Features essential omega 3 polyunsaturated fatty acids content and glucose level in adult residents of the Arctic region

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Abstract. The study aims to determine the level and identify the nature of the relationship between the content of ω-3 polyunsaturated fatty acids (PUFA) and the glucose level in practically healthy people of mature age in the Arctic region. Materials and methods: The study covered 1,689 individuals, of whom 939 are residents of the Arctic Region and 750 of the sub-Arctic Region. The content of essential omega-3 PUFA was determined by gas-liquid chromatography in serum, while the level of glucose was determined by spectrophotometry. Results: Regardless of region of residence, the age-related increase in glucose levels, their values in the Arctic region being abnormally high, are associated with an increase in the content of essential ω-3 PUFAs, which is confirmed by the majority of direct correlations between glucose and omega-3 PUFAs C18: 3n3, C205n3, C226n3), compared with sub-Arctic region (C226n3).

1. Introduction
ω-3 PUFAs are a part of cellular membranes designed to strengthen their cytoprotective properties (integrity, fluidity, elasticity, permeability, passive transfer of substances, etc.) [1, 2, 3]. In addition, ω-3 PUFAs have a positive effect on a number of metabolic disorders that underlie the development of diabetes. These effects include insulin sensitizing effects [4,5] and the potential prevention of insulin resistance through anti-inflammatory effects [6].

According to the results of previous studies, adaptive rearrangements of metabolic processes occur in practically healthy North Americans, which is characterized by a decrease in antiatherogenic and increased atherogenic lipid fractions and minimization of the carbohydrate link of metabolism with a decrease in glucose, pyruvate and increased blood lactate [7-10]. Thus, according to numerous studies [11–16], carbohydrate metabolism in residents of the northern areas is characterized by a reduced level of glucose. At the same time, the age-specific relationship between ω-3 PUFA and carbohydrate metabolism remains underexplored.

Our study aim to determine the level and identify the nature of the relationship between the content of ω-3 polyunsaturated fatty acids (PUFAs) and the level of glucose in practically healthy people of mature age residing in climatically different territories.

2. Materials and methods
For the purpose of our study, the made use of the material from expeditions conducted between 2002 and 2018. A total of 1,689 individuals were surveyed. Depending on the region of residence, the
surveyed were divided into 2 groups: the Arctic region (AR) – 939, and the sub-Arctic Region (SAR) - 750. The Arctic region included the Nenets Autonomous District (Nelmin-Nos, Nes); Mezen District of the Arkhangelsk Region (Sovpolye, Soyan, and Dolgoschelie); and the Yamal-Nenets Autonomous District (Nadym, Seyakha, Tazovsky). The sub-Arctic Region included Arkhangelsk and Pinega. To eliminate the influence of photoperiodic factor, all expeditions were conducted during the period when daylight hours were on the increase. The cohorts had to be healthy men and women aged 22 to 60 years permanently residing in the territories indicated. It was a requirement that the cohorts were devoid of individuals with endocrinological issues, cardiovascular diseases and diabetes mellitus. All of the participants were questionnaire with regard to age, height, weight, blood pressure, bad habits (smoking, alcohol), actual nutrition; they also underwent physical examination by a doctor, on the basis of whose conclusion judgements were made about the state of health of the surveyed. Blood sampling was carried out on an empty stomach from the cubital vein (between 8:00 a.m and 10:00 a.m). The samples were placed in vacutainers "Beckton Dickinson BP". The study was carried out with the consent from the participants and in accordance with the requirements of the Helsinki Declaration of the World Medical Association on the ethical principles of medical research (2000).

Based on the classification adopted at the VII All-Union Conference on the problems of age morphology, physiology and biochemistry of the USSR Academy of Pedagogical Sciences (Moscow, 1965), the surveyed were divided into 3 age groups: group 1 - 22-35 years (1st stage of adulthood) - 270 individuals in AR and 224 individuals in SAR; group 2 - 36-45 years (2nd stage of adulthood) - 259 in AR and 168 in SAR; group 3 - 46-60 years old (3rd stage of adulthood) - 410 people in AR and 358 in SAR.

The content of essential ω-3 polyunsaturated fatty acids (PUFA) – linolenic (C183n3), eicosapentaenoic (C205n3), and docosahexaenoic (C2266) – was determined using liquid gas chromatography, with lipid preliminarily extracted from blood serum and FA methyl ethers subsequently obtained. The analysis of methyl derivatives of FAs was carried out on an Agilent 7890A gas chromatograph (flame ionization detector — FID, Agilent DB-23 capillary column 60 * 0.25 * 0.15) in the mode of programming the temperature and velocity of the nitrogen carrier gas. The identification of PUFAs was performed using Supelco 37 FAME C4-C24 (USA) and GLS-569B standards (Nu-Chek-Prep., INC, USA). The quantitative calculation of FAs was performed using the internal standard method (nonadecanoic acid) B.03.01 program (USA). In the serum, the glucose level (Glu) was determined on the Mars and Furuno CA-270 biochemical analyzers using Chronolab AG, Switzerland.

Statistical processing of the obtained data on ω-3 PUFA and carbohydrate metabolism parameters in practically healthy residents of the sub-Arctic and Arctic regions with regard to age was performed using the SPSS 13.0 software package [18]. For most of the indicators, the normal distribution of values was not observed, the analysis using non-parametric methods. The data are described in median values, as well as in 25 and 75 percentiles. The statistical significance of the differences (p) between the samples was determined using the Mann-Whitney U-test. The threshold value of the significance level was considered to be 0.05, and a trend value – over 0.05 but under 0.1. To clarify the relationship between the parameters of carbohydrate metabolism and the level of PUFAs, Kendall correlation analysis (τ-Kendall coefficient) was used.

