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THE ROLE OF *FADS* GENE POLYMORPHIC VARIANTS IN ADAPTATION TO THE NORTHERN CLIMATE AND METABOLIC DISORDERS

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The review summarizes the studies of the role of the *FADS* gene in the metabolism of polyunsaturated fatty acids, as one of the mechanisms of human adaptation to the environmental conditions, in particular, a cold climate. A comparative analysis of the distribution of the most significant for circumpolar ethnic groups polymorphic variants rs7115739, rs174570 of the *FADS* 2-3 genes in various ethnic groups, including the Inuits and Yakuts, was carried out. The results of studies of the *FADS* polymorphic markers effect on lipid metabolism, the risk of cardiovascular diseases and type 2 diabetes mellitus in different world populations are systematized.

Keywords: *FADS* genes, desaturases, polyunsaturated fatty acids, rs7115739, rs174570, metabolism, adaptation, cold, North, Yakuts.

Introduction. Currently, the contribution of *FADS* cluster genes associated with the synthesis of long-chain polyunsaturated fatty acids (LC-PUFAs) in the development of metabolic disorders, increased risk of cardiovascular disease (CVD) and type 2 diabetes mellitus (DM2) is being actively studied. LC-PUFAs are involved in many physiological processes: they are part of cell membranes, serve as a substrate for the synthesis of inflammatory eicosanoids (leukotrienes and prostaglandins), act as signaling molecules, and regulate gene expression [42]. One of the main LC-PUFAs are eicosapentaenoic (EPA), docosahexaenoic (DHA) and arachidonic (AA) acids, the last two are necessary for the full functioning of the central nervous system [43]. These fatty acids are not synthesized in the body *de novo*, therefore, they must be supplied with food, or in the form of their 18-carbon substrates for endogenous biosynthesis (omega-6 linoleic (LA) and omega-3 alpha-linolenic acids (ALA)) [42]. The content of LC-PUFAs and their precursors in the traditional diet of various world populations varies greatly depending on the geography and type of economic activity. EPA and DHA,

found in seafood and fish, are an important component of the diet of coastal populations, especially those in the circumpolar regions.

A key role in the metabolism of LC-PUFAs is played by desaturase enzymes, which catalyze the conversion of a single bond between carbon atoms (C-C) of a fatty acid substrate into double bonds (C=C), and are encoded by genes of the *FADS* family [38]. *FADS* genes regulate numerous physiological processes associated with metabolism: they enrich membrane phospholipids with PUFAs, influence to lipoprotein metabolism and lipogenesis, inflammation, levels of circulating monocytes and T cells, and regulate the functions of macrophages, fatty acids, and cholesterol [13, 38, 42, 50]. It has been shown that the *FADS* genes belong to the genes involved in adaptation to a cold climate, which is associated with energy metabolism and the content of LC-PUFAs in food [18, 29, 30]. Thus, the selection of some polymorphic variants in the *FADS* gene cluster in the Greenlandic Inuit has been shown; the strongest signal is associated with rs7115739 T > G in the *FADS3* gene and rs174570 C > T in the *FADS2* gene [30].

One example of populations adapted to harsh climatic conditions are the peoples of Yakutia, whose traditional diet is dominated by foods characterized by a high content of proteins and fats. The population of the Arctic zone has the features of the so-called northern adaptive type, which is characterized by: dense body type, high basal metabolic rate, high content of high-density lipoprotein cholesterol (HDL cholesterol), low content of triglycerides (TG) and atherogenic index [2, 4, 44]. Currently, the diet of the indigenous population of the North, as well as throughout the world, is undergoing global westernization with an increase in the proportion of carbohydrates in the diet and a change in the ratio of fatty acids, which suggests an imbalance of LC-PUFAs. In this regard, the possible influence of desaturase gene activity on the metabolic health of circumpolar peoples, including Yakutia, is of interest.

The purpose of the study is to evaluate the possible relationship of polymorphic variants of the *FADS 1-2-3* genes with adaptation to the extreme conditions of the North and the development of metabolic disorders in modern conditions based on a review of the literature data.

