protivopozharnoj sluzhby` MChS Rossii [Bulletin of the St. Petersburg University of the State Fire Service of the Ministry of Emergency Situations of Russia. 2020; 3: 1-5 (In Russ.).]

9. Malkhazova SM, Mironova VA, Bashmakova IKh. Prirodnoochagovy`e bolezni v Arktike v usloviyax menyayushhegosya klimata [Natural focal diseases in the Arctic in a changing climate]. Vestnik Moskovskogo universiteta. Seriya 5: Geografiya [Bulletin of Moscow University. Episode 5: Geography. 2022; 1:43-57 (In Russ.).]

10. Markin VV, Silin AN, Vershinin IS. Zdorov`e lyudej v Arktike: social`no-prostranstvenny`j diskurs (na primere Yamalo-Neneczkogo avtonomnogo okruga) [Human health in the Arctic: socio-spatial discourse (using the example of the Yamalo-Nenets Autonomous Okrug)]. E`konomicheskie i social`ny`e peremeny`: fakty`, tendencii, prognoz [Economic and social changes: facts, trends, forecast. 2020; 13 (5): 182–199 (In Russ.).] doi: 10.15838/esc.2020.5.71.11

11. Polozhentseva OA. Uroven` i kachestvo zhizni kak faktor samorazvitiya mestny`x soobshhestv Murmanskoj oblasti [Level and quality of life as a factor in the self-development of local communities in the Murmansk region]. Vestnik Altajskoj akademii e`konomiki i prava [Bulletin of the Altai Academy of Economics and Law. 2020; 10-1:69-75; URL: https://vaael.ru/ru/article/view?id=1348 (date of access: 02/29/2024) (In Russ.).]

12. Savvina MT, Maksimova NR, Sukhomyasova AL, et al. Nasledstvenny`e bolezni i programmy` molekulyarno-geneticheskogo skrininga v geneticheski izolirovanny`x popu1yaciyax [Hereditary diseases and carrier's screening programs in genetically isolated populations]. Medicinskaya genetika [Medical Genetics. 2022; 21(1):3-13 (In Russ.).] https://doi.org/10.25557/2073-7998.2022.01.3-13

13. Sleptsov SS, Andreev MN, Sleptsova SS. Vliyanie kachestva zdravooxraneniya na ottok naseleniya iz otdalenny`x rajonov Yakutii (na primere Ojmyakonskogo ulusa) [The influence of the quality of healthcare on the outflow of the population from remote areas of Yakutia (on the example of the Oymyakonsky ulus)]. Uspexi sovremennogo estestvoznaniya [Advances in modern natural science. 2023; 7: 42-48 (In Russ.).] doi: 10.17513/use.38069.

14. Solonin YuG, Boyko ER. Mediko-fiziologicheskie problemy` v Arktike [Medical and physiological problems in the Arctic]. Izvestiya Komi nauchnogo centra UrO RAN [News of the Komi Scientific Center of the Ural Branch of the Russian Academy of Sciences. 2017; 4(32): 33-40 (In Russ.).]

15. Tikhonov DG. Arkticheskaya medicina [Arctic medicine. Ed. V.A. Galkina, M.I. Tomsky; RAMS, SO, YSC CMP. Yakutsk: Publishing house YSC SB RAS, 2010: 313 (In Russ.).]

16. Tomsky MI. Naselenie promy`shlenny`x rajonov Yakutii i «sindrom polyarnogo napryazheniya [Population of industrial regions of Yakutia and the "polar voltage syndrome]. E`konomika Vostoka Rossii [Economics of the East of Russia. 2015; 1:78-81 (In Russ.).]

17. Fedorov AI. Sukhomyasova AL, Golikova PI, et al. Rasprostranyonnost` spinocerebellyarnoj ataksii 1 tipa v Yakutii: sovremennoe sostoyanie [Prevalence of spinocerebellar ataxia type 1 in Yakutia: current state]. Medicinskaya genetika [Medical genetics. 2020; 19(7): 29-30 (In Russ.).] doi: 10.25557/2073-7998.2020.07.29-30.

I.V. Averyanova, O.O. Alyoshina

ANALYSIS OF CORTISOL AND DEHYDROEPIANDROSTERONE-SULFATE LEVELS IN MALE NORTHERNERS: THE INFLUENCE OF GENERATION LIVING IN THE NORTH

DOI 10.25789/YMJ.2024.87.20

UDC: 612.45; 57.017.3

Relevance. The body's ability to resist the effects of harsh climatic and geographical conditions is determined by characteristics of adaptive mechanisms and the process of their change based on the hypothalamic-pituitary-adrenal axis and depending on the length of residence in the North.

