

G.P. Evseeva, O.A. Lebedko, S.V. Suprun, E.I. Yakovlev,
N.I. Kuderova, E.V. Knizhnikova, R.S. Telepneva, T.V. Pivkina

ESTIMATION OF THE MITOCHONDRIA MEMBRANE POTENTIAL OF GRANULOCYTES IN CHILDREN WITH CHRONIC INFLAMMATORY DISEASES OF THE LUNGS

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EVSEEVA Galina Petrovna – doctor of Medical sciences, Professor, D.Sc. (Med.), Deputy Director on Scientific Work, Main Staff Scientist of the Group of Health and Environmental Problems of Mother and Child Health, Khabarovsk Branch of Far Eastern Scientific Center of Physiology and Pathology of Respiration – Research Institute of Maternity and Childhood Protection; e-mail: evceewa@yandex.ru. ORCID: 0000-0002-8076-3555, **LEBEDKO Olga Antonovna** – doctor of Medical sciences, Professor, D.Sc. (Med.), Director of the Khabarovsk Branch of Far-Eastern Scientific Center of Physiology and Pathology of Respiration – Research Institute of Maternity and Childhood Protection; e-mail: iomid@yandex.ru. ORCID: 0000-0002-8855-7422, **SUPRUN Stefaniya Viktorovna** – doctor of Medical sciences, Professor, D.Sc. (Med.), Main Staff Scientist of the Group of Health and Environmental Problems of Mother and Child Health, Khabarovsk Branch of Far Eastern Scientific Center of Physiology and Pathology of Respiration – Research Institute of Maternity and Childhood Protection; e-mail: iomid@yandex.ru. ORCID: 0000-0001-6724-3654, **YAKOVLEV Evgenii Igorevich** – junior researcher of the group of medical and environmental problems of mother and child health; eyakovlev1993@gmail.com. ORCID: 0000-0002-2427-8141, **KUDEROVA Natalia Ivanovna** – research associate of the group of clinical immunology and endocrinology Khabarovsk Branch of Far Eastern Scientific Center of Physiology and Pathology of Respiration – Research Institute of Maternity and Childhood Protection. E-mail: nataliya_kuderova@bk.ru. ORCID: 0000-0002-4225-3247, **KNIZHNIKOVA Elena Vladimirovna** – researcher of the Molecular Genetic Diagnostics Group, Khabarovsk Branch of Far Eastern Scientific Center of Physiology and Pathology of Respiration – Research Institute of Maternity and Childhood Protection. E-mail: 1904lenok@mail.ru. ORCID: 0000-0003-0377-4805, **TELEPNEVA Regina Sergeevna** – postgraduate student of the Institute of Maternity and Childhood Protection. E-mail: pupykin84@mail.ru. ORCID: 0000-0003-2873-2353, **PIVKINA Tatyana Vladimirovna** – Researcher of Group of health and environmental problems of mother and child health.

The article presents a study of the features of the mitochondrial membrane potential (MPM) of granulocytes in 72 children with congenital lung malformations (CLM). There was a 5-fold increase in the proportion of cells with reduced granulocyte MPM($\Delta\Psi_m$) compared to the control group. During periods of exacerbation of the disease, the number of granulocytes with reduced potential increased by 8 times. This was accompanied by an increase in luminol- and lucigenin-dependent chemiluminescence of whole blood phagocytes spontaneous, a significant decrease in the I-lum and I-luc stimulation indices by 30 and 25%. Negative dynamics of the stimulation index indicates the depletion of reserve capabilities of the phagocytic system in children of the study group. There are statistically significant direct correlations between the level of granulocytes with reduced MPM($\Delta\Psi_m$) and indicators of phagocytic activity of leukocytes.

Key words: children, congenital malformations of the lungs, neutrophilic granulocytes, mitochondrial membrane potential, oxidative metabolism of granulocytes, phagocytic activity.