Methods. The structure of the systematic review and the algorithm for information searching and selection are according to the PRISMA standard. The review includes the main sections: introduction, methods, results, discussion, conclusion, funding. The results of the review include the following sections: the geography of distribution of polymorphic markers of *FADS* genes in world populations and the association of *FADS* genes with the development of metabolic disorders in different ethnic populations.

Studies search and selection strategy. The studies were searched using keywords in the following databases: Russian scientific electronic library: elibrary.ru (https://www.elibrary.ru), Pubmed (https://pubmed.ncbi.nlm.nih.gov/), Google scholar (https://scholar.google.com/). Key words for sources in Russian were: gene* FADS*; in English for the Pubmed database: (FADS) AND (gene) with filters: species - human, language - English; for Google scholar search: human FADS gene, metabolism. The systematic review included studies of the association of polymorphic variants of FADS genes with adaptation and the development of metabolic disorders. The authors independently assessed the titles and abstracts of publications for compliance with the inclusion criteria, all disagreements were resolved through negotiations. A manual search was also carried out in the reference lists of the found articles to identify additional sources on the topic. The last search was carried out on August 15, 2022.

Inclusion Criteria. The studies selection criteria for the systematic review were: 1. language: Russian, English; 2. Type of study: cross-sectional and case-control; 3. Age of the subjects over 18 years old; 4. In case-control studies, individuals with type 2 diabetes mellitus (DM2), metabolic syndrome (MS) and cardiovascular diseases (coronary heart disease (CHD), ischemic stroke (IS)) were taken as cases.

Extraction of research data. In the initial screening, using the search queries described above, 241 publications were selected from the PubMed database and 24,100 results from the Google Scholar database. After assessing titles and abstracts, duplicate publications and publications that did not correspond to the search topic were excluded. After filtering, 160 studies remained that corresponded to the purpose of the review. After detailed examination of the full texts, 11 cross-sectional studies and 12 case-control studies fulfilling the inclusion criteria and theme of review were selected.

Search in Russian-language databases for the keywords: "gen* FADS*" found 8 articles, of which 3 publications were selected on the topic of the study.

Results of a systematic review Geography of Distribution of Polymorphic Markers of *FADS* Genes in Various World Populations. Studies of genetic variants of the long-chain unsaturated fatty acid desaturase gene region have revealed the evolutionary history of the *FADS* gene region. In different human populations, two common and very different haplotypes (A and D) were identified, covering the *FADS* gene region and closely related to the level of LC-PUFA synthesis. Haplotype A is considered to be the ancestral haplotype, while haplotype D is specific only for humans and appeared after the separation of the common ancestor of humans and Neanderthals [22]. Currently, haplotype D is most common in Africa and is closely associated with low levels of linoleic and alpha-linolenic acids, which act as substrates for fatty acid synthesis, and higher levels of production of AA, EPA, DHA, and gamma-linolenic acids [7]. Individuals homozygous for the D haplotype had 24% higher levels of DHA and 43% higher levels of AA in the blood than those homozygous for the ancient A haplotype [22]. It is assumed that the modern D haplotype was formed approximately 85,000 years ago, during the development of the continental part of the African continent, as one of the means of survival, during the period of unavailability of a diet rich in arachidonic and docosahexagenic acids, necessary for the development of the brain [7, 22].

The ancestral haplotype A is now generally less common and has been preserved with the highest frequency in populations whose traditional diet is marine mammals and fish with a high content of LC-PUFAs, while it is associated with lower desaturase activity. The natives of America have the lowest frequency of haplotype D, up to 0.01%. The low frequency of haplotype D in this population indicates that this haplotype may have been lost due to the bottleneck effect during the colonization of the American continent [22], and haplotype A was retained under conditions of a diet rich in essential LC-PUFAs. East Asian populations, in whose diet seafood plays a significant role, also have increased frequencies of polymorphisms, which determine lower desaturase activity, compared with European and African populations. A striking example of the influence of a diet high in LC-PUFAs on the maintenance of haplotype A is the Greenlandic Inuit population, in which its frequency reaches 99.9% [30]. Climatic conditions could also play a role in the preservation of haplotype A, requiring an effective ener-

gy balance in the conditions of available food resources. In 2018, studies were conducted on the distribution of variants of two polymorphisms (rs174546 *FADS1* and rs174568 *FADS2*) in Siberian populations. A wider distribution of variants related to haplotype A was shown with a frequency of 57% in South Siberian populations and 97% in West Siberian and northeastern populations [3].

