V.M. Nikolaev, S.I. Sofronova, L.D. Olesova, S.D. Efremova, A.S. Gol'derova, F.V. Vinokurova, E.D. Ohlopkova, L.I. Konstantinova, A.I. Yakovleva, A.V. Efremova, E.K. Rumyancev, K.M. Stepanov, A.A. Grigor'eva, N.K. Chirikova, A.S. Popova, S.A. Fedorova

INDICATORS OF LIPID PEROXIDATION OF NON-NATIVE RESIDENTS OF THE REPUBLIC SAKHA (YAKUTIA)

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In the article lipid peroxidation of native people and non-natives in Yakutia was compared. The obtained data clearly indicate existence of lengthening of the adaptation phase under modern socio-economic conditions of life of the population of Yakutia compared to similar studies of the several decades before. It is likely that adaptation to the harsh conditions of the North is associated with the activation of an antioxidant-responsive element that induces the expression of proteins responsible for maintaining internal homeostasis.

Materials and methods. Samples of blood were collected in biomedical expeditions during simultaneous examination of the population of Yakutia in the spring. 357 people were examined.

The intensity of free radical lipid oxidation was determined by the content of TBARS, the antioxidant defense was determined by the total content of low molecular weight antioxidants in serum, also ascorbic acid and catalase activity were studied. The activity of alanine aminotransferase and aspartate aminotransferase enzymes was studied.

Results. The level of TBARS and indicators of antioxidant protection (LWMAO, ascorbic acid and catalase) of people who moved to reside to studied area were higher, compared to indigenous people. There is an increase in the level of TBARS, catalase activity, AST / ALT coefficient in the first 5 years after relocation to Yakutia from other regions. The stabilization period of the biochemical parameters occurred in the period from 5 to 10 years.

Conclusion. Obtained data indicate a lengthening of the adaptation phase in modern socio-economic conditions of life of the population of Yakutia in comparison with scientific studies of previous years. It is likely that adaptation to the harsh conditions of the North is associated with the activation of an antioxidant-responsive element, which increases the expression of proteins responsible for maintaining internal homeostasis.

Keywords: adaptation, TBA-active products, TBARS, total content of low molecular weight antioxidants, ascorbic acid, catalase, Nrf2, antioxidant-responsive element.

Introduction. The modern geopolitical strategy of the state is aimed to develop Northern regions of the country, therefore one of the most important tasks of medical science at the present time is to help to maintain health and working capacity of the population living under extreme conditions of the North. In this regard, close attention is paid to research and activities aimed at shaping the quality of life of the population in the context of globalization and increasing population mobility.

As an integral criterion of health, the adaptive capabilities of organism, which reflect the degree of its dynamic equilibrium with the environment, are increasingly being considered. Adaptation is directly related to the background, which ultimately determines the risk of developing diseases, and therefore the level of health. Consequently, the approach to quantifying the adaptive capabilities of people can be a key point on which the gradual assessment of health depends.

The Republic Sakha (Yakutia), with its inherent set of climatic and geographical conditions, belongs to the regions of the Far North, which defines the impact of a number of adverse health factors of residing people.

According to the results of previous decades studies, it was found that the populations of the Northern people, living for thousands of years in the North, were formed by natural selection as a result of centuries of evolution [18]. They have developed a number of adaptations, that are genetically fixed and accordingly inherited. However, recent decades have been characterized by socio-economic transformations, urbanization of the indigenous population and change of the traditional way of life, all of which affect their health [13, 21].

Currently, study of nonspecific reactions of human organism that underlie adaptive-compensatory mechanisms in healthy people, such as changes in pro-oxidant-antioxidant balance, is of great interest [17].

The **objective** of the research was to study the indicators of lipid peroxidation of non-native residents depending on the duration of their residence in the Republic Sakha (Yakutia).

Material and methods of the research

This work was carried out at the Yakut Science Centre of Complex Medical Problems in Research: "Regional features of normal and pathological biochemical and immunological indicators in the indigenous and non-indigenous population of the Republic of Sakha (Yakutia)".

Samples of blood were collected in biomedical expeditions in the course of a cross-sectional study of the population of Yakutia in spring. 357 people between the ages of 18 and 77 were examined, including 253 native and 102 non-native residents. The native inhabitants in this work are people who were born and permanently reside in the territory of Yakutia, and non-native residents are people who, for one reason or another, came to Yakutia for permanent residence from other regions of Central Russia and living in Yakutia for at least a year. The ethnicity of the residents of both groups was heterogeneous and not taken into account.