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Introduction. The pathogenesis of most chronic non-specific lung diseases (CNSLD) is based on a long-term inflammatory process that forms in the structurally altered tissue of the lungs and bronchi due to congenital malformations of the lungs (CLM). One of the key positions in the immune response belongs to phagocytosis, which today is considered not only as a tool of anti-infection immunity, but also as a universal homeostasis effector that responds to numerous signals about destabilization of the internal environment of the body [5]. The constancy of immune homeostasis as a whole depends on the adequate implementation of the physiological functions of neutrophilic granulocytes (NG) [13]. During the inflammatory process in the lungs, when alveolar macrophages do not have time to control invading pathogens, resting neutrophils are attracted to the affected area of the lungs, which are activated and absorb microorganisms through phagocytosis due to a combination of the production of toxic oxygen radicals, proteolytic enzymes and other bactericidal peptides. The degree of neutrophil activation, generation of reactive oxygen species (ROS), and release of granule proteins play a key role in the clearance of microbial pathogens [15]. NG do not live long and in normal conditions, after performing their functions in the inflammatory focus, neutrophils die. Thanks to apoptosis, it is possible to prevent the release of cytotoxic contents of neutrophils

into the surrounding tissues and timely eliminate the dying cells through tissue macrophages. Therefore, neutrophil apoptosis can be considered as one of the mechanisms for controlling inflammatory responses. Violations of the mechanisms that regulate apoptosis of immune cells can be a central pathogenetic factor in the initiation and (or) exacerbation of various inflammatory processes and persistence of inflammation [2, 4, 5].

One of the ways to violate the mechanisms of neutrophil apoptosis is to decrease the mitochondrial membrane potential (MMP, $\Delta\Psi_m$) [10]. It was assumed that neutrophils do not contain at all or contain an insignificant number of mitochondria that do not play an active role in their life, but it was shown that neutrophil mitochondria, despite their limited number, are actually involved in apoptosis [2, 14].

Maintenance of the membrane potential serves as an indicator of the level of metabolic activity of cells and a drop in the value of the mitochondrial membrane potential is one of the main indicators of the initiation of the mitochondrial pathway for triggering apoptosis [6, 11]. During inflammation, the life span of neutrophils increases or neutrophil death is delayed to fight infection and inflammation. However, on the other hand, delayed apoptosis of neutrophils can lead to an exacerbation of the inflammatory process [15]. In this regard, it is relevant to study the mitochondrial membrane potential

of granulocytes in children with CPL as one of the most important mechanisms for the development of an inflammatory response that provides effective antimicrobial protection of the body in CNSLD.

The purpose of this study was to study the features of the mitochondrial membrane potential of granulocyte in children with CLM.

Materials and research methods.

The survey of 72 children with CLM in the clinic Institute of Maternity and Childhood Protection. The patients underwent complete clinical examination, morphological test, bronchoscopy/bronchography, and spiral computed tomography. The nosological unit of the defect sections Q32-34 ICD-10 was considered to be the criterion for the inclusion of a case in the study group. There were 38 children (52.8%) in prolonged remission, 34 patients (47.2%) suffered from frequent inflammatory bronchopulmonary diseases. The average age of children was 8.2 ± 0.54 years, of which 32 girls (44.4%) and 40 boys (55.6%). The controls were indicators of 23 healthy children, comparable by sex and age. The study was conducted under the principles of the current revision of the Declaration Helsinki (64th WMA General Assembly, Fortaleza, Brazil, October, 2013) and approved by the Ethics Committee, Research Institute of Mother and Child Health Care.

The mitochondrial membrane potential ($\Delta\Psi_m$) was determined on the BD FACS Calibur cytometer (USA) in the Cell Quest Pro program in heparinized blood using JC-1 dye (5.5', 6.6'-tetra-chloro-1.1', 3.3' tetraethylbenzimidazole carbocanine iodide / chloride) (Becton Dikcenson, USA). JC-1 is a cationic dye, the absorption of which by mitochondria is directly related to the size of the mitochondrial membrane potential [7].

The study of luminol-and lucigenin-dependent of whole blood phagocytes was carried out using the method chemiluminescence method (CML) [9], registering the light sum of spontaneous (S-lum, S-luc) and phagocytosis-induced opsonized zymosan CML (S-lumv+zym, S-luc+zym). CML was registered using a luminescent spectrometer PERKIN ELMER LS 50B.

