the Yakut science center of complex medical problems. Patients with different stages of dementia accounted for about 18 % of the total number of patients treated in the hospital of YSC CMP, and elderly patients with dementia – 10%. Ways to solve complex issues should be taken to develop ethical rules for the provision of specialized medical care, taking into account the psychosocial, cultural and ethnic characteristics of the population in the Republic Sakha (Yakutia).

Keywords: patient, bioethics, dementia, neurodegenerative diseases.

At present, there is a constant, steady increase in the number of elderly patients with cognitive impairment in need of specialized, high-tech medical care throughout the world. The problem of injustice in health care, primarily in the availability of high-quality medical care and modern achievements of biomedical science is of prime concern in contemporary bioethics [4].

Degradation of memory, thinking, behavior, and the inability to perform daily activities are the most common symptoms of dementia [6]. According to WHO, there are 47.5 million people with dementia worldwide, and 7.7 million people are diagnosed with it each year [2]. Dementia is a multifactorial pathology, including both the primary degenerative processes in the nervous system (Alzheimer's disease) and secondary degenerative changes in the cerebral circulatory system (vascular dementia). In addition, dementia, as a syndrome, is characteristic of several hereditary neurodegenerative diseases, such as Chorea Huntington, myotonic dystrophy, hereditary spastic paraplegia and others.

"Dementia 2012", a WHO report [10], has a separate chapter devoted to ethics. Protecting the rights of persons with dementia is one of the highest priorities of the medical community and our society. It is emphasized that patients with dementia and their caretakers share the same human rights as everyone else. The UN Convention on the Rights of Persons with Disabilities obliges governments to ensure the realization of all human rights and fundamental freedoms of all people with disabilities. Different examinations of the ethical aspects of dementia often focus on such major problems as the right to refuse treatment and euthanasia.

While these issues are very important, there are also other problematic ethical situations that arise in the course of scientific research, the routine treatment of patients and daily care [12,13]. These include: autonomy, capacity, consent, advance directive, disclosing truthful information, confidentiality, artificial feeding and hydration, genetic screening, behavior control, car driving, wandering, research, determination of diet, problems associated with the decision to leave this world, namely, euthanasia and voluntary death with the assistance of special painkillers that is approved by the attending doctor [9].

An analysis of the bioethical aspects of old age dementia is most fully reflected in the review [4], which presents contemporary foreign and Russian research on the ethical issues of gerontology.

Various ethical problems are described in these studies [15,18], they are divided depending on the stage and severity of the clinical signs of the disease.

Predictive stage - the development of a wide range of molecular and neurobiological biomarkers can provide the ability to identify not only preclinical, but also the presymptomatic state of the illness [7]. In particular, the safety and effectiveness of the diagnosis of preclinical state of the Alzheimer's disease (AD) is the most challenging issue in bioethics. One of the first questions is: who is to be considered as candidates for testing and for the diagnosis of preclinical AD. The ethical challenge is that receiving the results of Alzheimer's biomarker tests can potentially be traumatic, with subsequent manifestations of anxiety, depression, or even suicidal thoughts in patients. Surveys have shown that among Americans, the fear of Alzheimer's disease is superi-

or to the fear of heart disease, diabetes, stroke, and in people over 55, this fear is stronger than, for example, the fear of cancer [4].

The mild and moderate stages of dementia - here the bioethical problem of decisions made by the patients themselves is most frequently discussed. So-called joint decision making is perceived as most ethically acceptable. It is defined as a partnership that clarifies possible treatment options, provides information about options, results and uncertainties, taking into account the patient's own set of values and preferences, which allows clinicians, patients and caregivers to make joint decisions on treatment [1, 11, 14, 20].

The severe stage of dementia - the complex moral aspects of maintaining the life of the patient at the end of his life are discussed, especially in those countries where euthanasia of hopelessly ill patients is legalized [21]. Studies of this issue in Russia show that the attitude of relatives of patients with dementia and AD to euthanasia is ambiguous. Respondents are less likely to see a medical problem in euthanasia, highlighting its ethical and legal aspects more. They positively assess the moral level of medical workers, paying attention to the imperfections of modern medicine. The attitude of people towards euthanasia is determined by the existence of multidirectional ideas about euthanasia in the field of legal, socio-cultural, spiritual and personal aspects of this problem [5].

Stigmatization of patients with dementia is the constant subject of research in the International Alzheimer's Association studies [22], including the research of criticism in patients and caregivers, various attempts to address different aspects of

stigma and search for ways to overcome it. Stigma is seen as one of the main barriers in understanding the problems of the disease, seeking help, getting a diagnosis and accessing support services. This closes the path of open discussion of the disease and makes doctors think that they have nothing to offer [4].

Factors predisposing to the development of the disease are still not completely clear, but the severe moral and social consequences of dementia are obvious [17, 3]. The primary goal of this publication is to outline the main bioethical problems of scientific research and medical care after patients with dementia in the department of neurodegenerative diseases of the Hospital YSC CMP.

Since November 1st, 2018, the Department of Neurodegenerative Diseases has been functioning in the Hospital YSC CMP, in the span of three months from December 3, 2018 till March 5, 2019, 11 patients with different stages of dementia, from mild to severe, received medical help, of which 5 people were middle aged (30-55 years) and 6 people were of old age (63-79 years); nationality: Yakuts - 7 people, Russians - 2 people, other nationalities - 2 people; place of residence: Yakutsk - 7 people, districts of Yakutia - 4 people. Patients had the following diagnoses: frontotemporal dementia - 1 person, neurodegenerative diseases (NDD) - 6 people, Parkinson's disease - 2 people, neuromyelitis optica - 1 person, polyneuropathy of unclear genesis - 1 person. Patients with different stages of dementia accounted for approximately 18% of the total number of dementia patients who received treatment in the inpatient department of the YSC CMP, and elderly patients with dementia - 10%.

Elderly patients with dementia belong to the group of vulnerable patients who need special treatment and care, both from family and medical staff. You can include at least three questions into the framework of the modern ethical approach towards deciding on medical intervention for an elderly patient:

- 1) clearly identify the purpose of the intervention;
- 2) assess the effectiveness of the procedure or intervention;
- 3) determine whether the risks and benefits of the intervention will be balanced.

If all three questions are answered positively, the intervention and quality of care regarding the proper treatment and examination of an elderly patient will be ethical [19].

In the initial stages of dementia, it is

important for patients to be under the care of the caregiver and remain involved in the society as much as possible. The provision of relatives with accurate information about the disease, their involvement in the treatment plan and medical care, discussion and preparation of advance directives beforehand is of the highest ethical priority. As the disease progresses, the goal is to ease the stress for the patient and relatives. The method of providing negative information is up to the individual choice of the attending physician. The role of the doctor is not to make decisions for the patient, but to facilitate and participate in joint decision-making by the doctor, patient and family members. In addition, an important aspect is that the doctor or the researcher should consider the educational, cultural, ethnic and religious characteristics of the patient.

The treatment of patients with cognitive impairment in the conditions of the inpatient department of the YSC CMP is carried out according to the standards of medical care and the principle of equitable distribution of resources. It is known that in some cases, in the conditions of resource shortage, elderly patients are in a disadvantageous situation. Several hidden forms of discrimination against elderly patients is the refusal of hospitalization and appointment of expensive treatments [3,4]. In the future, palliative care is planned for the disabled and hopelessly ill patients of the YSC CMP.

Participation of patients with dementia in scientific clinical research is one of the more complex bioethical problems. Patients with cognitive disorders and elderly patients belong to the vulnerable group of participants in clinical trials, epidemiological and genetic studies. The issue lies in obtaining informed consent. The process of informed consent requires: confirmation of the ability to make decisions, disclosure of sufficient information, understanding of the information provided, voluntary choice between the options and, on these grounds, consent to or refusal of medical intervention [8,16]. Patients with cognitive impairment cannot fully comprehend large amounts of complex information, therefore researchers and the Ethics Committee should carefully weigh the risks and benefits for these patients and consider modifying clinical research protocols to protect patients, and that is the reason why family members or so-called "Surrogate" caretakers should actively participate in obtaining of informed consent. The term "surrogate decision maker" is a legal term for the

healthcare authority or agent who is the advocate for an incompetent patient. It is used in Western countries, but in Russia this practice finds itself in the concept of guardianship.

Conclusion

Apparently, about 20% of the total number of patients admitted for treatment and examination in the neurological department of the YSC CMP will be patients with various disorders of cognitive function, and elderly patients with dementia will account for 10% of it. Accordingly, it will be necessary to create certain conditions for patients in the hospital: constant around the clock monitoring and the provision of special equipment that facilitates patient care. In addition, special training is needed for medical personnel to care for elderly patients and people with disabilities.

Currently, the field of research on bioethical issues of application of new medical technologies in medical practice is expanding due to the study of new pathologies and the possibility of applying clinical trials of new diagnostic and treatment methods. It is necessary to outline a range of basic bioethical problems that undoubtedly arise in clinical practice and research of a number of diseases which impair cognitive functions, including senile dementia in elderly patients. We can resolve such problems with the development and adoption of ethical rules for the provision of specialized medical care, while also considering the psychosocial, cultural and ethnic characteristics of the population of the Republic of Sakha (Yakutia).