Purpose. This study examined male Northerners to assess fluctuations in their cortisol and dehydroepiandrosterone-sulfate mean levels in the increasing reliance on the generation of residence in the North.

Methods. Seventy male residents of the Magadan Region (mean age 40.0±0.8 yrs) participated in the survey and made up subgroups varying with the length (generation) of residence in the North: the 0th generation (n=15), the 1st generation (n=35), and the 2nd-3rd generation (n=20). Immunochromatographic and immune enzyme analyses were applied in the research.

Results. Subjective mean levels of serum cortisol and dehydroepiandrosterone-sulfate and their ratio tended to significantly fluctuate based on the generation of residence in the North: the highest values were observed in examinees with the longest period of residence (2nd-3rd generation), and the lowest – in representatives with a shorter period of adaptation to the North extremes (0th generation). In addition, the cortisol concentrations in the evening saliva test were optimized according as we traced them in representatives of 0th to 2nd-3rd generations.

Conclusion. The study has resulted in referring serum cortisol and dehydroepiandrosterone-sulfate concentrations, their ratio, as well as cortisol concentrations in the evening saliva tests to significant markers that reflect readjustments in the endocrine picture with increasing length of residence in the North, thus confirming the generally recognized role of glucocorticoids in hormonal support of the body adaptation to extreme factors including climatic environments.

Keywords: North, middle-aged men, cortisol, DHEA-S, the generation of residence

AVERYANOVA Inessa Vladislavovna – Doctor in Biology, head of the laboratory, chief researcher of the Laboratory of Physiology of Extreme Conditions Scientific Research Center "Arktika", Fareastern Branch of the Russian Academy of Sciences (SRC "Arktika" FEB RAS), e-mail: Inessa1382@mail.ru ORCID ID: 0000-0002-4511-6782; **ALYOSHINA Olga Olegovna** – junior scientist at the Laboratory of the Physiology of Extreme Conditions Scientific Research Center "Arktika", Fareastern Branch of the Russian Academy of Sciences (SRC "Arktika" FEB RAS), e-mail: oalesina597@gmail.com; ORCID ID: 0000-0002-5718-5398

Introduction. The issue of the mechanisms of newcomers' long-term adaptation to the harsh conditions of the north remains relevant and requires further study. Currently, in addition to the indigenous peoples in the Magadan Region, the permanent residents are made up of quite numerous ethnic groups of Caucasians: migrants and those born to them in the north in different generations [1]. In the course of our long physiological research, we found that migrants and north-born Caucasians have their own specific characteristics and also much in common in their body functional adaptive readjustments. As we were examining young male adults from Caucasian migrants and those born to migrants in the 1st-3rd generations, all being residents of the Magadan Region, we identified the main components of the adaptation strategy according as the examinees be-

longed to a particular generation. Those components showed optimization in the studied body functional performance as effectiveness of adaptive changes to the harsh impact of natural and climatic environments and were characteristic of generation-related subjects in the range from 0th generation to 2nd and 3rd generations: increased contribution of the parasympathetic component with a fall in the hypertensive focus in the cardiovascular system, reduced total energy costs, and lowered atherogenicity of the lipid picture [1].

It is known that successful adaptation of a human body to extreme climatic and geographical conditions varies with the state of adaptive mechanisms which are based on the hypothalamic-pituitary-adrenal axis (HPA). The structure of adaptive neurohormonal and endocrine reactions is quite plastic and is subject to changes depending on the duration of residence in the northern regions [7, 26]. Cortisol and dehydroepiandrosterone (DHEA) are considered valuable markers of the hypothalamus-pituitary-adrenal axis [19] with cortisol as the main biomarker of its activity [14] and the hormone that performs to ensure physiological homeostasis and adaptation to stressful situations. However, maintaining high levels of these hormones is energetically inefficient and prevents other physiological processes [32, 29]. Measuring the cortisol level provides important information on a person's capability to adapt to various environmental requirements [17] since its concentration is influenced by psychological and physiological stress factors [28]. To keep the energy balanced when exposed to hormones of the HPA axis, various mechanisms of adaptation of their levels to environmental conditions work at different time scales, i.e. through generations, between parents and their descendants, and during the life of an individual [21]. Dehydroepiandrosterone (DHEA) is mainly present as sulfated ether (DHEA-S); it shows an anti-glucocorticoid effect in vitro and can protect against the side effects of elevated circulating cortisol [19].