The functional and metabolic activity of neutrophils was evaluated according to the generally accepted method, determining the phagocytic activity of neutrophils and number of phagocytes neutrophils, and the ability of a cell to complete phagocytosis was evaluated in a spontaneous and pyrogenal stimulated nitro-blue tetrazolium (NBT) test.

Statistical calculations were performed

using Statistica 10.0 (Statsoft, Inc., USA). Data were tested for normality and are expressed as mean, standard deviation. When evaluating the entire population, mean values (M) and standard deviation (m) were calculated. The statistical significance was evaluated using Student's T-test. The study of the relationship of the determined characteristics was carried out using the Spearman correlation coefficient. The statistical hypotheses test showed the significance level of $p < 0.05$.

Results and discussion. The results of the study showed that the development of an acute infectious process in only 44.5% of children with CLM was accompanied by an increase in the number of leukocytes to $7.93 \pm 0.49 \times 10^9/l$, in 22.2% of children the number of leukocytes did not exceed $5.5 \times 10^9/l$, that is, active inflammatory process in the lungs did not activate the phagocytosis system in them, and it is known that maintaining the corresponding number of neutrophils and neutrophil homeostasis is significant in the conditions of inflammation [15].

21 patients (29.2%) had a high level (more than 10%) of granulocytes with reduced MPM. In children with CLM (Fig. 1) revealed a 5-fold increase in the proportion of cells with reduced granulocyte MPM ($10.9 \pm 2.4\%$ and $2.2 \pm 0.4\%$, respectively, $p < 0.001$), which may lead to neutropenia [5].

The changes resulted from period of the disease: if during the long-term remission the level of cells with reduced MPM corresponded to the control group ($2.5 \pm 0.5\%$), then during periods of relapse of inflammation, the number of granulocytes with reduced potential increased to $18.2 \pm 4.2\%$ ($p < 0.001$). Moreover, if the exacerbation of the disease was accompanied by clinical symptoms of pneumonia, these changes were more pronounced ($22.9 \pm 5.2\%$) than in children, when the exacerbation of the disease proceeded only with impaired bronchial patency ($9.7 \pm 2.7\%$, $p < 0.05$).

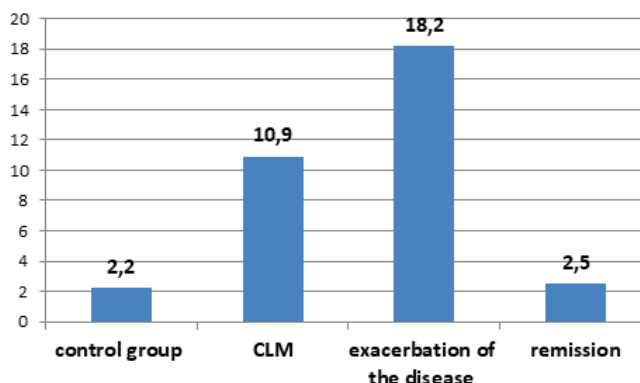
In other words, the number of granulocytes reflecting the processes of initiation of the mitochondrial pathway for triggering apoptosis increases significantly in the group of children with VPR during the inflammatory process in the lungs. Apparently, in the conditions of a chronic inflam-

matory state, cell-specific apoptosis is stimulated, when inflammatory mediators lead to an increase in the lifetime of neutrophils [12]. With adequate regulation of apoptosis, it supports tissue homeostasis. However, if the mechanisms of cell death are violated, it can lead to immunodeficiency, and an increase in the rate of apoptosis can lead to tissue destruction [1, 15].

According to the authors, mitochondrial dysfunction is accompanied by increased formation of reactive oxygen species [3]. Taking into account the significant changes in the MPM of peripheral granulocytes in children with VPR, we evaluated the functional activity of neutrophils (table 1). Indicators of oxidative metabolism of whole blood phagocytes demonstrated that the values of S-luc (1.1 ± 0.07 Rel. units) and S-lum (1.25 ± 0.09 Rel. units) in children with CPR in the period of exacerbation exceeded similar indicators in children in the period of remission (0.58 ± 0.07 Rel. units, and 0.59 ± 0.07 Rel. units, respectively, $p < 0.001$).