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Korostelev A.S., Potapov A.F., Ivanova A.A., Bulatov A.V.
**ACUTE KIDNEY INJURY IN PATIENTS WITH
CORONARY HEART DISEASE
AND METABOLIC SYNDROME DURING BYPASS
GRAFTING: CURRENT STATE OF THE PROBLEM**

Abstract

The article presents a review of literature on the current efforts in research of acute kidney injury (AKI) in patients with coronary heart disease (CHD) after myocardial revascularization with coronary artery bypass grafting (CABG). Different sources provided the data on the frequency of AKI during surgical methods of myocardial revascularization with the use of the cardio-pulmonary bypass (CPB) and off pump. The article describes the epidemiology of metabolic syndrome (MS) both in the world and in the Russian Federation. It also considers several options for making a MS diagnosis basing on various criteria, including the presence of CKD, as a likely predictor of developing MS and vice versa. An analysis of the current data showed the contribution of concomitant MS in the development of CKD and proved it an important risk factor for AKI. The study was based on the concept of endothelial dysfunction (ED), as a key element in the pathogenesis of cardiovascular diseases, MS and renal pathology. Concomitant proteinuria, microalbuminuria and decreased glomerular filtration rate (GFR), as well as the phenomenon of insulin resistance (IR) were proven to contribute to the development of perioperative AKI in patients with MS. The study covers the entire pathogenetic chain of development of cardiorenal syndrome (CRS), as an integral part of the cardiorenal continuum. It also considers the social and medical problem due to the high morbidity and mortality, as well as increased economic costs of treating this group of patients. The authors endeavored to determine the most rational approach when choosing the tactics of treatment and management of these patients. The methods for the prevention and treatment of AKI in patients with MS were considered. Based on the global positive experience of using statins, angiotensin converting enzyme (ACE) inhibitors, calcium antagonists and beta-blockers, these groups of drugs were considered as promising ones for pharmacological prevention of AKI in patients during myocardial revascularization with the use of bypass grafting.

Keywords: coronary heart disease, metabolic syndrome, off-pump coronary artery bypass grafting, acute kidney injury, statins.

Coronary heart disease (CHD) is a pathological condition characterized by an absolute or relative disorder of myocardial blood supply due to coronary artery diseases [22]. Amounting to 13.2%, or 7.4 million cases per year, CHD ranks first among causes of death in the world. According to official data, in 2015, the Russian Federation had the overall CHD incidence at 6,425.2 per 100 thousand of the population (Rosstat, 2015). From 2011 to 2015, the number of cases with CHD diagnosis established for the first time increased 1.5 times from 633.2 to 911.0 per 100 thousand of the population. The CHD structure is dominated by stable angina – 3,059.9 thousand people. In Russia annually registers an average of 520,000 new cases of acute coronary syndrome (ACS), breaking down into 63.6% cases of unstable angina and 36.4% cases of myocardial infarction [11].

Bypass surgeries are considered the most effective methods of CHD treatment. However, these surgeries are associated with a high risk of developing various undesirable dysfunctions of the organs and body systems, as well as with a number of serious complications, including acute kidney injury (AKI). In the recent years, off-pump bypass grafting surgeries have become widespread. Although less invasive, this method of surgical myocardial revascularization does not significantly reduce the risk of severe postoperative complications, including AKI. Thus, according to a number of international multifocal studies, off-pump

bypass grafting results in renal dysfunction in 28% of patients, and 1.2-2.9% of them need hemodialysis due to the AKI development [3].

The postoperative AKI leads to changed patient's management, longer duration of treatment and significantly worse prognosis, increasing hospital mortality from 7.6% to 26.3% among AKI patients [4]. The studies indicate a higher risk of developing perioperative renal complications in patients with concomitant chronic kidney diseases (CKD), diabetes mellitus, and overweight.

It has been established that one of the factors contributing to impaired renal function in patients with cardiovascular pathology is concomitant MS [23]. Patients with MS are 2.5 times more likely to have a high risk of developing CKD [6]. Therefore, for the patients with coronary artery disease and concomitant MS, who have undergone surgeries, in particular off-pump coronary artery bypass grafting, the management tactics requires a special approach, mandatory assessment of the initial state of the kidney function and the measures aimed at preventing their dysfunction in the pre- and postoperative periods.

1. Surgeries for CHD and acute kidney injury.

CHD surgeries involve shunting myocardial revascularization and percutaneous coronary intervention (PCI) with or without drug-eluting stents. Should PCI be impossible to perform due to technical difficulties or anatomical features,

an open-heart surgery using CPB or an off-pump operation is an option. As any cardiac surgery using CPB, coronary artery surgeries are always associated with a high risk of developing undesired dysfunctions of organs and systems, as well as a number of serious complications, with AKI being quite common [7].

In the recent decades, off-pump bypass surgeries have become an alternative to traditional operations on coronary vessels using CPB. These surgeries are less invasive, and up to 25% of all myocardial revascularizations in the world practice are performed off-pump [1]. However, despite the exclusion of major factors triggering AKI (platelet activation and damage, disruption of the blood coagulation system, production of free radicals, activated systemic inflammatory response), CABG still has the risk of postoperative kidney dysfunction [24].

The analysis of the information provided by various researchers on AKI following bypass grafting shows a large scatter of the data on frequency of this complication. Therefore, first, it is important to take into account the criteria of kidney injury that is used. For example, the AKI frequency following CABG with the use of the AKIN (Acute Kidney Injury Network) criteria is 26.3%, while with the use of RIFLE criteria (Risk, Injury, Failure, Lost of kidney function, End-stage renal failure) – 18.9% [16].

According to several authors, in terms of developing pronounced renal dysfunction, patients with concomitant MS make

another particular risk group [7]. The AKI following off-pump bypass grafting was observed in 17.5% of patients [12]. The combination of MS and cardiovascular diseases, and CHD in particular, is now a proven fact.

2. Relationship between metabolic syndrome and kidney failure.

MS is a topical issue in the modern medicine and is of interest for various specialists. According to epidemiological studies, nowadays, MS is characterized as a "XXI century non-infectious pandemic" and is regarded in many countries as a major socio-economic problem. The prevalence of MS in different countries varies from 10% to 84% among the total adult population and depends on ethnicity, age, gender, and race [25]. In Russia, according to the Ministry of Health, the MS prevalence varies from 20% to 35% among adults, its frequency increasing with age and being 2.5 times more common in women [5].

The World Health Organization (WHO) defines MS as a combination of type 2 diabetes mellitus (DM) with at least two of the following factors: arterial hypertension (AH), high blood lipids, obesity, and microalbuminuria [15]. The nature of MC is reflected most accurately and fully in the guidelines of the Russian Society of Cardiology (RSC). According to the RSC guidelines, MS is characterized by increased mass of visceral fat, decreased sensitivity of peripheral tissues to insulin and hyperinsulinemia, which causes the development of disorders of carbohydrate, lipid, and purine metabolism, and hypertension [10].

Along with the above clinical manifestations, MS also includes various renal dysfunctions, which often eventually leads to the development of CKD. MS has been linked with markers of chronic renal pathologies, including reduced GFR, proteinuria and/or microalbuminuria, as well as with histopathological markers, such as tubular atrophy and interstitial fibrosis [17].

Kidney injury can be considered both as one of the MS criteria and as an independent risk factor for CKD [18]. The presence of MS increases the likelihood of developing CKD in patients over 20 years of age by 2.6 times, and the risk goes higher with increasing MS criteria. With the MS lasting over nine years, the risk of developing CKD may increase by about 50% [19].

The early stages of CKD are most often asymptomatic and are not diagnosed during the initial examination of the patient. At the same time, it is not complete-

ly clear what develops earlier – CKD or MS. Indeed, there are common factors in the development mechanisms of the both pathologies: insulin resistance, inflammation, lipid metabolism, and hypertension [14]. In addition, obesity is accompanied by increased adipose tissue secretion of such pro-inflammatory cytokines as leptin, IL-6, and TNF, which also contributes to the production of type IV collagen, as well as the formation of reactive oxygen species, which in turn can lead to kidney endothelial cell (EC) dysfunction, secondary growth of mesangial cells and the formation of glomerulosclerosis [28].

Currently, it is recognized that endothelial dysfunction (ED) is one of the leading links in the pathogenesis of nephrosclerosis, as well as the majority of chronic forms of kidney pathology of both immune and non-immune genesis [2]. The unique position of endothelial cells at the interface between circulating blood and tissues makes them most vulnerable to various pathogenic factors in the systemic and tissue circulation. EC are the first to come in contact with free radicals, and are exposed to high hydrostatic pressure of blood with a high content of cholesterol and glucose. All these factors cause damage to the vascular endothelium, its dysfunction as an endocrine organ, and the accelerated development of angiopathy and atherosclerosis [29]. Thus, it can be stated that ED and MS syndrome are closely associated conditions and form a vicious circle leading to metabolic, cardiorenal and cardiovascular conditions.

In general, the existence of a close relationship between the development and progression of cardiac and renal pathology is a proven fact and must be taken into account in clinical practice. With the increased group of such patients, practitioners began to separate their condition into a single syndrome complex, which has been lately referred to in the Russian and international literature as cardiorenal syndrome (CRS), or cardiorenal continuum. Moreover, in 2008, the concept of cardiorenal interactions was adopted and developed, and various types of the CRS were identified [30].

This term is a collective one that emphasizes the interaction between the kidneys and the heart, when an acute or chronic dysfunction of one of these organs leads to an acute or chronic dysfunction of the other. MS patients have CKD without its manifestation and belong to the group with a high risk of perioperative renal complications [6].

In patients after myocardial revascu-

larization, the presence of latent renal dysfunction as a manifestation of chronic CRS can significantly worsen the immediate and late postoperative cardiorenal prognosis, and presents a medical and social problem due to high mortality and significant pharmaceutical and economic costs.

Thus, comorbidity in the form of a combination of CHD, MS and nephropathy in patients undergoing myocardial revascularization bypass grafting is a serious clinical problem.