We have considered the wide range of physiological effects of the above hormones, as well as the concept of optimization that occurs in the main physiological systems with the increasing duration of residence in the north. Based on this, we defined the aim of the present research as the analysis of saliva and serum cortisol, assessment of the DHEA-S level in the blood as well as the f DHEA-S/cortisol ratio in the population of male northerners in reliance on belonging to a particular generation.

Materials and Methods. During the scientific monitoring program for northerners entitled "The Arctic. Man. Adaptation" which is being implemented with the "Arktika" Scientific Research Center, the Far Eastern Branch of the Russian Academy of Sciences (the city of Magadan), we have studied the main hypothalamic-pituitary-adrenal system's indicators in northern men, all being permanent residents of the Magadan Region, and assessed the variables based on different periods of subjective living under the north conditions. The total sample involved 70 men (mean age 40.0±0.8 years) with the following anthropometric indicators: body height – 180.7±0.9 cm, body mass 87.5±2.1 kg, body mass index – 26.8±0.6 kg/m^2. The examined subjects made up two subgroups based on their generation of living in the north (0 generation (n=15), 1st generation (n=35), 2nd and 3rd generations (n=20). Subjects' venous blood was taken with a vacuum system in the laboratory of Unilab-Khabarovsk LLC. Saliva cortisol (ng/ml) was evaluated twice (morning and evening) using the IFA method on the Muitiscan FS immune enzyme analyzer (reader). Dehydroepiandrosterone sulfate (DHEA-S) (ng/ml) and cortisol (nmol/L) in serum were determined by the IHA method using an automatic immunochemiluminescence analyzer of Mindray CL 6000i. The index for DHEA-S (mmol/l) / cortisol (nmol/l) was calculated from the obtained data [6]. The numerical values of the ratio reflect various stages of adaptation (< 1.1 – adaptive reserves are depleted; from 1.1 to 2.1 – adaptive reserves are consumed; > 2.1 – adaptive reserves are preserved). The research protocol was approved by the Local Ethics Committee of the Federal State Budgetary Institution of Science of the Scientific Research Center "Arktika" of the Far Eastern Branch of the Russian Academy of Sciences (conclusion No. 002/021 dated 11/26/2021). The study was performed in accordance with the principles of the Helsinki Declaration (2013). Prior to inclusion in the study, all participants provided their written informed consent. The criterion for inclusion in the study was absence of chronic diseases in the acute stage and complaints about the state of health. All subjects were permanent residents of the Magadan Region living in comparable conditions and having the same mode of physical activity. The following subjective items were monitored: morning activity, caffeine intake, and smoking – factors that can affect morning cortisol and DHEA-S levels. Blood sampling was performed on an empty stomach before 10 a.m. The subjects were instructed to avoid unusual physical activity or stress for 24 hours before the blood tests. Samples of the morning saliva cortisol were taken by the subjects immediately after awakening, the evening saliva cortisol – before going to bed, independently, according to the instructions. Hormone levels in all samples were measured simultaneously to avoid variability among tests.

Statistical data processing was carried out using the standard statistical software package StatSoft Statistica 7.0. Checking for the normality of the distribution of measured variables was carried out based on the Shapiro-Wilk test. The results of parametric processing methods are presented in the form of an average value (M) and an arithmetic mean error (±m). In multiple comparisons, parametric one-factor analysis of variance (ANOVA) was used. To identify statistically significant differences between specific groups, a posteriori analysis using the Scheffe test for multiple comparisons was applied. The critical significance level (p) in the work was assumed to be 0.05.

Results. Table 1 presents blood serum cortisol and DHEA-S levels, as well as their ratio depending on the generation of residence in the north. The data obtained show raised levels of serum cortisol with the increasing period of residence, from representatives of the 0th to the 2nd-3rd generations. We can see the average value of the indicators in each group significantly exceeded the upper reference limit typical for residents of the north who had no pathologies (314 nmol/l) [10]. The DHEA-S level assessment revealed optimal concentration of this indicator with its significant growth in the next generations of residence in the north. A similar picture could be seen in the ratio of DHEA-S/cortisol. Based on the classification criteria, men of the 0th generation demonstrated the stage of depletion of adaptive reserves whereas subjects of the 1st, 2nd, and 3rd generations tended to preserve the adaptive reserves.