Matteo Fumagalli et al. showed that 6 SNPs in the Greenlandic Inuit in the *FADS* gene cluster underwent the greatest selection, of which the polymorphic markers rs7115739 (G/T) of the *FADS3* gene, rs174570 (C/T) of the *FADS2* gene [30]. As a result of a meta-analysis involving 10 largest studies among two ethnic groups (Greenland Inuit n= 4584 and Europeans n=207300), an association of these polymorphic variants with body mass index, with insulin, with LDL was revealed. It is also interesting that Caucasoids carrying T alleles of rs7115739 and rs174570 polymorphisms (n = 263451) showed a statistically significant association with short stature, and, conversely, no association with body weight was found. The possible association of these polymorphic variants with metabolic disorders and adaptation to cold climates determined our interest in them. Table 1 shows the frequency of minor alleles of these polymorphic variants in world populations, as well as in representatives of the Yakut ethnic group, which we identified in genome-wide studies.

Analysis of the distribution of rs7115739 of the *FADS3* gene shows a frequency from 0.03 in Europeans, including Russians, to 0.33 in the northern peoples of China, and 0.98 in the Greenlandic Inuit. In Yakuts, the frequency of the minor allele, which is considered to be associated with adaptation to cold, contrary to expectations, is 0.14, which is comparable with South Asian populations [28]. A more logical distribution of the frequency of the rs174570 polymorphism of the *FADS2* gene looks from 0.03 in Africans to 0.38 in East Asians, such as Han Chinese, and 0.99 in Greenlandic Inuit. In some Chinese populations, the frequency of the minor allele reaches 0.44 (Daurs), 0.49 (Evenki), and 0.77 (Dai of South China) [47]. In Yakuts, the minor allele occurs with a frequency of 0.43 [28]. It is suggested that the haplotype associated with low desaturase activity in combination with a traditional diet rich in LC-PUFA plays a protective role in reducing the risk of metabolic syndrome and CVD. This issue is relevant in modern conditions of changing nutrition and lifestyle, and is of great interest to researchers.

The Role of Polymorphic Markers of *FADS* Cluster Genes in the Development of Metabolic Disorders in Different Ethnic Populations. A systematic review of the results of cross-sectional and case-control studies on the analysis of the influence of the *FADS* genotype and desaturase activity on lipid metabolism and associated metabolic disorders revealed several publications with ambiguous results. Genetic polymorphisms in the *FADS 1-2-3* gene cluster are located mainly in intron regions and are linked by linkage disequilibrium. The main alleles conditionally belong to the D haplotype, and the minor alleles to the A haplotype. Table 2 shows the results of cross-sectional studies aimed at studying the relationship between *FADS* genotypes and the level of fatty acids (FA) in blood plasma, erythrocyte membranes, total cholesterol (TC), low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides (TG) and other indicators of metabolic health (body mass index (BMI), waist circumference, carbohydrate metabolism and others). The most studied are polymorphic variants of the *FADS1* gene [5, 6, 12, 15, 16, 19, 20, 25, 27, 32, 33, 45]. Most authors indicate that minor alleles of the *FADS* genes are associated with low desaturase activity, which is determined by the ratio of enzyme products to substrates. The only study we found in which minor alleles of the *FADS* genes showed an association with increased activity of desaturase enzymes was a study of the Eskimos of Alaska [48]. With regard to indicators of lipid metabolism, there is no such clear uniformity in the results of studies. However, most researchers have found lower levels of TC, LDL, and slightly less HDL in carriers of minor alleles [16, 19, 25, 27, 30, 33, 45]. The most conflicting data were obtained regarding the level of triglycerides; in the owners of minor alleles, it can be either increased or decreased [5, 6, 32, 34, 45].