Undoubtedly, improved surgical methods for the treatment of coronary heart disease, early detection of patients with a high risk of renal dysfunction and prediction of their development, elimination of nephrotoxic drugs, a more balanced approach to the use of radiopaque research methods have contributed to the reduction of postoperative AKI in MS patients [20]. Along with this, targeted prophylactic pharmacotherapy is an equally important direction in reducing perioperative renal complications, taking into account the mechanisms of its development, especially in patients with concomitant MS.

3. The use of statins as a preventive method for kidney injury following bypass grafting in CHD patients with concomitant MS.

The main measures for the prevention of perioperative kidney injury following surgical interventions are set out in the National Guidelines for the diagnosis, prevention and treatment of AKI, clinical guidelines for the management of patients with the risk of AKI [8], and the management of patients with MS [9].

The main objectives of treating MS patients are weight loss, better metabolic control, the maintenance of an optimal level of blood pressure, as well as the prevention of acute and remote cardiovascular complications. At the same time, taking into account the key pathogenesis of the syndrome, as well as the modern concept of ED, for patients with coronary pathology and concomitant MS, an important component of preventive measures is pharmacotherapy with drugs that can directly affect the state of the endothelium and its dysfunction, as well as correct lipid exchange.

There are several pharmacological groups used to correct ED. These are antioxidants, angiotensin II receptor blockers, angiotensin converting enzyme (ACE) inhibitors, calcium antagonists, beta-blockers, nonsteroidal anti-inflammatory drugs, and statins. The data on the effect of many medications in the presented groups on the endothelium

function are insufficiently studied and controversial. To date, there is evidence of various "pleiotropic" effects of statins. It has been revealed that statins regulate ED, proliferation of mesangial cells, have anti-inflammatory and immunomodulatory effect, as well as a positive effect on renal hemodynamics. The positive effect of statins in the event of perioperative AKI has been also revealed [17].

HMG-CoA reductase inhibitors are suitable for most patients with albuminuria and proteinuria, especially with the amount of protein in the urine exceeding 1 g/day [18].

The mediated nephroprotection and increased GFR with various signs of renal dysfunction observed in clinical practice [21] require further study of this effect of statins. Therefore, it continues to be relevant to study the effect of HMG-CoA reductase inhibitors on the course of AKI with its various etiologies. In addition, there is insufficient information about the optimal timing of statin administration from the standpoint of their nephroprotective effect.

Thus, currently the problem of kidney injury following bypass grafting in patients with coronary heart disease, especially with concomitant MS, remains relevant; there is no consensus on the choice of methods for its prevention, and the use of statins as nephroprotective agents remains the subject for discussion.

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POINT OF VIEW

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THE EFFECT OF PREGNANT AGE ON THE PROBABILITY OF THE OCCURRENCE OF COMPLICATIONS DURING PREGNANCY AND CHILDBIRTH

ABSTRACT

Until now, there has not been a consensus in the literature as to what plays a leading role in the occurrence of complications of pregnancy and childbirth in minors: biological immaturity or social risk factors. **The aim of this work** was to determine the influence of the age of the pregnant woman on the probability of complications of pregnancy and childbirth.

Materials and methods. Minors pregnant women surveyed (n=483) observed and gave birth in SPbGPU "Maternity hospital № 10" in 2004-2014 [1 group 13-15 years (n=49); 2 group - 16-17 years (n=434)]. The comparison group consisted of 110 women of middle reproductive age. Medical and social aspects of the life and behavior of patients were assessed by analyzing unified specially designed questionnaires. Statistical analysis of obtained data was performed using the programs STATISTICA V. 7.0 (Statsoft Inc., Tulsa, USA) and SPSS 19 (SPSS: An IBM Company, USA). Multivariate statistical analysis was performed using logistic regression for dichotomously dependent variables. In addition to age group indicators, the following control (independent) variables were used to separate the effect of age from other factors in the construction of regressions: age of menarche; the age of sexual activity; the period of registration in the women's consultation.

Results. In minors 13-15 years, compared with women of average reproductive age, significantly higher was the chance of occurrence of early rupture of membranes (OR=13,2; 95% CI: 2,1-81,9; p<0,01) and the implementation of perineotomy (OR=8,3; 95% CI: 2,6-27,0; p<0,01), and significantly lower the chances of occurrence polyhydramnios (OR=0,2; 95% CI: 0,1 to 0,6; p<0,01). In minors 16-17 years, compared with women of middle reproductive age, significantly higher were the chances of occurrence of chronic placenta insufficiency with hemodynamic disorders during pregnancy (OR=2,5; 95% CI: 1,3-5,0; p<0,05), premature (OR=3,3; 95% CI: 1,2-9,0; p<0,05) and early (OR=12,5; 95% CI: 2,7-57,1; p<0,01) rupture of membranes and production of perineotomy (OR=2,6; 95% CI: 1,3-5,1; p<0,01) during childbirth, and significantly lower chances of occurrence of polyhydramnios (OR=0,1; 95% CI: 0,1-0,3; p<0,01).

Conclusion. The results confirm the literature data on the complicated course of pregnancy and childbirth in minors. Moreover, it is likely that the morpho-functional immaturity of the reproductive system, as well as other body systems, homeostasis systems of minors pregnant women is most important, and adverse social factors are the background to which the work of the systems and organs is imposed on the limit of their functional capabilities with a rapid ability to decompensate.

Keywords: age of childbirth, childbirth in minors, pregnancy in minors.

Introduction. In 2016, In Russ. Federation women gave birth to 51 thousand children less than in 2015, which may be the beginning of the second "Russian cross". Another very important fact is of particular concern: in 2016, 175 thousand fewer marriages were registered than in 2015 [2, 5]. Therefore, every pregnancy is a value for the family and

society. Though small, but important segment in a cohort of women in labor occupy minors.

In Russia, 30-40 thousand minors give birth every year [2, 5].

Until now, there is no consensus in the literature on what plays a leading role in the occurrence of complications of pregnancy and childbirth in minors: biological

immaturity or social risk factors [1, 4, 6].

There are also conflicting opinions as to whether the frequency and severity of complications of pregnancy, childbirth and the postpartum period increases with the decrease in the age of the minor [1, 3, 7].

The aim of this work was to determine the influence of the age of the preg-

nant woman on the probability of complications of pregnancy and childbirth.

Materials and methods of research.

Minors pregnant women surveyed ($n=483$) observed and gave birth in SP-bGPU "Maternity hospital № 10" in 2004-2014 [1 group 13-15 years ($n=49$); group 2 – 16-17 years ($n=434$)]. The comparison group consisted of 110 women of middle reproductive age. Medical and social aspects of life and behavior of patients were evaluated by analyzing unified specially designed questionnaires. The questionnaire contained 52 questions combined into four blocks: living conditions; presence of bad habits; peculiarities of sexual behavior (reproductive attitudes); satisfaction from visiting a medical organization. 17 patients of group 1, 127 patients of group 2 and 110 women from the comparison group were surveyed. Statistical analysis of obtained data was performed using the programs STATISTICA V. 7.0 (Statsoft Inc., Tulsa, USA) and SPSS 19 (SPSS: An IBM Company, USA). To determine the significance of differences in quantitative traits we used Student t-test, Mann-Whitney U-test (nonparametric analog of Student t-test). The chi-square Pearson (χ^2) or Fisher (F) criterion was used to determine the reliability of differences in qualitative characteristics in two or more groups. Multivariate statistical analysis was performed using logistic regression for dichotomously dependent variables. The model for multivariate analysis included factors and complications of pregnancy and childbirth, between which statistically significant differences were found in the course of univariate analysis between groups. Logistic regression was used to explain the effect of age on dichotomously dependent variables (that is, 0/1 values). Accordingly, in this case, the dependent variables were binary indicators of the presence of the following diseases and features of the course of pregnancy and childbirth: anemia of pregnant women; preeclampsia; chronic placental insufficiency with hemodynamic disorders; polyhydramnios; oligohydramnios; premature rupture of membranes; early rupture of membranes; fetal distress; rapid delivery; perineotomy. In the construction of regressions, in addition to indicators of age groups, the following control (independent) variables were used to separate the effect of age from other factors: the age of menarche; the age of the beginning of sexual life; the period of registration in the women's consultation.

The results of the study and their discussion.

As a result of the study, it was found that at the time of pregnancy, every second 16-17-year-old minor (44.8%) and every fifth woman of middle reproductive age (20.9%) did not work or study ($p<0.001$).

Minors aged 16-17 were 1.6 times less likely to be married (35.4%) ($p>0.05$) than women of average reproductive age (55.4%). 16-17-year-olds lived in "civil marriage" 1.8 times more often (45.7%) ($p<0.01$) than women of middle reproductive age (25.5%). 13-15-year-olds were single 3.7 times more often (70.6%) ($p<0.001$) than 16-17-year-olds (18.9%) and women of middle reproductive age (19.1%).

Minors aged 13-15 started smoking 6.3 (11.3 ± 0.7 years) ($p<0.001$) and 16-17-year-olds 5.2 years earlier (12.4 ± 0.8 years) ($p<0.001$) than women of middle reproductive age (17.6 ± 1.0 years). During pregnancy, 13-15-year-olds continued smoking in 4.8 times more often (35.3%) ($p<0.001$), and 16-17-year-olds were 4.0 times more likely (29.1%) ($p<0.001$) than women of middle reproductive age (7.3%).