We also analyzed the saliva cortisol levels shown in Table. 2 and found the multidirectional trends in its concentration at different times during the day. We noticed that the content of the morning saliva cortisol remained unchanged with the increasing length of residence in the north, with its average values significantly exceeding the upper reference typical for this indicator, whereas the evening saliva cortisol significantly reduced in the row from representatives of the 0th to the 2nd and 3rd generations with the approach to the normal range. It is worth mention-

Table 1

Concentration of serum cortisol, DHEA-S and DHEA-S/cortisol ratio depending on the generation of residence in the north

Indicator	Generation			Level of significance of differences		
	0	1	2-3	0-1	1-(2-3)	0-(2-3)
Cortisol, nmol/l	383.6±28.0	397.7±15.3	450.8±23.9	p=0.47	p=0.04	p<0.001
DHEA-S, mcg/dl	275.2±21.9	370±20.4	419.0±23.3	p<0.001	p=0.06	p<0.001
DHEA-S mmol/l	7.47±0.59	10.04±0.55	11.37±0.63	p<0.001	p=0.06	p<0.001
DHEA-S, mmol/l / Cortisol, nmol/l	1.80±0.11	2.37±0.14	2.59±0.18	p<0.001	p=0.17	p<0.001

ing that daily fluctuations in saliva cortisol levels that vary with the generation of residence in the north conditions show the preservation of daily biorhythmology.

Discussion. In our study, we observed high blood cortisol levels in northern residents with an increase in mean values from representatives of the 0th to the 2nd-3rd generations, which indicate the signs of hypercortisolism reported in earlier studies performed in the northern territories [8, 9, 5, 2.]. It is believed that such increased activation of hormones of the hypothalamic-pituitary-adrenal axis is part of adaptive adjustments to adverse northern conditions aimed at maintaining basal metabolic parameters to compensate for the cold factor [9]. In previous (the 90s of the twentieth century) assessment studies on hormonal status of those living in the north (the Magadan Region) [5], the authors also observed increased blood cortisol concentrations characteristic of new coming people with its significant fluctuations during the first 15 years of living in harsh conditions. Interestingly, no significant differences between migrants and the north born were revealed.

This research has presented cortisol levels that are significantly lower than those obtained earlier [5]: for example, the mean values of serum cortisol in new coming Magadan residents ranged from 489.9±18.8 to 604.8±25.0 nmol/l varying with periods of residence in the north (under 3 years, from 3 to 10 years and more than 10 years), which was significantly higher than in modern residents who migrated to the territory as the 0th generation. Similar differences were exhibited by the north born population of the last century in comparison with modern representatives of the 1st generation. As we studied modern residents of the Magadan Region, only representatives of the 2nd and 3rd generations demonstrated significantly high values of blood cortisol levels. Some authors consider cortisol as the hormone that preserves energy resources and ensures long-term reactions to stimuli of various etiologies [32]. Following on from that, we can see raised cortisol concentration with longer residence in the north as a normal reaction to acute stressors to maintain survival functions. [23, 32].

Table 2

Concentration of saliva cortisol depending on the generation of residence in the north

	Generation			Level of significance of differences		
	0	1	2-3	0-1	1-2	0-(2-3)
Morning	42.9±3.1	44.0±2.6	41.0±4.1	p=0.39	p=0.27	p=0.57
Evening	11.8±1.2	10.4±1.3	8.3±0.9	p=0.21	p=0.09	p<0.01

For the first time in the Magadan Region, the saliva cortisol level in men was suggested a predictor of the intensed functional reserves, and its daily biorhythmology was assessed as an informative factor on the imbalance which occurs in chronobiological rhythms owing to the specific light periodicity of our region. Saliva cortisol level has long been used as a marker of stress system activity and often assumed to quantify the effects of "biological stress" [20]. However, tracking cortisol daily curves – peak values 30 minutes after awakening and decreasing values to a nighttime minimum – is obviously more valuable than single-point levels, which is necessary to identify characteristics of the HPA function [15].