Attempts were made to assess the risk of developing CVD, coronary heart disease, ischemic stroke and T2DM depending on the *FADS* genotype in case-control studies (Table 3). Such work was carried out in Chinese, Indian, Iranian and some European populations. In a number of publications, the association of the *FADS* genotype with CVD and DM2 is not detected or is not detected with all the studied *FADS* polymorphic variants [1, 26, 10, 17, 24, 37, 40, 41]. Some Chinese researchers have found a decrease in the risk of coronary artery disease and DM2 in carriers of minor alleles, accompanied by a reduced level of TC [10, 40]. Other data, also obtained in China, show an increased risk of coronary artery disease and IS in carriers of the minor T allele rs174546 of the *FADS1* gene and rs174601 of the *FADS2* gene [11]. At the same time, the frequency of the minor allele T of these two SNPs was higher than the frequency of the C allele both in the control group and in patients. The T allele in this study was associated with a decrease in serum HDL and ApoAI levels in groups of patients with coronary artery disease and IS [11]. Also, in the Chinese population, an increased risk of CHD was found in carriers of minor alleles of rs174547 in *FADS1* when adopting a recessive model [21]. In another study, on the contrary, carriers of the main allele rs174537 - patients with DM2 had an increased risk of developing coronary artery disease (odds ratio (OR) 1.763; 95% CI 1.143-2.718; p = 0.010) [41]. At the same time, the genotype with an increased risk was associated with an increased level of plasma LDL cholesterol.

The association of the *FADS* genotype with DM2 is much less common. Thus, other Chinese authors in studies of several SNPs showed an association of the minor allele only rs174616 of the *FADS2* gene with a reduced risk of DM2 in both codominant and dominant models after adjusting for age, sex, and BMI [40]. Detailed studies of the rs174575 *FADS2* gene have been carried out in the Indian population. In these studies, the minor allele rs174575 was associated with higher fasting blood glucose and HOMA-IR, while HOMA-β was lower [9]. In the recessive model, carriers of the minor allele rs174575 also had statistically significant elevated levels of total cholesterol, TG, LDL, VLDL [46]. Multivariate models of the rs174575 genotype (carriers of the minor allele) with insulin and the rs174575 genotype with insulin and triglyceride showed an association between the genotype and the risk of type 2 diabetes [46]. In other studies, the association of *FADS* polymorphisms was not revealed [24, 37, 41]. In studies performed by O. V. Kochetova et al. in Bashkir and Tatar women, no association of the polymorphic variant rs174550 (T/C) of the *FADS1* gene with metabolic syndrome was found, but a statistically significantly reduced level of triglycerides was shown in carriers of the minor allele in the recessive model (p =0.02) only in the group of women of the Bashkir ethnicity [1].

Analysis of data from cross-sectional studies of *FADS1-2* genotypes in different populations shows that minor alleles of disequilibrium linked SNPs of this clus-

Ассоциация полиморфизмов генов кластера FADS с риском развития ССЗ и СД2 по результатам исследований случай-контроль в различных мировых популяциях