Serum was used for all analysis. The intensity of free radical lipid peroxidation was determined by the contents of TBA-reactive substances (TBARS) [20], indicators of antioxidant protection of people were determined by the total content of low molecular weight antioxidants (LMWAO) [8], ascorbic acid level [16], catalase activity (CAT) [5] using the SPECORD 40 "AnalytikJena" (Germany) spectrophotometer. Transaminase activity: alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were determined on a "Labio" automated

biochemical analyzer using "Analyticon" reagents (Germany). The level of interleukin-6 (IL6) and interleukin-18 (IL18) cytokines was assessed on a "Multiscan" analyzer (USA) using the enzyme-linked immunosorbent assay utilizing "Vector-Best" CJSC (Russia) kits.

Statistical analysis of data was made using IBM SPSS Statistics. The significance of differences between the medians was evaluated using the Mann-Whitney U test. The data in the tables are presented as M±m, where M is the mean, m is the error of the mean. The differences were considered statistically significant at p <0,05.

Results and discussion. Indicators of lipid peroxidation in the population of the Republic of Sakha (Yakutia) were as follows: the TBARS level was equal to 3,572±0,122 μMol/l, the total content of LMWAO was 91,471±1,956 nmol/l, the activity of the antioxidant enzyme CAT was 0,490±0,010 μKat/l, the concentration of ascorbic acid was 0.255 ± 0.009 mg/dl (Table 1).

There is a strong opinion that the indigenous population of the Far North evolutionally adapted under extreme factors conditions, and people have formed a certain lifestyle that can inhibit reactions of lipid peroxidation [4, 9, 10]. The above statement is confirmed in our work. The level of end products of lipid peroxidation - TBARS and indicators of antioxidant protection (LMWAO, vitamin C and CAT) of non-indigenous people were higher compared to indigenous people (Table 2).

The staged nature of adaptation processes was described in study of researchers led by V. Yu. Kulikov et al. (16) and V.P. Kaznacheev (3). The first phase lasts on average up to six months and is characterized by destabilization of many physiological parameters. The second phase comes in 3-4 years. During this period, the normalization and synchronization of vegetative and somatic functions takes place in the conditions of physiological rest and moderate physical and psycho-emotional stress. After 8 - 10 years, the body's condition is relatively stabilized.

Data on the terms of adaptation of the non-native population in the 90s in Yakutia are given in the paper by A.S. Popova [7]. Comparison of physiological parameters was studied by dynamics of glucose and cholesterol in blood of non-native and native Yakutians. In this work, three phases of adaptation were distinguished among non-native residents. In the residing period up to 5 years, the level of cholesterol in blood was higher than that of native people (p <0.05). After 5 years of living in the North, content of these indicators decreased, after 10 years of living it increased. Thus, the first phase of adaptation took place before 5 years, the second phase - in the interval of 5-10 years, and the third after residing for more than 10 years [7].

In our study, we noted the intensification of free radical peroxidation of lipids of non-native residents for 5 years. Moreover, the peak increase of the level of the final product of lipid peroxidation occurred in the period of 2 to 5 years, as evidenced by the high content of TBARS (1.47 times (p=0.02) above the average value). At the same time, an increase in exogenous antioxidant - ascorbic acid, was observed. The concentration of ascorbic acid was 1.69 times higher than the average value (p = 0.01). At the same time, the total content of LMWAO and the activity of catalase did not change.

Subsequently, with an increase in the time spent in the North, the levels of TBARS and the antioxidant defense indices shifted to values close to the average biochemical indices of indigenous people (Table 2).

According to the concept of stress-limiting systems founded in the 1980s by F.Z. Meerson [6] a general stress response leads to the formation of an organism short-term adaptation, which, in turn, acts as a basis for a long-term adaptation formation. Moreover, the initiators of lipid peroxidation, reactive oxygen species, are linked to the development of short-term and long-term adaptation [1]. Long-term adaptation occurs gradually, as a result of prolonged or repeated action of environmental factors on the organism. It arises not on the basis of pre-existing physiological mechanisms, but on newly formed regulatory programs.