Currently, the fact that a daily cortisol level comes down by the evening time is considered as a fairly informative biomarker of inhibition of feedback in the HPA axis caused by cortisol, whereas its level upon awakening shows the sensitivity of adrenal receptors and their reactivity to the effects of adrenocorticotropic hormone (ACTH) [20]. The data in Table 2 confirm rather high mean values of the subjective morning saliva cortisol concentration through all the examined groups, which prove to not change in any reliance on a generation of residence in the north, thereby demonstrating the link to the increasing sensitivity of adrenal receptors.

Circadian fluctuations in cortisol, usually measured as the difference between the cortisol level at awakening and before bedtime, as well as cortisol reactivity to stress factors, are associated with the body health condition [11]. The smaller the difference between morning-evening cortisol levels, the worse the physical and mental health indicators [18]. The lowest variables of the difference were exhibited by the 0th generation men.

On the whole, the comparison study on the morning and evening saliva cortisol indicated that each examined group (0th, 1st, 2nd and 3rd generations) kept the circadian rhythm staying unchanged, despite the cortisol hypersecretion in the morning saliva test. The smallest cortisol levels in the evening sample were typical for men of the 2nd and 3rd generations, thereby showing an optimization of sensitivity to inhibition of the feedback of the HPA axis in men characterized by the longest residing experience in the northern conditions. The HPA axis performing activity is known to aim at relieving the adaptation of behavior over time, using past experience to prepare for expected challenges by changing system control points, shifting regulatory control and programming behavioral tendencies [25], as well as keeping hormonal levels within the safe limits by suppressing feedback [31, 24], which conforms with the evening cortisol test results in the examined men of the 2nd and 3rd generations.

It is believed that the universal mechanism of adaptation is the switching of steroidogenesis in the adrenal glands from the production of glucocorticoids to the secretion of androgens, in particular, DHEA-S [4] in order to provide a functional balance of catabolic and anabolic vectors of exchange; they are the stages of adaptive response [3]. The anti-stress mechanisms of DHEA-S include changes

in the metabolism of cortisol to its inactive metabolite cortisone, the resulting ratio of which redistributes energy and restores homeostasis [22]. In this research, the DHEA-S secretion tended to grow up in the increasing reliance on the period of the north residence, from the 0th to the 2nd and 3rd generations, which was probably a response to the raised blood cortisol concentration depending on the generation.

DHEA-S and cortisol have different and often antagonistic effects on each other [13] since these two hormones jointly regulate each other and their joint increase or imbalance determine the total effect on tissues; therefore the DHEA-S/cortisol ratio must be given emphasis in addition to absolute concentrations of both steroids [27]. The emphasis necessity is also backed up by the concept of anabolic balance which takes into account the ratio of anabolic and catabolic hormones and may indicate a susceptibility to diseases associated with stress and aging [13]. Nowadays, the ratio of the sulfated metabolite of DHEA and cortisol is used as an indicator of catabolic/anabolic balance [33]. High values of the ratio suggest an optimal anabolic balance, whereas low values are associated with chronic stress and declining health [33], with mortality [16, dementia [12], metabolic syndrome [16], and decrease in immunity after physical stress [30].

It is worth emphasizing the ratio of cortisol-DHEA as a key marker of human resistance to stress, because for adequate protection against stress, DHEA that works as a protector for the central nervous system must always prevail over cortisol which has a destructive effect on the hippocampus [22]. Calculation and interpretation of the DHEA-S/cortisol index based on the levels of the two antagonist hormones in the blood serum varying with the length of of residence in the north, have revealed that the 0th generation experience tension in the hypothalamus-pituitary-adrenal glands system, and the value of this index shows the expenditure of adaptive reserves whereas the 1st and 2nd-3rd generations exhibit the optimization of this system and keep their adaptive reserves.

Conclusion. Serum cortisol and dehydroepiandrosterone sulfate, their ratio, as well as evening saliva cortisol test have proved to be significant markers that reflect readjustments in a person's endocrine profile with the increasing length of residence in the north, which confirms the generally approved role of glucocorticoids in human adaptation to severe factors including climate extremes. This study has found pronounced tendency of activation of the hypothalamic-pituitary-adrenal axis in northern men who develop excessive cortisol production, report high mean values of DHEA-S and the ratio of DHEA-S/cortisol growing with the next generations of residence in the north. The numerical values of the DHEA-S/cortisol ratio indicate the stage of depletion of adaptive reserves experienced by male subjects of the 0th generation whereas representatives of the 1st, 2nd and 3rd generations tend to keep their adaptive reserves. In the process of adaptation to continuously unfavourable factors of the north, the cortisol hyper production promotes increased catabolic reactions that grow more intense with longer periods of adaptation. At the same time, powerful restorative anabolic processes are activated owing to the driving effect of DHEA-S in the population of northern men. This phenomenon requires further research for better understanding. It is worthy of note that the values of the DHEA-S/cortisol ratio growing from the representatives of the 0th generation to residents with longer residing experience in the north agree with the early identified optimization in physiological performance showing a strong link to the next generations, which allows us to consider the DHEA-S/cortisol indicator as a new criterion for the degree of adaptability.