During pregnancy, minors aged 16-17 continued to drink alcohol significantly more often (3.9%) ($p<0.05$) than women of middle reproductive age (0%), which is consistent with the data of the authors who considered alcoholization to be the most common scenario of early sexual contacts [4]. Minors aged 13-15 years grew in single-parent families 1.5 times more often (47.1%) ($p>0.05$), and minors aged 16-17 years – 1.9 times more often (59.8%) ($p<0.001$) than women of middle reproductive age (30.9%). The number of children in parental families was significantly higher in minors of both groups (2.2 ± 0.7 and 2.3 ± 0.9 respectively) ($p<0.05$) than in women of average reproductive age (1.8 ± 0.7).

Before pregnancy, 13-15-year-olds lived in a communal apartment in 6.6 (11.8%) ($p<0.05$), and 16-17-year-olds were 3.9 times more likely (7.1%) ($p<0.05$) than women of middle reproductive age (1.8%). Respectively, 5.9% and 5.5% of minors of both groups lived in an orphanage before pregnancy.

The current sexual partner was the father of a child at 1.8 (52.9%) ($p>0.05$) at 13-15 years of age and 1.4 times less (67.7%) ($p>0.05$) at 16-17 years of age than women of middle reproductive age (93.6%).

Our results are generally consistent with those of other authors who also pointed to a low social-economic standard of living and the chance of early

pregnancy in minors [4,5].

The results of the study are mainly consistent with the literature data on the higher incidence of complications of pregnancy and childbirth in minors than in women of middle reproductive age [6, 7].

Threatening abortion was observed in 13-15 years in 2.1 (36.7%) ($p<0.01$), and in 16-17 years in 1.9 times more often (32.9%) ($p<0.05$) than in women of middle reproductive age (17.3%). Preterm birth was detected in minors aged 13-15 years 2.0 times more often (8.2%) ($p<0.05$) than in minors aged 16-17 years (4.1%), and 2.3 times more often ($p<0.05$) than in women of middle reproductive age (3.6%).

The frequency of preeclampsia was higher in 13-15 years in 4.1 (10.2%) ($p<0.05$), and in 16-17 years in 3.9 times (11.1%) ($p<0.05$) than in women of middle reproductive age (2.7%), which is also consistent with the data of a number of researchers who showed in their works that in pregnancy in minors preeclampsia was more common than in women of middle reproductive age [3,6].

Chronic placenta failure with hemodynamic disturbances were observed in juvenile 13-15 years in 2.2 times more often (14.3%) ($p<0.05$), and minors 16-17 years – 1.7 times more often (11.1%) ($p<0.05$) than women of middle reproductive age (6.4%).

Premature discharge of amniotic fluid was observed in minors aged 16-17 years 1.9 times more often (17.1%) ($p<0.05$) than in women of middle reproductive age (9.1%). Early amniotic outflow was found at 13-15 years in 2.0 (36.8%) ($p<0.05$), and at 16-17 years in 1.5 times more often (28.1%) ($p<0.05$) than in women of middle reproductive age (18.2%), which corresponds to the results of other researchers indicating a higher rate of untimely amniotic outflow in minors [6, 7].

The rate of rapid labor was 3.8 times higher in 13-15-year-olds (10.2%) ($p<0.05$) and 4.2 times higher in 16-17-year-olds (11.3%) ($p<0.01$), compared with women of middle reproductive age (2.7%), which corresponds to the results of other researchers who also found a high rate of rapid labor in minors [3,6].

Fetal distress was detected at 13-15 years of age 3.0 times more frequently (12.2%) ($p<0.05$) than at 16-17 years of age (4.1%), and 3.4 times more frequently ($p<0.05$) than in women of middle reproductive age (3.6%).

Chorioamnionitis was observed in minors aged 13-15 years 2.2 times more

often (2.0%) ($p<0.05$), and in minors aged 16-17 years – 2.0 times more often (1.8%) ($p<0.05$) than in women of middle reproductive age (0.9%).

There were no statistically significant differences between the groups in the frequency of other complications of labor ($p>0.05$), which is at odds with the data of the authors who noted more frequent development of weakness of labor and more frequent occurrence of postpartum bleeding and maternal injuries in minors [3,6].

The frequency of cesarean section operations was 18.4%, 18.7% and 22.7%, respectively ($p>0.05$). Of them was planned 44.4%, 39.5% and 44.0% of transactions, respectively ($p>0.05$); the emergency – 56.6% and 60.6% and 56.0% of transactions, respectively ($p>0.05$). Indications to planned cesarean section were: scoliosis with retro-conversion, spine fracture history, and various options of contracted pelvis, hereditary cerebellar ataxia of Pierre Marie, myopia with peripheral chorioretinal dystrophy and other diseases, as well as – foot fetal presentation. The indications for emergency delivery were: the lack of effect of therapy of pre-eclampsia, fetal distress, clinical mismatch between the head of the fetus and the pelvis of the mother, the presence of uterine inertia, prolapsed umbilical cord loops.

The frequency of the imposition of an obstetric forceps made in groups of 2.0%, 1.6% and 0.9%, respectively ($p>0.05$). Vacuum extraction of the fetus was conducted of a minor 13-15 years old were 2.3 times more often (4.1 percent) ($p<0.05$) than women of average reproductive age (1.8 percent). In both groups of minors, the perineotomy rate in childbirth was significantly higher (34.7% and 29.0%, respectively) ($p<0.05$) than in women of middle reproductive age (17.3%).

The construction of a series of logistic regressions allowed to establish that the age group of patients statistically significantly affects the probability of occurrence of a number of features of the course of pregnancy and childbirth.

Table 1 presents an assessment of the impact of age on the probability of occurrence of features of pregnancy and childbirth.

Interpreting all the values of the odds ratio and paying attention to their statistical reliability, we can conclude that minors 13-15 years, compared with women of middle reproductive age, significantly higher were the chances of early rupture of membranes (OR=13,2; 95% CI: 2,1-81,9; $p<0,01$) and perineotomy (OR=8,3; 95% CI: 2,6-27,0; $p<0,01$), and significantly lower the chances of occurrence of polyhydramnios (OR=0,2; 95% CI: 0,1-0,6; $p<0,01$).

In minors 16-17 years, compared with women of middle reproductive age, significantly higher were the chances of occurrence of chronic placenta failure with hemodynamic disorders during pregnancy (OR=2,5; 95% CI: 1,3-5,0; $p<0,05$), premature (OR=3,3; 95% CI: 1,2-9,0; $p<0,05$) and early (OR=12,5; 95% CI: 2,7-57,1; $p<0,01$) rupture of membranes and production of perineotomy (OR=2,6; 95% CI: 1,3-5,1; $p<0,01$) during childbirth, and significantly lower chances of occurrence of polyhydramnios (OR=0,1; 95% CI: 0,1-0,3; $p<0,01$).

There is no consensus in the literature as to whether the minor age is the cause of obstetric and perinatal complications in itself [3], or the high incidence of complications is not directly due to the age of the primiparous, and the most important are social risk factors [6, 7].

The ability of a woman to bear and give birth to a healthy child is determined by many factors, the most important of which are the biological maturity of the

organs and systems of the body [8]. Juvenile age is the most important stage in the formation of the reproductive and neuroendocrine systems, which causes a high incidence of complications and adverse pregnancy outcomes [9]. It is shown that unplanned pregnancy at a minor age is associated with a higher incidence of obstetric complications during pregnancy and childbirth, perinatal and maternal mortality, fetal growth retardation with subsequent developmental disorders of the child [10].

Conclusion. Thus our results confirm the literature data on the complicated course of pregnancy and childbirth in minors. Moreover, it is likely that the morpho-functional immaturity of the reproductive system, as well as other body systems, homeostasis systems of minors pregnant women is most important, and adverse social factors are the background to which the work of the systems and organs is imposed on the limit of their functional capabilities with a rapid ability to decompensate.

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Assessment of the influence of age on the probability of occurrence of features of the course of pregnancy and childbirth

Complication	Complication 13-15 years (compared to women of average reproductive age)				16-17 years (compared to women of average reproductive age)			
	Odds ratio (OR)	Confidence 95% interval (CI)		p	Odds ratio (OR)	Confidence 95% interval (CI)		p
		min	max			min	max	
Chronic placenta insufficiency with hemodynamic disturbances	1,3	0,4	4,5	$p>0,05$	2,5	1,3	5,0	$p<0,05$
Polyhydramnios	0,2	0,1	0,6	$p<0,01$	0,1	0,1	0,3	$p<0,01$
Premature rupture of membranes	0,7	0,1	7,3	$p>0,05$	3,3	1,2	9,0	$p<0,05$
Early rupture of membranes	13,2	2,1	81,9	$p<0,01$	12,5	2,7	57,1	$p<0,01$
Perineotomy	8,3	2,6	27,0	$p<0,01$	2,6	1,3	5,1	$p<0,01$

Note-statistically significant differences were found between the groups

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CASE STUDY

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TAKAYASU ARTERITIS: ASSOCIATIONS WITH HEMOCOAGULATION GENES POLYMORPHISM

ABSTRACT

Takayasu arteritis (TA) is a systemic vasculitis (SV) subset with chronic granulomatous arteritis predominantly affecting the aorta and its main branches. Cardiovascular events are the leading cause of death in TA patients. The high incidence of cardiovascular events cannot be explained entirely by inflammatory vascular wall lesions. Thrombophilia genes polymorphism has been discussed as another factor of thrombotic events in TA.

The **aim** of the current paper is to demonstrate thrombophilia genes polymorphism identification relevance to better assess the propensity to thrombotic complications in TA patients.

Methods: three clinical cases of verified TA are presented. All had vascular complications. Thrombophilia genes polymorphism, MRI and angiograms assessment were performed.