The values of the light sum induced by CML zymosan: S-luc+zym (5.45 ± 0.23 Rel. units) and S-lum+zym (6.25 ± 0.22 Rel. units) in children with exacerbation exceeded by 2 times the values of the remission period (3.07 ± 0.11 Rel. units and 4.18 ± 0.15 Rel. units, respectively, $p < 0.001$). Both spontaneous and stimulated chemiluminescence of phagocytes was increased in cnczl, but the I-lum and I-luc stimulation indices were significantly reduced in comparison with the control values by 30 and 25%.

The determination of the phagocytic activity of peripheral blood leukocytes is an important diagnostic criterion. The functional state of phagocytic defense factors was characterized by the tension of the redox reactions of neutrophils, the increase in the spontaneous NBT test in patients with exacerbation was significantly increased compared with the



The percentage of granulocytes with reduced membrane potential (%) in children with CLM

Indicators of functional activity of granulocytes in children at different periods of the disease, (M±m)

Indicators	control group	CLM – exacerbation	CLM – remission
Sluc, rel.units	0.21±0.02ΔΔ,##	1.11±0.07**,##	0.58±0.02**,ΔΔ
Sluc+Z, el.units	2.02±0.10ΔΔ,##	5.45±0.23**,##	3.06±0.11**,ΔΔ
K-luc, rel.units	9.42±0.39ΔΔ,##	4.91±0.22**,##	6.05±0.28**,ΔΔ
Slum, rel.units	0.26±0.01ΔΔ,##	1.25±0.09**,##	0.59±0.03**,ΔΔ
Slum+Z, rel.units	2.67±0.11ΔΔ,##	6.25±0.22**,##	4.18±0.15**,ΔΔ
K-lum, rel.units	10.18±0.47ΔΔ,##	5.00±0.24**,##	7.03±0.19**,ΔΔ
NBT sp., st. units	17.87±0.92ΔΔ,##	38.72±2.83**,##	27.89±4.92*
NBT st., st. units	24.44±1.10ΔΔ,##	42.05±2.48**,##	34.78±2.80**
Number of phagocytes neutrophils sp., units	11.46±0.95	12.49±1.42#	9.13±0.80Δ
Number of phagocytes neutrophils st, cond. Units	13.03±1.40Δ	9.27±0.58*,#	11.83±1.00*,Δ
Phagocytic activity of neutrophils sp., %	51.16±0.89Δ	34.50±7.33 *,#	53.32±3.71*,Δ
Phagocytic activity of neutrophils st., %	53.55±3.62Δ,##	41.29±4.93*,##	71.93±1.01**,ΔΔ

Note: * - $p < 0.05$ in relation to the "control" group. ** - $p < 0.001$ in relation to the "control" group. Δ - $p < 0.05$ in relation to the group "CLM - exacerbation". ΔΔ - $p < 0.001$ in relation to the group "CLM - exacerbation". # - $p < 0.05$ in relation to the group "CLM remission" ## - $p < 0.001$ in relation to the group "CLM remission"

control (38.72±2.83 standard units and 17.87±0.92 standard units, respectively, $p < 0.001$). However, with additional stimulation of neutrophils, a 2-fold decrease in the coefficient of stimulation of NBT was determined (3.33±0.48 and 6.57±0.09, respectively, $p < 0.001$). According to the pyrogenal-stimulated NBT test, inhibition of oxygen-dependent phagocytic cell metabolism was determined in 50% of children (average values of stimulation indices are lower than 1.0). In addition, in the period of exacerbation of the disease, the lowest indicators of phagocytic activity of cells were determined.

In patients with inflammatory processes in the lungs against the background of CLM, there is suppression of the phagocytic activity of neutrophils to 34.5±7.3%, against 51.2±0.9% in control and 53.3±3.7% in remission ($p < 0.05$), a decrease in the absorption function of neutrophils in stimulated tests. The inhibition of the absorption function of phagocytes in the stimulated test and the absence of prodigiosan-induced response were determined. The average values of number of phagocytes neutrophils in the period of exacerbation were 12.5±1.4 units, in children in remission-9.1±0.8 units ($p < 0.05$), stimulated number of phagocytes neutrophils -9.3±0.6 units and 11.8±1.0 units accordingly ($p < 0.05$), which may cause a violation of the formation of an anti-infectious response and lead to the development of clinical signs of the disease. The correlation analysis revealed statistically significant direct relationships between

the level of granulocytes with reduced MPM and the indicators of the phagocytic activity of neutrophils $r = 0.361$ ($p < 0.05$) and number of phagocytes $r = 0.397$ ($p < 0.05$).