For the first time, the assessment study on morning and evening saliva cortisol levels has been conducted in northern residents. Despite the morning cortisol hypersecretion, the subjective circadian rhythm in each examined group remained unchanged, which was observed along with a significant fall in the evening cortisol level in men of the 2nd and 3rd generations. That was caused by the pronounced sensitivity of adrenal receptors in the entire population and the changes for optimization of sensitivity to inhibiting the feedback of the HPA axis in men who experienced the longest residing in the north conditions.

Thus, adaptive adjustments to the living conditions of the north develop with the activation of the pituitary-adrenal cortex system and vary with the generation depending on the duration of residence in harsh climate conditions and weather extremes.

We have considered all other equal things and concluded that analysis of the DHEA-S/cortisol ratio indicator can be valuable since its variables identify specific adaptation readjustments that northerners report in the increasing reliance on their duration of residence in severe climatic and natural conditions. In general, this ratio serves as a marker of the degree of adaptation, as well as a highly informative criterion when selecting volunteers to work in extreme living conditions in the Arctic regions.

References

1. Averyanova IV, Maksimov AL Strategija adaptivnyh perestroek funkcional'nyh sistem ukorenjonnyh evropeoidov – urozhencev razlichnyh pokolenij Severo-Vostoka Rossii [Adaptation of functional systems in different generations of Caucasians in the North-East of Russia]. Ekologiya cheloveka [Human Ecology. 2023;30(4): 259-273. DOI: https://doi.org/10.17816/humeco321856 (In Russ.).]

2. Volkova NI, Bichkaeva FA. Analiz soderzhanija kortizola i gljukozy v syvorotke krovi u zhitelej arkticheskogo i priarkticheskogo regionov Severa zrelogo vozrasta [Analysis of the blood serum content of adult Arctic and Arctic North]. V sbornike: Global'nye problemy Arktiki i Antarktiki. Sbornik nauchnyh materialov Vserossijskoj konferencii s mezhdunarodnym uchastiem, posvjashhennoj 90-letiju so dnja rozhdenija akad. Nikolaja Pavlovicha Lavjorova [In the collection: Global Problems of the Arctic and Antarctic. Collection of scientific materials of All-Russia conference with international participation, dedicated to the 90th anniversary of academician Nikolay Pavlovich Laverov. 2020; 956–961 (In Russ.).]

3. Goncharov NP, Katsiya GV Degidrojepiandrosteron: biosintez, metabolizm, biologicheskoe dejstvie i klinicheskoe primenenie (analiticheskij obzor) [Dehydroepiandrosterone biosynthesis, metabolism, biological effects, and clinical use (analytical review). Andrologija i genital'naja hirurgija [Andrology and Genital Surgery. 2015;16(1): 13–22 (In Russ.).] doi: 10.17650/2070-9781-2015-1-13-22.

4. Zaychik ASh, Churilov LP Obshhaja patofiziologija (s osnovami immunopatologii): Patofiziologija. V 3-h tomah [General pathophysiology (with the basics of immunopathology): Pathophysiology. In 3 volumes. Ed. 4th. SPb: JeLBI-SPb. 2008 (In Russ.).]

5. Maksimov AL, Bartosh TP Invarianty normy gormonal'nogo statusa cheloveka na Severo-Vostoke Rossii: nauchn.-prakt. Rekomendacii [Invarianty normy gormonal'nogo statusa cheloveka na Severo-Vostoke Rossii: nauchn.-prakt. Rekomendacii. Magadan: SVNC DVO RAN, 1995. (In Russ.).]

6. Aleksanin SS, et al. Ocenka adaptacionnyh rezervov organizma muzhchin: teoreticheskie osnovy, tehnologija: metodicheskie im. A.M. Nikiforova MChS Rossii Variations of the norm of human hormonal status in the North-East of Russia: scientific –practical recommendations]. SPb.: IPC Izmajlovsky, 2022; 19 (In Russ.).]