According to the results of genotyping, the patients were given recommendations on lifestyle modification, further laboratory studies, followed by consultation with the doctor of the rheology laboratory and hemostasis for the selection of personalized therapy with antiplatelet agents or anticoagulants.

The presented cases reflect the undoubted relevance of genetic research. Further research is needed into the specific features of thrombophilic gene polymorphism in patients with Takayasu arteritis.

Keywords: Takayasu's arteritis, thrombophilia genes, polymorphism.

Introduction

Takayasu arteritis (TA) is a systemic vasculitis (SV) subset with chronic granulomatous arteritis primarily affecting the aorta and its main branches [4]. The disease has been reported to occur more often in females [15]. Cardiovascular events are the leading cause of death in TA patients [10]. TA patients have a higher incidence of cardiovascular diseases than in the general population and a significantly higher risk of vascular events

on the Score scale at the time of the establishment of the disease in comparison with the general population [6].

Currently, the study of thrombophilia markers is an actual problem. A number of studies have proved the role of polymorphisms of thrombophilia genes and the risk of thrombotic complications in children and young people [3.5], in pregnant women [1, 2].

Clinical case 1

Subject N., a Caucasian female born

in 1972. Swelling and pain in the ankle joints occurred in 1998 at the age of 26 a few days after acute cystitis symptoms onset. Small joints of the hands and knee were gradually involved. Non-steroidal anti-inflammatory drugs (NSAIDs) administration had a short-term effect. During 2002-2003 a subfebrile fever was persisting. In April 2005 the subject was regarded as having a chronic course urogenic reactive arthritis. At the same time, a systolic murmur on the right subclavian artery, radial arteries pulse asymmetry,

and humeral arteries 40 mm Hg blood pressure (BP) asymmetry were registered, subfebrile fever persisting. The aorta and its branches ultrasound revealed the visceral branches stenosis, including left renal artery hemodynamically insignificant (<60%) lumen reduction. The above mentioned data being available, no TA has been registered.

The patient has received 3 plasmapheresis procedures accompanied by 3 intravenous 240 mg methylprednisolone infusions and oral sulfasalazine and hydroxychloroquine administration. Though effective, the treatment was discontinued after the discharge. Until February 2012, the subject had been feeling well, unless occasional volatile pains in the small joints of the hands, feet, knees, ankles well controlled by oral NSAIDs.

In February 2012, knees, feet and hands joints polyarthritis occurred, cervical and thoracic spine pain, frequent occipital pain to gradually commence. Dizziness and the evening subfebrile fever up to 37.2 °C also were registered. Total blood count revealed leukocytes = $11.8 \times 10^9/L$, platelets = $601 \times 10^9/L$, ESR = 36 mm/h. Serum tests were: hsCRP 3 mg/L, AST 63 IU, ALT 81IU, negative rheumatoid factor (RF), ELISA for chlamydia antibodies was also negative. Chest radiogram was normal. The subject consumed nimesulide on a daily basis.

In 2012 she was hospitalized to the Regional Hospital 1 Rheumatology Dept. BP on the legs was 170/130 mm Hg. In connection with the inflammatory activity (increased ESR, CRP, fibrinogen), it is recommended to prednisone 40 mg / day to normalize the inflammation, then gradually reduce the dose to 7.5 mg / essence. The patient had articular syndrome with involvement of the joints of the hands and feet, peri-arthritis, pain in the spine. Radiological erosive arthritis of the foot joints was revealed, whose debut was chronologically associated with cystitis, and a urogenital infection was diagnosed several years ago. Patient was recommended radiography of the thoracic spine, the sacroiliac joints. After further examination, taking into account the revealed 2-sided sacroiliitis, grade 1-2, arthritis, enthesitis, urogenital infection, a history of diagnosis was diagnosed.

In November 2013 she was treated in the rheumatology department; pulse therapy was carried out with a metered 250 mg intravenous No. 3. In December 2013, she was transferred to the vascular surgery department, where on December 10, 2013, a brachiocephalic trunk was performed. In the postoperative period

(December 11, 2013), an acute disorder of cerebral circulation developed in the basin of the left internal carotid artery. Since that time, I constantly took clopidogrel 75 mg / day. After discharge from the hospital she took prednisone 20 mg / day. Recommendations were followed. She was regularly observed by a rheumatologist.

In March 2015, due to clinical and laboratory activity (ESR = 15 mm / h, ASLO = 165), it was recommended to increase the dose of prednisolone to 15 mg / day. At the same time, she was consulted by an anesthetist. Computer tomography (CT) scan of the brachiocephalic vessels revealed signs of occlusion of both common carotid arteries (OCA) with the development of collateral blood flow in both internal carotid arteries (ICA). Ultrasound of the upper extremities arteries hemodynamically significant disorders of the main arteries were not detected. Surgical treatment is not needed, it is recommended to continue receiving clopidogrel.

Hemostasiogram from 10/17/2016: hematocrit = 30%, platelets = $420 \times 10^9 / l$, platelet aggregation with adf = 21%, TTPA = 27.6 seconds, prothrombin time = 14.3 seconds, the Kvik test = 94% , INR = 0.99 , thrombin time = 16.4 seconds, fibrinogen 3.34 g / l, SFC = 5.5 mg / 100 ml, plasminogen activity = 113%. Conclusion: the chronometric parameters of coagulation hemostasis are within the normal range, thrombocytosis is moderately elevated.

Thus, the association of inflammatory lesions of large arteries with the presence of genetically determined thrombophilia led to the development of an acute

violation of cerebral circulation. AT and thrombophilia verification allowed us to prescribe anti-inflammatory and anti-platelet therapy and, at least, delay the need for surgical treatment.

Clinical case № 2

Patient A., female, born in 1963. From her youth, she noted chest pain and shortness of breath during exercise. During the examination in 1994 she noted headaches, severe weakness, accelerated ESR up to 50 mm / h. During the examination, asymmetry of the pulse was noted, the stenosis of the right internal carotid artery (PASA), the right subclavian artery, the left subclavian artery, arterial hypertension up to the maximum figures of 240/130 mm Hg. However AT was not diagnosed.

Since 2002, the patient began to notice intermittent claudication of the lower extremities. Conservative therapy in the form of vascular preparations — Trental 5.0 IV, Cavinton 5.0 IV, and verapamil 80 mg was without effect. On the USDG of the arteries of the lower extremities - stenosis of the iliac arteries, occlusion of the superficial femoral arteries on both sides.

In the spring of 2007, a rheumatologist was examined - taking into account the survey data: noise during auscultation of the carotid arteries, asymmetry of the pulse, young age, stenosis according to instrumental studies, increased ESR in history with exclusion of infection and other causes diagnosed with arteritis Takayasu, started taking prednisone at 30 mg / day In 2007, due to hemodynamically significant stenosis, a bifurcation prosthesis was performed on femoral arteries. Acetylsalicylic acid at a dose of 100 mg / day has been added to therapy. In 2008, a recurrent ultrasound showed signs of stenosis of the internal carotid artery, subclavian arteries on both sides, stenosis of the common carotid artery on the left, left renal artery. 07/11/2008 endovascular stenting of the common carotid artery was performed. Blood flow in the left common carotid artery was restored. In 2013, she began to re-note pain in the lower extremities, during the examination revealed thrombosis of the right branch of the aorto-femoral (AB) shunt. An operative intervention was performed on June 20, 2013: from the incision in the projection of the femoral access, the right arm of the prosthesis AB, the common femoral artery (OBA), the deep femoral artery. The latter are passable, suitable for reconstruction. In the field of prosthetic and femoral anastomosis were observed occlusion, thrombotic masses. Distal anas-

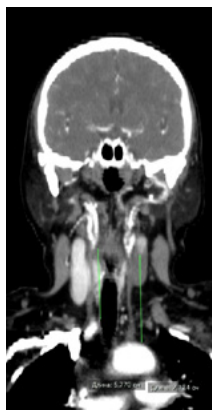


Fig.1. CT Angiography of the head and neck of patient N, coronary projection: long stretches of obliteration of both common carotid arteries



Fig.2. CT Angiography of the head and neck of patient N, axial projection: narrowed gaps of common carotid artery with a pronounced circular thickening of walls

tomosis of the cross - shunt of the type "end to end" was formed.

Up to this day, she continues to observe rheumatologist, angiologic surgeon SOKB No. 1, continuous intake of prednisone 7.5 mg, aspirin, clopidogrel.

Coagulogram from 2013: hematocrit 39% (35-47), TTPA 41.5 (28-40), the Kvik test 77 (75-120%), INR 1.18 (0.9-1.2), thrombin time 16.4 s (14-21), fibrinogen 3.0 (2-4), SFC 8 mg / 100 ml (0-4.5), plasminogen activity 93% (75-140). Conclusion: increased platelet aggregation, chronometric normal coagulation, increased levels of thrombinemia markers.

In this case, the development of vascular occlusion after reconstructive surgery for hemodynamically significant stenosis was also due to a genetic predisposition to hypercoagulation.

Patient S., female, born in 1959. Ill in 1991: acutely developed fever, weakness. She began to notice pain, paresthesia of the upper limbs. To the doctor did not address. A few months later, an acute violation of cerebral circulation in the PVA pool developed, during the examination there was a decrease in pulsation in the upper limbs, arterial hypertension, systolic murmur over the subclavian arteries. A clinical diagnosis is formulated: AT with lesions of the subclavian arteries, the internal carotid artery on the right. Intake of prednisone was started orally at a dose of 20 mg / day, vascular therapy (Curantil, Cavinton). In satisfactory condition discharged home with the recommendations of observation by a rheumatologist; In view of the complete clinical and laboratory activity, the patient no longer appeared in the Regional Rheumatological Center (RRC). At the telephone contact she complained of shortness of breath, pain retrosternal during physical activity. She was recommended examination by a cardiologist.