Thus, the changes in the level of granulocytes with reduced mitochondrial membrane potential were revealed in children with CLM. This was accompanied by an increase in oxidative metabolism of phagocytes of whole blood in the period of exacerbation that was a reaction to the inflammation, however, the decrease in stimulation index I-lum I-luc, NBT-test, the phagocytic activity of neutrophils points to the depletion of the reserve capacity of the phagocytic system in children from the studied group and may be an important pathogenetic link in diseases of the respiratory system, causing constriction and inflammation of bronchi, destruction of lung parenchyma.

Conclusion. In the children with CLM the disease is accompanied by higher percentage of granulocytes in the peripheral blood with a reduced mitochondrial membrane potential, which indicates the activation of the mitochondrial pathway of apoptosis. The mitochondrial dysfunction of granulocytes affects their functional properties, reduces the intensity of phagocytic reactions, leads to depletion of adaptive reserves of immunocompetent blood cells and can lead to increased susceptibility to viral-bacterial bacterial infection and frequent exacerbations of the disease.

References

1. Апоптоз в иммунологических процессах / Р.И. Сепиашвили, М.Г. Шубич, Н.В. Колесникова [и др.] // Аллергология и иммунология. – 2015. – Т. 16, № 1. – С. 101-107. [Apoptosis in immunological processes / R.I. Sepiashvili, M.G. Shubich, N.V. Kolesnikova [et al.] // *Allergologiya i immunologiya*. – 2015. – Vol. 16, № 1. – P. 101-107].
2. Маянский Н.А. Митохондрии нейтрофилов: особенности физиологии и значение в апоптозе / Н.А. Маянский // Иммунология. – 2005. – № 5. – С. 307-311. [Maianik N.A. Neutrophil mitochondria: the characteristics of physiology and significance in apoptosis / N.A. Maianik // *Immunologiya*. – 2005. – № 5. – P. 307-311].
3. Мембранный потенциал митохондрий лимфоцитов и процессинг-активных форм кислорода в периферической крови у детей с хроническими воспалительными заболеваниями легких / М.С. Кузнецова, Е.И. Яковлев, Н.П. Мищенко [и др.] // Российский вестник перинатологии и педиатрии. – 2018. – Т. 63, № 4. – С. 245-246. [Membrane potential of mitochondria of lymphocytes and processing of reactive oxygen species in peripheral blood in children with chronic inflammatory lung diseases / M. S. Kuznetsova, E. I. Yakovlev, N. P. Mishchenko [et al.] // *Rossiyskiy Vestnik Perinatologii i Pediatrii*. – 2018. – Vol. 63, № 4. – P. 245-246].
4. Нейтрофил как «многофункциональное устройство» иммунной системы / И.И. Долгушин, Е.А. Мезенцева, А.Ю. Савочкина [и др.] // Инфекция и иммунитет. – 2019. – Т.9, №1. – С. 9-38. DOI: 10.15789/2220-7619-2019-1-9-38 [Neutrophil as a multifunctional relay in immune system / I.I. Dolgushin, E.A. Mezentseva, A.Yu. Savochkina [et al.] // *Infektsiya i immunitet*. – 2019. – Vol. 9, № 1. – P. 9–38]. DOI: 10.15789/2220-7619-2019-1-9-38
5. Новый взгляд на нейтрофильные гранулоциты: переосмысление старых догм. Часть 1. / И.В. Нестерова, Н.В. Колесникова, Г.А. Чудилова [и др.] // Инфекция и иммунитет. 2017. – Т. 7, № 3. – С. 219–230. DOI: 10.15789/2220-7619-2017-3-219-230. [A new look at neutrophilic granulocytes: rethinking old dogmas. Part 1. / I.V. Nesterova, N.V. Kolesnikova, G.A. Chudilova [et al.] // *Infektsiya i immunitet*. 2017. – Vol. 7, № 3. – P. 219–230. DOI: 10.15789/2220-7619-2017-3-219-230
6. Современные методы и подходы к изучению апоптоза в экспериментальной биологии / И.В. Кудрявцев, А.С. Головкин, А.В. Зурочка [и др.] // Медицинская иммунология. – 2012. – Т. 14, № 6. – С. 461-482. [Modern technologies and approaches to the study of apoptosis in experimental Biology / I.V. Kudriavtsev, A.S. Golovkin, A.V. Zurochka [et al.] // *Med. Immunol.* – 2012. – Vol. 14, № 6. – P. 461-482].
7. Altered mitochondrial membrane potential, mass, and morphology in the mononuclear cells of humans with type 2 diabetes / M.E. Widlansky, J. Wang, S.M. Shenouda // *Translational Research*. – 2010. – 156(1). – p. 15–25. DOI:10.1016/j.trsl.2010.04.001
8. An Integrated Imaging Approach to the Study of Oxidative Stress Generation by Mitochondrial Dysfunction in Living Cells / W.-Y. Cheng, H. Tong, E.W. Miller [et al.] // *Environmental Health Perspective*. – 2010. – № 7. – P. 902-908.
9. Dahlgren C. Measurement of respiratory burst products generated by professional phagocytes / C. Dahlgren, A. Karlsson, J. Bylund //