Популяция (общее кол-во исследованных n)	Случай (кол-во n, возраст, лет); Контроль (кол-во n, возраст, лет)	Исследованные гены *FADS* и их SNP (основная /минорная аллель)	Ассоциация генотипа *FADS* с риском случая	Ассоциация генотипа *FADS* с метаболическими нарушениями	Ссылка
Швеция, городское население (n=24032)	ССЗ (n=2648, 44-74) Контроль (n=21384, 44-74)	*FADS1* rs174546 (C/T)	нет		[26]
Китай (n=992)	ИБС (n=497, 67.0 (18.0)); Контроль (n=495, 58.5(22.0))	вблизи *FADS1* rs174537 (G/T), *FADS1* rs174547 (T/C), *FADS2* rs1535 (A/G), rs174575 (C/G), rs174602 (T/C), *FADS3* rs174450 (A/C), rs7115739, (G/T), rs1000778 (A/G)	↓ риска ИБС у носителей минорного аллеля rs1000778 *FADS3*	↓ ОХ у носителей аллелей rs174575-G *FADS2* и rs174450-C и rs7115739-T *FADS3* в контроле	[10]
Китай, южная популяция (n= 1 669)	ИБС (n = 534, 61.93 ± 10.69); ИИ (n = 553, 62.54 ± 12.11); Контроль (n=582, 61.40 ± 10.54)	*FADS1* rs174546 (C/T), *FADS2* rs174601 (C/T)	↑ риск ИБС и ИИ у носителей аллелей Т двух SNP	↓ ЛПВП и АроАI в сыворотке крови в группах пациентов ИБС и ИИ у носителей аллеля Т двух SNP и генотипа rs174601 ТТ.	[11]
Китай (n=1660)	ИБС (n=515, 66.7±10.0); Контроль с высоким риском (n=524, 50.2±12.5); Контроль с низким риском (n=621, 49.8±12.4)	*FADS1* rs174547 (T/C)	↑ риск ИБС у носителей генотипа rs174547 CC в рецессивной генетической модели	↓ ЛПВП и ↑ ТГ у носителей минорного аллеля С	[21]
Китай (n=872)	ИБС (n=200, 59.47 ± 10.53); СД2 (n=234, 57.74 ± 12.76); СД2 и ИБС (n=185, 60.30 ± 9.73); Контроль (n=253, 59.73 ± 10.06)	вблизи *FADS1* rs174537 (G/T), *FADS2* rs174616 (C/T), rs174460 (T/C), rs174450 (A/C)	↑ риск ИБС у пациентов СД2 с генотипом rs174537 GG (основной аллель)	↑ ЛПНП, АК и дельта-6 десатуразы у носителей генотипа rs174537 GG	[41]
Китай (n=772)	СД2 (n=441, 58 (11.0)); Контроль (n=331, 56 (12))	*FADS1* rs174545 (C/G), *FADS2* rs2072114 (A/G), rs174602 (A/G), rs174616 (C/T)	↓ риск СД2 у носителей минорного аллеля Т rs174616 как в кодоминантных, так и в доминантных моделях после корректировки на возраст, пол и ИМТ	↓ ОХ у носителей минорных аллелей. ↓ ЛПВП у гомозигот по минорному аллелю rs174546 и rs3834458.	[40]
Китай (n=1158)	СД2 (n=758, 58.25±12.31); Контроль (n=400, 51.99 ± 8.41)	вблизи *FADS1* rs174537 (G/C), *FADS2* rs174575 (C/G), *FADS3* rs174455 (G/A)	нет		[24]
Индия (n=429)	СД2 (n=213, 51.03 ± 8.25); Контроль (n=216, 47.44±10.16)	*FADS2* rs174575 (C/G)	Не показано.	↑ глюкоза натощак и HOMA-IR, ↓ HOMA-β у носителей минорной аллели rs174575.	[9]
Индия (n=429)	СД2 (n=213, 51.03 ± 8.25); Контроль (n=216, 47.44± 10.16)	*FADS2* rs174575 (C/G)	↑ риск СД2 в многомерных моделях генотипа rs174575 (носители минорного аллеля) с инсулином и генотипа rs174575 с инсулином и ТГ.	↑ ОХ, ТГ, ЛПНП, ЛПОНП у носителей минорного аллеля rs174575 в рецессивной модели.	[46]
Иран (n=190)	СД2 (n=95, 53.23±10.87); Контроль (n=95, 53.67±8.47)	*FADS2* rs174583 (C/T)	нет		[37]
Германия (n = 2653)	СД2 (n=673, 55.1 ± 7.4); Контроль (n=1980, 50.0 ± 8.9)	*FADS1* rs174546 (C/T)	Нет. Но более низкая активность фермента D6D предсказывала более низкий риск СД2 у носителей минорного аллеля.		[17]
Татары (женщины), n=375; башкиры (женщины), n=166	МС (n=243, 52.92±7.22); Контроль (n=298, 54.14±6.91)	*FADS1* rs174550 (T/C)	нет	↓ ТГ у носителей минорного аллеля в рецессивной модели (p=0,02) только в группе женщин башкирской этнической принадлежности	[1]

ter are associated with low desaturase activity and, probably, a more favorable lipid profile. This conclusion is supported by a Mendelian randomization study to investigate the associations between plasma FA levels of phospholipids and 15 cardiovascular diseases, which showed that carriers of the *FADS1* minor allele rs174547 (T/C) have a reduced risk of ischemic stroke, large artery stroke, and venous thromboembolism, and evidence feedback on ischemic heart disease, abdominal aortic aneurysm, and aortic valve stenosis [39].