In this case, the association of inflammatory lesions of large arteries with the presence of genetically determined thrombophilia caused the development of an acute violation of cerebral circulation at a young age.

We carried out the determination of polymorphisms of hemocoagulation genes in 3 patients with verified AT. All those examined at a young age developed vascular complications in 2 cases in the form of ischemic stroke and in 1 patient thrombosis of the aorto-femoral shunt.

All our patients were carriers of at least 3 allelic variants of thrombophilia genes. It is believed that the risk of recurrent strokes increases in carriers of multigene

combinations by 3-7 times [9].

Genetic combinations involving all 3 hemostasis were recorded in all patients: plasma (heterozygous variant of FGB fibrinogen in the first patient, heterozygous variant of the F13 gene in the second patient, and heterozygous variant of the F7 gene in the third patient); platelet (a heterozygous version of the ITGA2 gene is fixed in all patients, a heterozygous version of the ITGB3 gene in the first patient and a homozygous version of the ITGB3 gene in the third); fibrinolysis systems (heterozygous variants of the PAI-I gene in the first and third patients and the homozygous variant of the PAI-I in the second).

Polymorphisms on 7 and 13 clotting factors are considered protective in

terms of thrombus formation. Their role as thrombophilic polymorphisms is still under discussion.

It is interesting that ITGA2 and PAI-I polymorphism were noted in all patients. Option ITGA2: 807 (C to T) leads to an increase in the density of collagen receptors on the platelet membrane [7], which, if there is a defect in the endothelial lining, leads to an increased adhesion of platelets and the development of thrombosis in situ.

The PAI-1: 675 variant (5 G to 4 G) acts as an inhibitor of fibrinolysis [14]. Currently, the role of this polymorphism in the development of the immunopathological process is being studied. There is evidence that with the participation of PAI-1, activation of the pre-forms of the

Table 1

Subject N. thrombophilia genes polymorphism assessment (2018)

Factor	Identified subject's genotype	Wild type
F2: 20210 (G на A)	GG	GG
F5: 1691 (G на A)	GG	GG
F7: 10976 (G на A)	GG	GG
F13: (G на T)	GG	GG
FGB: 455 (G на A)	GA	GG
ITGA2: 807 (C на T)	CT	CC
ITGB3: 1565 (T на C)	TC	TT
PAI-1: 675 (5 G на 4 G)	5G4G	5G5G

Table 2

Genetic testing for the determination of genetic markers of thrombophilia from patient A in 2018

Factor	Patients genotype	Wild type
F2: 20210 (G на A)	GG	GG
F5: 1691 (G на A)	GG	GG
F7: 10976 (G на A)	GG	GG
F13: (G на T)	GT	GG
FGB: 455 (G на A)	GG	GG
ITGA2: 807 (C на T)	CT	CC
ITGB3: 1565 (T на C)	TT	TT
PAI-1: 675 (5 G на 4 G)	4G4G	5G5G

Table 3

Genetic testing for the determination of genetic markers of thrombophilia from 2018 patient S

Factor	Patients genotype	Wild type
F2: 20210 (G на A)	GG	GG
F5: 1691 (G на A)	GG	GG
F7: 10976 (G на A)	GA	GG
F13: (G на T)	GG	GG
FGB: 455 (G на A)	GG	GG
ITGA2: 807 (C на T)	CT	CC
ITGB3: 1565 (T на C)	CC	TT
PAI-1: 675 (5 G на 4 G)	5G4G	5G5G

enzymes of the matrix metalloproteinase system is possible [10]. The role of PAI-1 as an inhibitor of cell migration and phagocytosis is also discussed, which also contributes to immunopathological processes [11, 13].

Cases of association of AT and mutations of Leiden were described earlier [16]. However, in the cases presented by us this association was not traced.

In recent years, the characteristic of modern medicine has been given using the "4 P" concept: predictive, personalized, preventive, participatory [12].

From the standpoint of the "4 P" concept, timely examination of patients for polymorphism of thrombophilia marker genes is highly relevant, since an adequate assessment of the risk of vascular complications will allow the timely prevention of condemned events. In addition, evidence has been obtained that the platelet glycoprotein ITGB3 (homo or heterozygous) mutation causes the development of resistance to the anti-aggregant effect of aspirin [8]. Identification of genetic markers of thrombophilia allows a personalized approach to the appointment of disaggregant therapy to patients at high risk of thromboembolic complications.

The study of patterns of polymorphism of hemocoagulation genes also allows us to concretize the further scope of laboratory research. For example, the first patient, based on the data of genotyping, should monitor the levels of fibrinogen, SFC, prothrombin time, concentration of plasminogen activator inhibitor, platelet count, thromboelastogram, and platelet aggregation tests.

The study of patterns of polymorphism of hemocoagulation genes also allows us to concretize the further scope of laboratory research. For example, the first patient, based on the data of genotyping, should monitor the levels of fibrinogen, SFC, prothrombin time, concentration of plasminogen activator inhibitor, platelet count, thromboelastogram, and platelet aggregation tests.

According to the results of genotyping, the patients were given recommendations on lifestyle modification, further lab-

oratory studies, followed by consultation with the doctor of the rheology laboratory and hemostasis for the selection of personalized therapy with antiplatelet agents or anticoagulants.

The cases presented reflect the undoubted relevance of genetic research. Further research is needed into the specific features of thrombophilic gene polymorphism in patients with Takayasu arteritis.

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A.G. Markhaev, M.V. Badleeva

UNUSUAL CASE OF IN VIVO DETECTION OF INTRADURAL INTRAMEDULLARY TUBERCULOMA

ABSTRACT

The article presents a review of the literature about observations of spinal tuberculomas. Intramedullary spinal tuberculoma – thus is a rare diagnosable form of extrapulmonary tuberculosis. Review of the literature describes about 40 patients with spinal cord tuberculoma. In 1956, Cascino and Dibble identified intramedullary spinal tuberculoma of a patient. MacDonell et al. reviewed about 20 cases of this disease for 30 years. Fifteen cases of spinal tuberculosis were reported by Ramdurg et al. In clinic there are extradural and intradural forms of spinal tuberculoma. Intramedullary tuberculosis occurs ten times more often. In the pathogenesis of the development of intramedullary spinal tuberculoma it may be blood- dissemination and the spread of MBT through the cerebrospinal fluid are possible. According to some data, they are detected more often in women. Intramedullary tuberculomas were not previously diagnosed in Buryatia.

The purpose of the study: a description of the clinic and methods of diagnosis of intraspinal tuberculoma.

The materials of research described a history of the clinical picture of a 34-year-old patient with a relapse of pulmonary tuberculosis in 2003, with the formation of fibrous-cavernous pulmonary tuberculosis in 2013 in TBC (+) II B GDU, MLU-HRS.

During hospitalization in the hospital there were neurological symptoms with deterioration.

After screening of the chest organs on both sides by X-ray tomograms, on the right revealed multiple confluent polymorphic focal shadows with decay cavities were discovered more. Neurological status: cranial nerves without pathology. Neurologically - muscle tone is sharply reduced in the lower limbs, reflexes are sluggish. Cerebellar tests, sensitivity testing without pathology, meningeal and radicular symptoms have not been identified.

On MRI with contrasting at the level of Th3, intramedullary a volumetric formation with a ring-shaped accumulation of contrast with dimensions of 7x8 mm was discovered. It was small infiltration perifocally.

Based on this data, a diagnosis of spinal cord tuberculosis was exposed. Pathologic examination was confirmed the diagnosis.

In result findings showed that a patient with widespread respiratory tuberculosis, against the background of blood- dissemination in the lungs, nerve tuberculosis was joined – this is intramedullary tuberculosis with typical neurological symptoms and diagnosis of spinal cord lesion became possible using the magnetic resonance imaging with contrast.

Keywords: tuberculoma, spinal cord, MRT, Buryatia.

Introduction. Tuberculosis remains an important pathological problem in developed and developing countries [1]. According to some estimates, part of the central nervous system in patients with tuberculosis is about 10%, with the most common manifestation of tubercular meningitis. Spinal tuberculoma is also a manifestation of extrapulmonary tuberculosis involving the central nervous system and characterized as jekstraduralnaja or intramedullary, depending on their location [2,3].

Extramedullary tuberculoma is extremely rare. In literature, it was found only 30 such localization tuberculoma.

Tuberculoma tuberculoma is also a rare form of the disease. In the world described more than four dozen cases of tuberculoma of the spinal cord. Cascino and Dibble in 1956, for the first time described the intramedullary spinal tuberculoma [7]. MacDonell et al. for 30 years have identified 18 cases of this pathology [8]. Ramdurg et al. for 21 year presented 15 cases [9]. Intramedullary spinal tuberculoma develops due to hematogenous dissemination of the pathogen or infection of spinal fluid. The ratio of intracerebral tuberculoma to spinal is 42 to 1 [5]. Among women the pathology occurs more often [11, 12, 13]. In Buryatia intramedullary tuberculoma was not

previously diagnosed.

The purpose of the study: description of the clinical picture, diagnosis methods, intramedullary tuberculoma.

Materials research. Patient n., 34 years old man in his childhood had primary tuberculosis. Relapse of tuberculosis identified in 2003 year, in places of deprivation of liberty (MLS), short courses of treatment ineffective. To 2013 year formed a fibro-cavernous pulmonary tuberculosis BK + II b GDU, MDR-HRS. In December 2014, in connection with the

grave condition of the patient was released for health reasons.