7. Pirogov AB Nejrojendokrinnaja organizacija adaptacii zhitelej Severo-Vostoka Rossii [Neuroendocrine structure of adaptation of Russian north-eastern population] Bûlleten' fiziologii i patologii dyhaniâ [Bulletin of physiology and pathology of respiration] 1998;1:14-27. (In Russ.).]

8. Dogadin SA, et al. Soderzhanie insulina, S-peptida i kortizola v dinamike testa tolerantnosti k gljukoze u korennyh i prishlyh zhitelej Krajnego Severa [Levels of insulin, C-peptide, and hydrocortisone in the course of glucose tolerance test in indigenous population of the Extreme North and in newcomers]. Problemy jendokrinologii [Problems of Endocrinology]. 1997;43(2):7–10 (In Russ.).]

9. Hasnulin VI. Osobennosti psihojemocional'nogo stressa u zhitelej regionov severa i Sibiri s diskomfortnym klimatom pri vysokom i nizkom soderzhanii gormonov stressa v krovi [Features of emotional stress in the residents of the north and siberian regions with discomfortable climate at high or low content of hormones in the blood]. Mir nauki, kul'tury, obrazovanija [The world of science, culture, and education. 2012;5(36): 32–35 (In Russ.).]

10. Hasnulin VI, Hasnulin PV. Sovremennye predstavlenija o mehanizmah formirovanija severnogo stressa u cheloveka v vysokih shirotah [Modern concepts of the mechanisms forming northern stress in humans in high latitudes]. Jekologija cheloveka [Human ecology]. 2012;1:3–11 (In Russ.).]

11. Adam EK, Kumari M Assessing salivary cortisol in large-scale, epidemiological research. Psychoneuroendocrinology. 2009;34:1423-1436. DOI: 10.1016/j.psyneuen.2009.06.011

12. Ferrari E, et al. Age-related changes of the hypothalamic-pituitary-adrenal axis: pathophysiological correlates. Eur J Endocrinol. 2001;144(4):319–329. DOI:10.1530/eje.0.1440319

13. Aldwin CM, Park CL, Spior. A Handbook of Health Psychology and Aging, Guilford Publications, Inc, New York. 2007: 119-141 DOI:10.1348/000712607X246

14. Ghiciuc CM, et al. Awakening responses and diurnal fluctuations of salivary cortisol, DHEA-S and α-amylase in healthy male subjects. Neuroendocrinol Lett. 2011; 32(4): 475–480.

15. Stalder T, et al. Clow Assessment of the cortisol awakening response: expert consensus guidelines. Psychoneuroendocrinology. 2016;63:414-432. DOI: 10.1016/j.psyneuen.2015.10.010

16. Phillips AC, et al. Cortisol, DHEA sulphate, their ratio, and all-cause and cause-specific mortality in the Vietnam Experience Study. Eur J Endocrinol. 2010;163(2):285–292. DOI: 10.1530/EJE-10-0299

17. de Bruijn R, Romero LM. The role of glucocorticoids in the vertebrate response to weather. General and Comparative Endocrinology. 2018;269:11-32, https://doi.org/10.1016/j.ygcen.2018.07.007.

18. Adam EK, et al. Diurnal cortisol slopes and mental and physical health outcomes: a systematic review and meta-analysis. Psychoneuroendocrinology. 2017;83: 25-41. DOI: 10.1016/j.psyneuen.2017.05.018

19. Wilcox RR, et al. Diurnal patterns and associations among salivary cortisol, DHEA and alpha-amylase in older adults. Physiology & Behavior. 2014;129:11-16, https://doi.org/10.1016/j.physbeh.2014.02.012.

20. Abelson JL, et al. Do diurnal salivary cortisol curves carry meaningful information about the regulatory biology of the HPA axis in healthy humans? Psychoneuroendocrinology. 2023;150. https://doi.org/10.1016/j.psyneuen.2023.106031.

21. Homberger B, Jenni-Eiermann S, Jenni L Distinct responses of baseline and stress-induced corticosterone levels to genetic and environmental factors. General and Comparative Endocrinology. 2015;210: 46-54. https://doi.org/10.1016/j.ygcen.2014.09.020.

22. Kamin HS, Kertes DA Cortisol and DHEA in development and psychopathology. Horm. Behav. 2017;89: 69–85. doi: 10.1016/ j.yhbeh.2016.11.018.