Modern data support the concept of stress-limiting systems, clarifying the mechanisms of regulatory processes controlled by reactive oxygen species [23]. The mechanisms for protecting human from the negative effects of extreme factors of the North depend on the expression of transcription factors that are responsible for the functional state of protective systems [2]. Exposure to extreme factors can activate the redox-sensitive signaling system of the antioxidant-responsive element Keap1/Nrf2/ARE, which includes the transcription factor Nrf2, which is constantly monitored by the Keap1 repressor protein [2, 14]. Nrf2 regulates the expression of many protective

Table 1

Indicators of lipid peroxidation of indigenous and non-indigenous people of the Republic of Sakha (Yakutia)

Indicators	native	M+m	P
TBARS (nmol/l)	non-native residents	3.089±0.153	0.551
	native	3.920±0.213	
LMWAO (mEq/mg)	non-native residents	90.090±2.288	0.032
	native	101.94±3.886	
CAT (μKat/l)	non-native residents	0.444±0.018	0.551
	native	0.496±0.032	
Ascorbic acid (mg/dl)	non-native residents	0.151±0.013	0.151
	Приезжие	0.246±0.025	

Table 2

Indicators of lipid peroxidation of non-indigenous people of the Republic of Sakha (Yakutia) depending on the duration of residence

Duration of residence in the Republic of Sakha (Yakutia)	TBARS (nmol/l)	LMWAO (mEq/mg)	CAT (μKat/l)	Ascorbic acid (mg/dl)
less than 2 years	4.28±0.75	83.29±2.16	0.55±0.07	0.43±0.11
from 2 to 5 years	5.78±0.98	87.82±4.18	0.52±0.06	0.41±0.11
from 5 to 10 years	3.75±0.77	100.00±8.56	0.50±0.03	0.13±0.04
from 10 to 20 years	3.86±0.41	103.10±1.00	0.47±0.05	0.23±0.05
20 and more years	3.57±0.28	99.22±0.40	0.53±0.06	0.29±0.03
P	p_{1-5}=0.05 p_{2-5}=0.04	-	p_{2-4}=0.04	p_{1-3}=0.03 p_{3-5}=0.04

Table 3

Serum activity of alanine aminotransferase and aspartate aminotransferase levels among residents of Yakutia

Indicators		ALT (U/l)	AST (U/l)	AST/ALT ratio
Duration of residence in the Republic of Sakha (Yakutia)	less than 2 years	17.85±1.47	26.78±1.90	1.54±0.08
	from 2 to 5 years	15.65±1.03	25.13±1.58	1.65±0.06
	from 5 to 10 years	18.05±1.95	26.64±2.14	1.53±0.04
	from 10 to 20 years	20.75±2.46	27.93±2.44	1.38±0.08
	20 and more years	18.21±1.14	23.26±0.90	1.27±0.11
	Native	19.08±0.51	25.52±0.42	1.36±0.02
p		-	-	p_{1-5}=0.03 p_{2-5}=0.04 p_{2-6}=0.05 p_{3-5}=0.03

systems genes: antioxidant and immune defenses [24], detoxification of xenobiotics [24], molecules controlling DNA repair [15]. According to scarce publications other Nrf2 functions were mentioned as: the effect on ATP production and cellular respiration; removal of damaged or improperly folded proteins by regulating the expression of proteasomes; regulation of NADPH content in the cell by activation of transcription factor-4 (ATF4), which stimulates the expression of phosphoglycerate dehydrogenase; affects the transcriptional vibrations of circadian genes in human cells and mouse tissues, etc. [22].

According to published data, the intensification of free radical processes activates the redox-sensitive signaling system of the antioxidant-responsive element [26]. Reactive oxygen species and lipid peroxidation metabolites are capable of modifying the sensitive thiol groups of Kear1 protein, which hinders its ability to inhibit the transcription factor Nrf2 of the antioxidant-responsive element [19].

In addition, there is evidence that reactive oxygen species and lipid peroxidation products are capable of activating other redox-sensitive transcription factors NF-kB (nuclear factor kappa-light-chain-enhancerofactivated B cells), AP-1 (Activator protein 1) and P53 [22].