He entered the hospital with complaints of paraplegia, lack of control over the functions of the pelvic organs, chills, fever, weight loss, expressed by general weakness, cough with phlegm. From the history it was established that appeared a few months ago pain in thoracic and lumbar spine. The condition worsened: pain in the spine exacerbated, weakness in the limbs, growing to no active movements in the lower extremities. Pelvic dis-



Fig. 1. Review lung X-ray

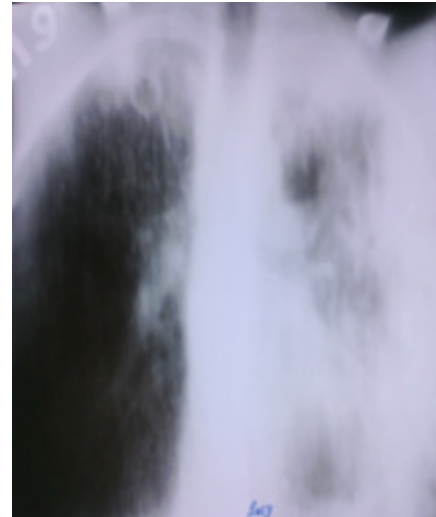


Fig. 2. Lung CT



Fig. 3. MRI of the spine

order not noted.

Diagnosis at admission: disseminated pulmonary tuberculosis in the disintegration phase of MBT (+), MDR – HRSPas, 11B GDU. Cachexia, multiple organ failure.

On the X-ray tomograms of the chest, there is a presence on both sides of more to the right of multiple polymorphic focal shadows, cavities with thick walls on both sides (Figure 1, 2).

Neurological examination noted that the cranial nerves are not affected by the pathological process. Muscle tone is reduced in all the limbs, reflexes are sluggish. Cerebellar tests, sensitivity testing were normal, meningeal and radicular symptoms were not revealed.

With MRI with intravenous contrasting, omniscan revealed at the level of Th3 a volume formation with a ring-shaped accumulation of contrast measuring 7x8 mm. Perifocal small infiltration (Figure 3).

Differential diagnostics was performed between new formation, multiple sclerosis and spinal tuberculosis.

Cerebrospinal fluid analysis was not performed due to patient failure. Based on the data obtained, a diagnosis of spinal cord tuberculosis was made. Tuberculosis therapy did not produce results due to the serious condition of the patient, a far-

gone tuberculosis process. The patient died of tuberculosis. Pathologic examination confirmed the diagnosis.

Results and discussion

In a patient with chronic widespread pulmonary tuberculosis, due to refusal of treatment on the background of hematogenous dissemination in the lungs, the nervous system tuberculosis joined - intramedullary tuberculoma with typical neurological symptoms.

Diagnosis of lesions of the spinal cord has become possible due to the use of magnetic resonance imaging with contrast.

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EXPERIENCE EXCHANGE

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ROENTGENOSURGICAL TREATMENT OF CHRONIC PELVIC PAIN CAUSED BY PERIMETRIUM VENOUS CONGESTION

ABSTRACT

A 36-year-old female patient (having two children) presented with a permanent pain in hypogastric region, which increased during sexual intercourse. The woman had recurrent pains of such nature from the puberty age. The pain became permanent after the second childbirth. In this regard, sexual intimacy proved almost impossible. The occurrence and increase of pain were not associated with meal, physical exercise, menstrual periods or weather conditions. Dyspepsia was absent. Multiple consultations with medical specialists, including gynecologists were ineffective.

Complex radiation study (doppler ultrasound, multispiral computed tomography, angiography) diagnosed the signs of hyperemia - disorders in the drainage via the left gonadal vein. Superselective occlusion of the dilated vessel resulted in recovery: the pains discontinued, sexual function became normal.

Keywords: venous congestion, chronic pelvic pain, endovascular occlusion.

Varicose pelvic disease or pelvic congestion syndrome (PCS) is a pathological condition that is difficult to diagnose. The main symptoms of the syndrome is a chronic pelvic pain lasting more than 6 months independently of menstrual period, dyspareunia and dysmenorrhea [1, 6]. Louis Alfred Richet was the first to describe this condition in 1857. Pelvic venous hyperemia is caused by renal hypertension and valvular failure of the left ovarian vein [2, 4, 5]. Pelvic venous hypervascularization is the reason of abdominal pain in adolescent girls in 4% of follow-ups [2].

According to Lechter (1999), 70000 hysterectomies were performed annually in the United States for chronic pelvic pain resulted from undiagnosed pelvic varicosities. Currently, the main method for treating pelvic venous hyperemia and chronic pain is an intervention on the gonadal veins based on endoscopic or endovascular procedures. Radiologic surgical occlusion of gonadal veins is technically successful in 92-95% of patients, and its clinical efficacy ranges from 40 to 82% [3, 7].

Case Report

A 36-year-old female patient (having two children) presented with a permanent pain in hypogastric region, which increased during sexual intercourse. The woman had recurrent pains of such nature from the puberty age. The pain became permanent after the second childbirth. In this regard, sexual intimacy proved almost impossible. The occurrence and increase of pain were not associated with meal, physical exercise, menstrual periods or weather conditions. Dyspepsia was absent. Multiple consul-

tations with medical specialists, including gynecologists were ineffective.

Objective status: habitus is regular, normosthenic; the abdomen of normal form is painful in hypogastrium in palpation, peritoneal symptoms are absent. Urination is painless, urine is transparent, straw-yellow in color. Defecation is normal. Rectal examination: perianal skin is not changed, sphincter tone is ordinary. The anterior wall of the rectum is moderately painful with indistinct prolapse. Gynecologic examination did not reveal any acute pathology.



Fig. 1. Selective contrast enhancement of the left renal artery. Retrograde injection of the dilated left gonadal vein during the venous phase

Clinical blood analysis: moderate increase of erythrocytes up to $4.86 \times 10^{12}/l$, decrease in blood hemoglobin to 110 g/l. Other rates correlated with the reference values. Clinical urine analysis, biochemical blood analysis, coagulogram were without abnormalities.

Multispiral computed tomography of the abdominal cavity showed varicose pelvic veins, arteriovenous shunts between the left gonadal vein and the arteries of the left kidney (?). Screening ultrasonography of the abdominal cavity did not reveal any pathological changes.

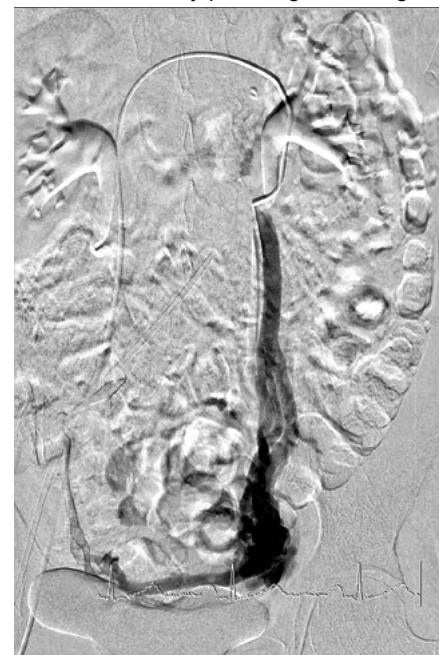


Fig. 2. Selective contrast enhancement of the left renal vein. Injection of ovarian vein and varicose plexus of the small pelvis



Fig. 3. Selective contrast enhancement of the left renal vein. Occlusion of gonadal inflow by spiral element (arrow)

A detailed instrumental examination was performed. Duplex scanning of renal arteries did not reveal hemodynamic disorders. The diameter and hemodynamic parameters of the abdominal aorta were without changes.

Ultrasound duplex scanning of the superior mesenteric artery showed that it branched off the aortic wall at an acute angle, compressing the left renal vein in the proximal segment, the diameter of which was 1,8 mm in its narrowing. In the preaortic part, the left renal vein was dilated to 1,0 cm, there was a shunt into the left gonadal vein, which was dilated to 0,8 cm. Right renal vein was of ordinary diameter (0,6 cm) with preserved blood flow.

The inferior vena cava was patent in every segment. Common and external iliac veins were without changes on either side. Varicose alterations of pelvic veins: right veins were tortuous and dilated to 7,0 mm; left veins were dilated to 8,0 mm; blood flow was spontaneous, reduced, located on both sides.

Considering the above findings in the venous bed and clinical data, the diagnosis was made: aorto-mesenteric compression of the left renal vein; varicose dilation of the left ovarian vein; pelvic veins varicosity; pelvic venous hyperemia (pelvic congestion syndrome); chronic pelvic pain. It was decided to carry out radiologic surgical intervention for diagnostic and

therapeutic purposes.

Selective rheovasography (SRVG) revealed no pathology on the right. Left SRVG showed renal artery without changes. The venous blood outflow from the left kidney was via renal and dilated ovarian veins. The latter was drained into a varicose network of pelvic veins (Fig. 1). Then the contrasted blood entered the inferior vena cava by several collectors. Angiography of the left renal vein was performed from venous access. Varicose ovarian vein originated from its proximal part (closer to the kidney portal) (Fig. 2).

It was decided to embolize the left ovarian vein. Amplatzer vascular plug 2 (8 mm in diameter) was positioned in its proximal part. Monitoring SRVG showed the absence of shunting into the ovarian vein. Monitoring angiography from the renal vein (venous access) showed that renal vein was intact, ovarian vein stump was visualized on the left (Fig. 3).

The early postoperative period was uneventful. The patient was inspected in 24 hours after the manipulation. She complained of moderate pain in the puncture sites on the right thigh. Abdominal pain was not manifested. The abdomen was soft and painless in palpation. The patient was discharged two days after manipulation in good condition.