In some cases, the *FADS* genotype is not associated with the disease, but the activity of desaturases has a statistically significant association with T2DM. Thus, the work of J. Kroger et al showed a positive relationship between D6D activity, encoded by *FADS2*, and a clear inverse relationship between D5D (*FADS1*) activity and the risk of diabetes, while the relationship with the genotype was not proven [17]. A recent Mendeleev randomized study revealed the overall effects of increased activity of both D6D and D5D on the risk of T2DM and the effect of D6D activity on the risk of CHD [14]. According to the authors, the influence of desaturase activity on the risk of diabetes is probably mediated by changes in the composition of FAs in cell membrane phospholipids, which affect cellular function, including insulin signaling and receptor binding affinity. [14, 17]. In addition, long chain PUFAs can act as biological ligands for PPAR-γ, which is associated with adipogenesis and lipogenesis. PUFAs also block NF-kappa B, reducing inflammation. Together, all factors can increase insulin sensitivity, and when the activity of desaturases changes, lead to metabolic disorders. Another Mendeleev randomized study showed that a decrease in the synthesis of omega-6 LC-PUFAs was not significantly associated with the risk of developing DM2, however, the authors concluded that in a predominantly white European population, the synthesis of omega-6 LC-PUFAs is not a major risk factor for developing DM2 [49].

Discussion. An analysis of the prevalence in world populations of haplotypes covering the region of *FADS* genes and closely related to the level of LC-PUFA synthesis reflects both the historical processes of migration of modern humans and the influence of available food sources and processes of adaptation to climatic conditions on the selection of the most energetically advantageous polymorphisms. The spread of a derivative of the D haplotype with high desaturase activity is associated with the development of agriculture and farming and an increase in the share of plant foods in the diet, which contributed to the development of new continental territories.

The fixation of the ancestral haplotype A in modern Native Americans and circumpolar peoples has been interpreted as evidence of selection from their Siberian or Beringian ancestors [23, 31]. However, it is not excluded that the ancestral haplotype was preserved from the Paleolithic Eurasians, in whom the derived alleles probably did not yet become common until the time of separation of the ancestors of the indigenous inhabitants of America and the Eurasians [35]. In northern populations, this haplotype, which is responsible for a lower level of LC-PUFA biosynthesis, is adapted to the availability of LC-PUFA in the diet and, accordingly, to higher levels of accumulation in the body of 18-carbon precursors and other fats capable of being actively deposited in adipose tissues. of the body as an energy source that provides thermogenesis of the body in cold conditions and energy consumption during traditionally active physical activity.

It should be noted that there is an insufficient number of studies of *FADS* genes in Russian populations, while the diversity of climatic conditions and ethnic groups in Russia could make a significant contribution to the coverage of this topic. As part of a project to study the entire genome of Russian populations, an analysis was made of the frequency of the two most significant polymorphic variants rs7115739 (G/T) of the *FADS3* gene and rs174570 (C/T) of the *FADS2* gene involved in adaptation to cold climates in Yakuts and Russians. It was shown that the frequency of minor alleles rs7115739 and rs174570 in Yakuts is higher (14% and 43%, respectively) than in Russians (3-4% and 7-23%), and is close to that in East Asian peoples [28]. It can be assumed that this is influenced by a common origin with the East Asian peoples, but the frequencies obtained cast doubt on the selective selection for these variants in the Yakut population. However, about half of the Yakut population have a genetically predetermined low desaturase activity in the *FADS2* gene.

A systematic review of the results of studies of the association of polymorphic variants of the *FADS* genes with metabolic disorders in different world populations did not give an unambiguous answer to what extent the effect of the ancestral haplotype A is favorable on lipid metabolism and the risk of developing DM2 and CVD. This haplotype with low desaturase activity can be associated with both a favorable lipid profile and an unfavorable one. It is likely that the relationship between the *FADS* genotype and the risk of metabolic disorders is complex and is affected by diet, lifestyle, and the state of the human immune system. In general, it seems that the carriers of minor alleles, i.e. ancestral haplotype A are more sensitive to lipid metabolism disorders and the associated risk of CHD and IS. The haplotype that causes low desaturase activity, which is compensated by the intake of LC-PUFAs with traditional foods, has a protective effect on CVD, but under conditions of westernization of the diet and low physical activity, it has a negative effect on metabolic health.