Our results have confirmed those defined in the literature. We noted an increase in the coefficient showing the AST/ALT ratio (de Ritis ratio) indicating the predominance of anabolic processes over catabolic of non-native residents in the first 5 years of their stay in Yakutia. The optimal ratio of kata and anabolic processes of non-native residents is established in the period from 5 to 10 years. Moreover, the de Ritis coefficient has a positive correlation r = 0.32 (p = 0.03) with the content of TBARS, which, in our opinion, is evidence of the influence of the antioxidant-responsive element on the adaptation of non-native residents to the extreme conditions of Yakutia.

Thus, the level of TBARS and indicators of antioxidant protection (NMAO, ascorbic acid and catalase) of non-native residents were higher compared to native people. There is an increase in the level of TBA-AP, catalase activity, AST / ALT coefficient in the first 5 years of people after relocation. The stabilization period of the biochemical parameters occurred in the period from 5 to 10 years. The results indicate lengthening of the adaptation phase in modern socio-economic conditions of life of the population of Yakutia in comparison with scientific studies of previous years. It is likely that adaptation to the harsh conditions of the North is associated with the activation of an antioxidant-responsive element, which increases the expression of proteins responsible for maintaining internal homeostasis.

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Yakutsk, Russian Federation: **NIKOLAEV Vyacheslav Mikhailovich** – candidate of biological sciences, chief researcher - head of the department for studying adaptation mechanisms, Yakut Science Center of Complex Medical Problems (YSC CMP), Nikolaev1126@mail.ru. **SOFRONOVA Sargylana Ivanovna** – candidate of medical sciences, chief researcher - head of the Science-organizational and information-publishing department, Yakut Science Center of Complex Medical Problems (YSC CMP), sara2208@mail.ru. **OLESOVA Lyubov Dygynovna** – Candidate of Biological Sciences, Leading Researcher, Yakut Science Center of Complex Medical Problems (YSC CMP), oles59@mail.ru. **EFREMOVA Svetlana Dmitrievn**a – Junior Researcher, Yakut Science Center of Complex Medical Problems (YSC CMP), esd64@mail.ru. **GOLDEROVA Aitalina Semenovna** – Doctor of Medical Sciences, Professor of the Department of Public Health and Health Care, General Hygiene and Bioethics of the Medical Institute of the North-Eastern Federal University named after M.K. Ammosov, hoto68@mail.ru. **VINOKUROVA Fekla Vasilievna** – Researcher, Yakut Science Center of Complex Medical Problems (YSC CMP), pfv@mail.ru. **OKHLOPKOVA Elena Dmitrievna** – candidate of biological sciences, leading researcher, Yakut Science Center of Complex Medical Problems (YSC CMP), elena_ohlopkova@mail.ru. **KONSTANTINOVA Lena Ivanovna** – Researcher, Yakut Science Center of Complex Medical Problems (YSC CMP), konstanta.l@mail.ru. **YAKOVLEVA Alexandra Ivanovna** – Researcher, Yakut Science Center of Complex Medical Problems (YSC CMP), sashyak@mail.ru. **EFREMOVA Agrafena Vladimirovna** – PhD in Biology, PhD, Senior Researcher, Yakut Science Center of Complex Medical Problems (YSC CMP), a.efremova@mail.ru. **RUMYANTSEV Egor Konstantinovich** – Junior Researcher, Yakut Science Center of Complex Medical Problems (YSC CMP), tzeentch1993@mail.ru. **STEPANOV Konstantin Maksimovich** – Doctor of Agricultural Sciences, Senior Researcher, Yakut Science Center of Complex Medical Problems (YSC CMP), stenko07@mail.ru. **GRIGORYEVA Anastasia Anatolyevna** – Researcher, Yakut Science Center of Complex Medical Problems (YSC CMP), nastiagrigoryeva@gmail.com. **CHIRIKOVA Nadezhda Konstantinovna** – Doctor of Pharmaceutical Sciences, Leading Researcher at the Institute of Natural Sciences of the North-Eastern Federal University named after M.K. Ammosov, hofnung@mail.ru. **POPOVA Alexandra Semenovna** – PhD, Senior Researcher at the Institute of Natural Sciences of the North-Eastern Federal University named after M.K. Ammosov, alexandra.s.popova@gmail.com. **FEDOROVA Sardana Arkadevna** – Doctor of Biological Sciences, leading researcher at the Institute of Natural Sciences of the North-Eastern Federal University named after M.K. Ammosov, sardaanafedorova@mail.ru.