Methods Mol Biol. – 2007. – Vol. 412. – P. 349–63. DOI: 10.1007 / 978-1-59745-467-4_23

10. Elmore S. Apoptosis: a review of programmed cell death / S Elmore // Toxicol. Pathol. – 2007. – Vol. 35, № 4. – P. 495–516. DOI: 10.1080/01926230701320337

11. Ly J.D. The mitochondrial membrane potential ($\Delta\psi_m$) in apoptosis; an update / J.D. Ly, D.R. Grubb, A. Lawen // Apoptosis. – 2003. – Vol. 8. – P. 115–128. DOI: 10.1023/A:1022945107762.

12. Neutrophil Apoptosis: Relevance to the Innate Immune Response and Inflammatory Disease / S. Fox, A.E. Leitch, R. Duffin [et al.] // J Innate Immun. – 2010. – Vol. 2. – P. 216–227. DOI:10.1159/000284367

13. Neutrophils in the activation and regulation of innate and adaptive immunity / A Mantovani, MC Cassatella, C Costantini [et al.] // Nat. Rev. Immunol. – 2011. – Vol.11. – P. 519–531. DOI: 10.1038/nri3024

14. Newmeyer D.D. Mitochondria: releasing

power for life and unleashing the machineries of death / D.D. Newmeyer, S. Ferguson-Miller // Cell. – 2003. – Vol. 112, № 4, P. 481–490. DOI: 10.1016 / S0092-8674(03)00116-8

15. Understanding the roles of cytokines and neutrophil activity and neutrophil apoptosis in the protective versus deleterious inflammatory response in pneumonia / J. Bordon, S. Aliberti, R. Fernandez-Botran [et al.] // Int J Infect Dis. – 2013. – Vol. 17, № 2. – P. e76–83. DOI: 10.1016 / j.ijid.2012.06.006.

S.D. Efremova, V.M. Nikolaev, S.I. Sofronova, E.K. Rumyantsev, E.D. Oxlopkova, N.K. Chirikova, S.A. Fedorova

SMOKING AND ITS INFLUENCE ON THE LEVEL OF ONCOMARKERS IN BLOOD SERUM OF THE POPULATION OF THE REPUBLIC OF SAKHA (YAKUTIA)

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Our results indicate that smoking stimulates the expression of tumor markers in the serum of smokers. The level of tumor markers increases with the increase in smoking history. In the body of smokers, the concentration of tumor markers increases at a young and middle age, rather than in the elderly. The decrease in the indicators of tumor markers in old age is explained by the natural premature dropout of smokers from the population.

Keywords: smoking, tumor markers, cancer-embryonic antigen (CEA), alpha-fetoprotein (AFP), prostate specific antigen (PSA), ovarian tumor marker (CA125).