Conclusion. In circumpolar ethnic groups, the distribution of an ancestral haplotype with low desaturase activity was shown. Although this haplotype is generally considered favorable for lipid metabolism, a review of studies suggests that its holders may be more vulnerable to CVD. This is probably due to the fact that in modern conditions, with a global shift in the diet towards the Western diet and a decrease in the level of consumed LC-PUFAs, low deaturase activity, combined with a decrease in physical activity, also leads to lipid metabolism disorders. When developing preventive measures and technologies for personalized medicine to reduce the prevalence of risk factors for cardiovascular diseases and alimentary-dependent pathology, genetically determined desaturase activity should be taken into account. As the example of the Yakut population shows, the prevalence of one or another haplotype is determined not only by geographical factors and environmental conditions, therefore, the development and implementation of personalized approaches to each population is more justified.

The study was carried out within the framework of the basic part of the state task of the Ministry of Education and Science of the Russian Federation on the topic "Genetic characteristics of the population of the north-east of Russia: reconstruction of genetic history, mechanisms of adaptation and aging, age-dependent and hereditary diseases." (FSRG-2023-0003).

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POINT OF VIEW

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THE ROLE OF SOCIAL FACTORS IN THE FORMATION OF CONGENITAL HEART DISEASE IN THE REPUBLIC OF SAKHA (YAKUTIA)

The article presents the results of the study of the association of some socio-demographic factors with risk of congenital heart disease in children in the Republic of Sakha (Yakutia). The analysis was carried out on the basis of the Perinatal Center of the Republican Hospital No.1-NCM). The study includes all cases of congenital defects among newborns born alive in two time periods – from 2001-2003 and 2011-2013. In the first period, 697 cases were registered, in the second period there were 1127 cases of congenital heart disease.

The first group included newborns with persistent fetal communications without signs of heart failure, without expansion of the heart cavities and without hemodynamic disorders. The second group was represented by newborns with congenital heart disease with signs of heart failure and functional class of various degrees. This group was divided by severity of heart failure and functional class stages into two subgroups which were 2A and 2B respectively.

The factors such as the education of parents, the number of births in the history, the presence of a full and incomplete family, were analyzed.

The compared groups were not statistically significantly different by age of the parents. The median values of the mothers' age at the time of birth of a child with congenital heart disease were 27 years in the first group, 26 years in the 2A group, and 28 years in the 2B group. The median age of the father in all groups was 29 years.

The structure of categories of social status is represented mainly by employees, non-workers, workers and students. An analysis of the parents of the education factor as a possible predictor of the birth of a child with congenital heart disease was also conducted.

According to the results of the study, social factors affecting the risk of birth of children with congenital heart defects were an incomplete family without a sign of marriage (registered and unregistered marriage), the level of education of the mother in the case of simple heart defects, the number of births and the social status of the mother in complex diseases.

Keywords: congenital heart disease, social factors, parents, statistical analysis.

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Introduction. Children's health is formed under the influence of the interaction of endogenous and external factors. The leading place among the endogenous are genetic factors, parents' health, the course of antenatal and perinatal periods. The external environmental factors also can increase the likelihood of disease [1,9,14].

Congenital heart disease is one of the global problems of modern neonatology and pediatrics. Most of the risk factors influencing the formation of CHD in the fetus can be managed, as evidenced by numerous multicenter studies, which reinforces the importance of preventive measures aimed at preventing further growth of CHD prevalence [2, 7].

The etiology of congenital heart disease is still unclear. In addition to genetic or chromosomal abnormalities, maternal factors such as drug intake during pregnancy, viral infections in the first trimester of pregnancy, smoking, alcohol abuse, and others can contribute to CHD development [4, 5, 6, 8, 13]. There is an evidence of an increased risk of heart defects in children of mothers with diabetes