The patient was surveyed in 7 months: pain is absent, sexual life is comfortable.

Discussion. The patient was admitted to the hospital with a long history of chronic pelvic pain. Arteriovenous shunt between the left renal artery and the left gonadal vein was supposed, but was not confirmed in a subsequent examination.

However, an anomalous angle of the superior mesenteric artery origin from the aorta was revealed, which resulted in compression of the left renal vein with the formation of a collateral blood outflow via the left gonadal vein. Subsequently, the pelvic venous congestion developed, which clinically manifested as the progressing syndrome of chronic pain.

Detailed examination allowed an accurate diagnosis and an adequate management. Direct angiography verified the findings of non-invasive radiation methods and enabled minimal invasive correction of hemodynamic disorders and as a result the relief of the permanent pain.

Thus, women with chronic pelvic pain syndrome need obligatory duplex ultrasound examination of the venous bed of the small pelvis with an assessment of hemodynamic parameters. Angiography of the venous bed with the material occlusion of the pathological venous shunt

allows effective and fast relief of clinical manifestations of pelvic congestion syndrome and pain.

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OUR EXPERIENCE OF LAPAROSCOPIC SUTURING PERFORATIVE GASTRODUODENAL ULCER IN THE MULTIDISCIPLINARY URGENT SURGICAL CENTER OF THE REPUBLIC SAKHA (YAKUTIA)

ABSTRACT

The **aim** of the study was to evaluate the results of surgical treatment of patients with perforated gastroduodenal ulcer, taking into account the use of the laparoscopic method in a multi-field surgical center of the Republic of Sakha (Yakutia).

Material and methods. The work is based on the analysis of the results of treatment of 108 patients with perforated gastroduodenal ulcer, of which 45 (41,7%) underwent laparoscopic suturing of the perforated opening.

Results. The first experience of laparoscopic suturing of perforated gastroduodenal ulcer demonstrated the promise of the method, as well as its high efficiency and safety. **Conclusion.** The introduction of the method allowed to reduce the number of postoperative complications by 1,7 times, and to reduce the length of stay in a multidisciplinary surgical hospital by 28,6%.

Keywords: perforated gastroduodenal ulcer, laparoscopic suturing.

Introduction. In urgent surgical practice, operations for perforated gastroduodenal ulcers are still relevant. According to a number of researchers [1], the incidence of gastric ulcer and duodenal ulcer among the adult population in the Russian Federation is 3-15%, in 5-15% of patients the disease course is complicated by ulcer perforation, while postoperative mortality ranges from 1,3 to 19,4%, depending on the time of admission of the patient to the hospital [6], and the number of postoperative complications reaches 17% [8].

It is worth noting that, at present, the treatment of this complication of peptic ulcer disease is one of the many unsolved problems of surgical gastroenterology [4]. The operation of choice in most clinical cases is laparoscopic suturing of the perforation hole. Technically, suturing is fairly easy to do and provides favorable immediate results of treatment [7]. The need to perform more complex operations rarely arises (a combination of perforated ulcers with stenosis of the output section of the stomach and duodenum, multiple and callous ulcers, widespread purulent peritonitis). The disadvantage of the suturing operation is the high purity of the recurrence of peptic ulcer - up to 45% [4]. At present, with the advent of a new generation of drugs that have a proven ability to significantly accelerate the processes of repair and healing of ulcers, as

well as prevent their relapses, prospects have opened up for improving the long-term results of the treatment of perforative ulcers after they are sutured [3].

In the Republic of Sakha (Yakutia), as well as in other regions of the Russian Federation, the perforation of the gastroduodenal ulcer is one of the leading places among urgent surgical pathology. According to the Yakutsk Republican Medical Information and Analytical Center (YRMIAC), in recent years there has been a slight decrease in the incidence of gastric ulcer and duodenal ulcer – 6,3‰ in 2017 compared to 7,8‰ in 2010, but the problem is significant degree complicates the formation of various forms of severe complications, including perforation, bleeding and malignancy. The current situation is alarming and creates the need to search for more effective diagnostic methods, as well as to improve the principles and methods of conservative and surgical treatment that exist today.

Research materials and methods. The presented work is based on a retrospective analysis of the results of complex treatment of 108 patients with perforated gastroduodenal ulcer who were treated in the emergency surgery department of the Republican Hospital № 2 - Emergency Medical Center of the Republic of Sakha (Yakutia) from 2010 to 2019. The average age of patients

was 35.2 ± 5.5 years, while there were 73 men (67,6%) and 35 women (32,4%). The diagnosis, perforated gastroduodenal ulcer, is verified on the basis of a modern multi-level comprehensive examination. Patients were divided into study groups. The main group consisted of 45 (41,7%) patients who underwent laparoscopic suturing (LS) of the perforation hole, and 63 (58,3%) patients with the control group who underwent perforation ulcer excision (PUE), including duodenoplastic (according to Judd-Tanaka, Judd-Horsley) depending on its location. Perforation of gastric ulcer during surgery was found by us in 27 (25%) and duodenal ulcers - in 81 (75,0%) patients. At the same time, in 39,7% of cases, local serous-fibrinous peritonitis was detected, in 55,0% - diffuse and 5,3% - widespread purulent. The diameter of the perforation hole, when conducting LS and PUE, averaged 5.0 ± 1.4 mm.

All operations were performed using the endoscopic system Karl Storz Endovision® DCI® with the autorotation system (ARS) - a digital single camera, PAL, NTSC color systems with an integrated digital image processing module. A set of DCI® HOPKINS®II laparoscopes (10 mm large format optics), trocars, forceps, scissors, dissectors, Karl Storz Click'Line® extractors under combined endotracheal anesthesia. We considered contraindications to the performance of

traditional laparoscopic suturing (LS) of perforated gastroduodenal ulcer: the time of the time from perforation is more than four hours, difficult localization of the ulcer, large diameter of the perforated hole, suspicion of ulcer malignancy, callas ulcer, perifocal inflammation of the intestinal wall more than 10 mm, purulent diffuse or widespread peritonitis, sepsis, the presence of associated diseases and conditions that prevent the imposition of carboxyperitoneum.

Statistical processing of the material was made using the IBM.SPSS.Statistiks.v22 software package. The coefficient of reliability of differences (p) was determined by the t-criterion of Student.

Results and discussion. During the operation of the LS perforated gastroduodenal ulcer, the transition to laparotomy (conversion) took 3 (6,7%) patients, and in which, despite a three or four hour exposure, the prevalence and nature of the inflammatory process in the abdominal cavity corresponded to diffuse purulent peritonitis. In all cases of conversion, laparotomy access was used. At the same time, in all three cases, ulcer perforation was detected in the projection of the duodenal bulb, which required the implementation of an operation commonly used in our clinic, such as Judd-Horsley, followed by rehabilitation and drainage of the abdominal cavity.

From the moment the patient arrived at the surgical hospital (taking into account the necessary examination) and until the surgical intervention was completed, no more than 60 minutes passed. The time of surgical intervention when performing LS ranged from 45 to 125 minutes and averaged 98.5 ± 24.8 minutes. Operation of PUE took from 60 to 130 minutes (average of 75.3 ± 22.1 minutes). The time difference was statistically significant ($p < 0.05$). It should be emphasized that the duration of the laparotomy wound closure has the main influence on the duration of the PUE operation; this fact is confirmed by other researchers [5, 9].

Another important parameter is the average time of activation of patients after surgery, as indicated by many researchers [2, 10]. In our case, the time of activation of patients after the LS was 1.6 ± 0.6 days. After the operation of the PUE – 2.1 ± 0.7 days. ($p < 0.05$). The increase in bed rest after PUE was largely due to pain from the laparotomy wound.

Along with such a parameter as the time of activation of the patient, one of the important aspects is the time of appearance of active intestinal motility [2], the ability to take liquid and solid food

in order to maintain energy balance and plastic function of the body. In our case, after the operation of the LS, this time was 1.0 ± 0.3 days, and after the operation of PUE – 1.2 ± 0.5 days.

The total number of complications in the main group was 3 (6,7%), in all three cases the complications were associated with the failure of the sutures of the previously sutured perforated hole, which required a laparotomy, excision of the ulcer, followed by Judd-Horsley or Judd -Tanaka, depending on its location, with subsequent rehabilitation and drainage of the abdominal cavity. In the control group, the total number of complications was 5 (7.9%). At the same time, only 1 (1,6%) intra-abdominal complication was recorded - sluggish peritonitis, which required carrying out a program of rehabilitation of the abdominal cavity, the patient subsequently recovered. In the remaining 4 (6.3%) cases, complications from the operating wound (infiltration, suppuration) were recorded. There were no deaths in both groups. The average length of stay in the in-patient department after the LS was 5.0 ± 1.0 bed-days, after the operation of PUE – 7.0 ± 2.0 bed-days. Patients after LS were on average 2 bed-days less than those who underwent PUE.

Thus, the following **conclusions** can be made that with the widespread introduction of minimally invasive technologies into clinical practice, along with performing such operations as: laparoscopic appendectomy, hernioplasty and many others, the operation of LS perforated gastroduodenal ulcer is becoming more and more stable. First of all, this is facilitated by the positive results of treatment: reduction of postoperative complications and length of stay in the surgical hospital, reduction of the rehabilitation period and early rehabilitation. Comprehensive introduction into the practice of urgent surgical clinics of the LS perforated gastroduodenal ulcer should be considered a priority for modern technological medical care. The data we obtained allow us to consider surgical operations in which special attention should be paid to the theoretical and practical training of surgeons, as well as the use of common tactical approaches and solutions in various clinical situations.

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