23. King SL, Hegadoren KM Stress hormones: how do they measure up? Biol Res Nurs 2002;4: 92–103.

24. McEwen BS. Protective and damaging effects of stress mediators. N. Engl. J. Med. 1998;338:171-179. DOI:10.1056/NEJM199801153380307

25. McEwen BS, Akil H. Revisiting the stress concept: implications for affective disorders. J. Neurosci. 2020;40:12-21. DOI:10.1523/JNEUROSCI.0733-19.2019

26. Møller N, Jørgensen JOL. Effects of growth hormone on glucose, lipid, and protein metabolism in human subjects. Endocr Rev. 2009;30:152-177. DOI:10.1210/ er.2008-0027

27. Maninger N, et al. Neurobiological and neuropsychiatric effects of dehydroepiandrosterone (DHEA) and DHEA sulfate (DHEAS). Frontiers in Neuroendocrinology. 2009;30(1): 65-91. https://doi.org/10.1016/j.yfrne.2008.11.002.

28. Obayashi K. Salivary mental stress proteins. Clin Chim Acta. 2013;425:196–201. doi: 10.1016/j.cca.2013.07.028

29. Oyola MG, Handa RJ. Hypothalamic–pituitary–adrenal and hypothalamic–pituitary–gonadal axes: sex differences in regulation of stress responsivity. The International Journal on the Biology of Stress. 2017;20: 1-19. DOI:10.1080/10253890.2017.1369523

30. Butcher SK, et al. Raised cortisol:DHEAS ratios in the elderly after injury: potential impact upon neutrophil function and immunity. Aging Cell. 2005;4(6):319–324. DOI:10.1111/j.1474-9726.2005.00178.x

31. Herman JP, et al. Regulation of the hypothalamic-pituitary-adrenocortical stress response. Compr. Physiol. 2016;6:603-621. DOI:10.1002/cphy.c150015

32. Sapolsky RM, Romero LM, Munck AU. How do glucocorticoids influence stress-responses? Integrating permissive, suppressive, stimulatory, and preparative actions. Endocrinol. Rev. 2000;21:55-89. DOI:10.1210/edrv.21.1.0389

33. Wolkowitz OM, Epel ES, Reus VI. Stress hormone-related psychopathology: pathophysiological and treatment implications. World J. Biol. Psychiatry. 2001;2:115-143. 10.3109/15622970109026799

SCIENTIFIC REVIEWS

M.Yu. Kislitsyna, A.V. Mikhailenko, E.G. Gavrilova

ACUTE ENDOTHELIAL CELL INJURY IN CARDIAC SURGERY PATIENTS UNDER ARTIFICIAL BLOOD CIRCULATION: THE CURRENT STATE OF THE PROBLEM

DOI 10.25789/YMJ.2024.87.21

UDC:53.7

KISLITSYNA Marina Yu. – student of I.P. Pavlov St. Petersburg First State Medical University; e-mail: kislitsynamari0412@yandex.ru; **MIKHAILENKO Anna V.** – student of I.P. Pavlov St. Petersburg First State Medical University, e-mail: annamikhailenko94@gmail.com; **GAVRILOVA Elena G.** – MD, PhD in Medicine, Associate Professor of Anesthesiology and Intensive Care Department, Head of Anesthesiology and Intensive Care Department No. 2 of the Research Clinical Center of Anesthesiology and Intensive Care, Head of Intensive Care Department of the COVID Treatment Medical Center, E-mail: egavrilova70@mail.ru

This study summarizes the existing literature data on endothelial damage and its etiology, pathophysiology, and diagnosis in patients undergoing cardiac surgery with cardiopulmonary bypass (CPB). Data on endothelial dysfunction and the history of its study were obtained from various medical databases, including PubMed, Cochrane, Elibrary, and Cyberleninka. We suggest that endothelial injury that occurs during and after the surgery predicts poor clinical outcomes, and should therefore be considered by anesthesiologists, intensivists, cardiac surgeons, and transfusion medicine specialists.

Keywords: endothelium, endothelial dysfunction, cardiopulmonary bypass (CPB), endothelial glycocalyx (eGCX).

Introduction. Numerous studies conducted in recent decades have demonstrated the crucial role of endothelium in physiological and pathological processes in the body. The endothelium constantly counteracts the effects of damaging factors and produces multiple biologically active substances thus preventing negative impacts of these factors on the vascular wall and regulating its functions.