Introduction. Smoking is a risk factor for many chronic diseases such as chronic obstructive pulmonary disease, hypertension, cardiovascular disease, atherosclerosis, diabetes, cancer and

microbial infections (respiratory tract infections, bacterial meningitis), etc. [4, 5]. According to the World Health Organization (WHO), more than 8 million people die annually from tobacco-related diseases, of which more than 7 million are smokers and more than 1.2 million are passive smokers (non-smokers) [27]. Tobacco smoke contains about 4,000 known chemicals; 250 of them are known to be harmful to health and more than 50 cause cancer in humans [23].

There is sufficient evidence of the involvement of smoking in the development of the following cancers: lung [13, 16], oral cavity [7,10], pharynx [18,25], larynx [4,7], esophagus [5, 8], nasal cavity and nasal sinuses [7,18], stomach [5,8], liver [20], kidney [24], cervix [15], etc. Smoking is especially dangerous at a young age, because addiction develops very quickly (cravings, withdrawal symptoms). It has been proven that nicotine contained in tobacco products causes addiction symptoms. Analysis of the sources has shown a directly proportional relationship between the age of onset and the duration of smoking [16]. It should be noted that the World Health Organization and the American Psychiatric Association classify nicotine addiction as a “substance use disorder” [27].

According to various researchers, stopping tobacco use reduces the risk of developing cancer and increases the life expectancy of individuals [13, 14]. Smok-

ing electronic cigarettes, pipes, hookahs and cigars can also cause lung cancer, but the highest risk of developing carcinogenic diseases is caused by cigarette smoking, since it is the most widespread form of tobacco use in the world [16,19]. In developed countries, long-term programs aimed at reducing the number of smokers contribute to a decrease in mortality from tobacco smoking [9,12,15].

According to the sources, researchers have noted a significant increase of tumor markers in the blood serum of patients with cancer: carcinoembryonic antigen (CEA), alpha-fetoprotein (AFP), prostate-specific antigen (PSA) and ovarian tumor marker (CA125) [3,26]. An increase in cancer markers among smokers has been noted [26, 28].

The aim of this study is to assess the level of tumor markers in smokers and nonsmokers in the Republic of Sakha (Yakutia), depending on age.

Material and Research Methods. This work was carried out within the framework of the research: “Epidemiological aspects of malignant tumors in the Far North, development of modern methods of early diagnosis and prevention with the usage of highly informative fundamental research methods” in the Department of Adaptation Mechanisms Research, Yakutsk Scientific Center for Complex Medical Problems. We examined 175 residents of Megino-Khangalass district, aged 22 to 66, of which 83 were

EFREMOVA Svetlana Dmitrievna - Junior Researcher, Yakutsk Scientific Center for Complex Medical Problems (YSC CMP), esd64@mail.ru, **NIKOLAEV Vyacheslav Mikhailovich** - Candidate of Biological Sciences, Chief Researcher - Head of the Department for the Study of Adaptation Mechanisms, Yakutsk Scientific Center for Complex Medical Problems (YSC CMP), Nikolaev1126@mail.ru, **SOFRONOVA Sargylana Ivanovna** - Candidate of Medical Sciences, Chief Researcher - Head of the Scientific and Organizational and Information and Publishing Department, Yakutsk Scientific Center for Complex Medical Problems (YSC CMP), sara2208@mail.ru, **RUMYANTSEV Egor Konstantinovich** - Junior Researcher, Yakutsk Scientific Center for Complex Medical Problems (YSC CMP), tzeentch1993@mail.ru, **OKHLOPKOVA Elena Dmitrievna** - Candidate of Biological Sciences, Leading Researcher, Yakutsk Scientific Center for Complex Medical Problems (YSC CMP), elena_ohlopkova@mail.ru, **CHIRIKOVA Nadezhda Konstantinovna** - Doctor of Pharmaceutical Sciences, Leading Researcher at the Institute of Natural Sciences of M.K. Ammosov North-Eastern Federal University, hofnung@mail.ru, **FEDOROVA Svetlana Arkadyevna** - Doctor of Biological Sciences, Chief Researcher of the Institute of Natural Sciences, M.K. Ammosov North-Eastern Federal University, sa.fedorova@s-vfu.ru