3. Results
The content of all essential ω-3 PUFA in residents of AR is significantly higher than that in all mature age groups of SAR (Table 1).

The comparison of Me (25.75) α-linolenic (C18: 3n3), which is the substrate for the formation of the remaining ω-3 PUFA, showed its statistically significant increase in people of mature age (22-35, 36-45 and 46-60 years) in both the regions – 36-45- and 46-60-year-olds relative to 22-35-year-olds (SAR p = 0.011 p <0.001; AR p = 0.009, p <0.001). Despite this increase, the limits of its fluctuations in 22-35-year-old AR and SAR were multidirectional: in SAR they were wider, shifting to a greater extent towards lower limit (17.50% vs. 6.60%, p <0.001), while in AR, oppositely, towards higher limit (14.30% versus 7.30%, p = 0.017). At the same time, for 36-45- and 46-60-year-olds of both the regions,
the C18: 3n3 content tended to shift only towards higher level values, while the proportion of SAR individuals with excessive content of C18: 3n3 was less than in the AR (10.40% and 15.80% vs. 14.80% and for 26.40%, p = 0.216, p = 0.001).

Eicosapentaenoic acid was found to be increasing with age in mature residents of both the regions – in 36-45 and 46-60-year-olds compared to 22-35-year-olds (SAR p = 0.019, p < 0.001; AR p < 0.001, p < 0.001). Despite the increase in its level in blood serum, the limits of fluctuations in all the age groups of the SAR were varying greatly in the direction of lower standard limit from 23.20% to 15.60%, respectively, in 22-35 to 46-60-year-olds (p = 0.003, p = 0.001, p < 0.001). In the AR, such a dynamics was observed only in 22-35-year-olds with a 11.20% share of individuals with its deficit, while in 36-45- and 46-60-year-olds, on the contrary, the values tended to be higher than normal in 9.50% and 12.30% of individuals, respectively.

The analysis of the content of docosahexaenoic acid (C22: 6n3) in people of mature age in both the regions, has shown its significant increase in 46-60-year-olds compared to 22-35-year-olds (p < 0.001, p < 0.001); in the AR residents, the increase was found in 36-45-year-olds relative to 22-35-year-olds (p < 0.001). At the same time, the range of fluctuations of C22: 6n3 level in adult individuals of the SAR and the AR was found to shifted towards the lower limit; the proportion of people with its deficit in the SAR was 22.30%, 16.0% and 15.80% and in the AR 18.10%, 9.80% and 9.20%, respectively, in age groups 22-35, 36-46 and 46-60. At the same time, the largest proportion of individuals with excessive content of this acid was found in 13.0% of cases – in 46-60-year-old residents of AR.

The comparison of Me (25; 75) of glucose levels did not reveal any major differences between AR and SAR residents. However, cases of abnormally low glucose levels is found to decrease among 22-35 years and older – from 6.30% to 5.3% in SAR and from 13.3% to 8.8% in AR, whereas the percentage of individuals with abnormally high levels is found to increase – from 6.7% to 9.80% in SAR residents and from 8.1% to 15.6% in AR.

The correlation analysis showed a weak positive correlation in AR residents aged 22-35 between the glucose levels with eicosapentaenoic (r = 0.125, p = 0.003) and docosahexaenoic acids (r = 0.107, p = 0.011), and linolenic acid (r = 0.090, p = 0.031). The 36-45 year-olds showed weak positive correlation between glucose and linolenic acid (r = 0.115, p = 0.008) and eicosapentaenoic acid (r = 0.094, p = 0.029). A similar pattern was found in age group 46-60, where an increase in glucose level was influenced by an increase in linolenic (r = 0.167; p < 0.001) and eicosapentaenoic (r = 0.172; p < 0.001) and docosahexaenoic (r = 0.183; p < 0.001) acids. At the same time, SAR residents showed a weak positive relationship with docosahexaenoic acid only among 35–45 year-olds (r = 0.112, p = 0.046).

### Table 1: N- number of surveyed; Me (25; 75) - median values of indicators; p - level of significance of differences between regions; P(1-2),(1-3),(2-3) - level of significance of differences between age groups; *- boundaries of normal content.

| Parameter   | Region | n     | Me (25; 75)          | Quartile | Statistical significance (p) |
|-------------|--------|-------|----------------------|----------|-------------------------------|
|             |        |       |                      | 25       | 75                            |
| **22-35 (1)**|        |       |                      |          |                               |
| C183n3      | AR     | 259   | 4.64                 | 2.98     | 6.62                          | 0.000                      |
| (1,51-9,57)*| PR     | 206   | 3.54                 | 1.86     | 5.72                          |                           |
| C205n3      | AR     | 258   | 13.80                | 6.48     | 27.12                         | 0.000                      |
| (3,36-71,38)*| PR     | 203   | 7.11                 | 3.25     | 12.31                         |                           |
| C226n3      | AR     | 259   | 29.30                | 13.89    | 53.05                         | 0.048                      |
| (8,86-138,9)*| PR     | 206   | 20.56                | 9.40     | 50.81                         |                           |
| GLU         | AR     | 270   | 4.61                 | 4.05     | 5.22                          | 0.494                      |
| (3,9-6,1)*  | PR     | 224   | 4.67                 | 4.26     | 5.12                          |                           |
| **36-45 (2)**|        |       |                      |          |                               |
| C183n3      | AR     | 244   | 5.38                 | 3.53     | 7.17                          | 0.001                      |
| (1,51-9,57)*| PR     | 144   | 4.26                 | 2.50     | 6.35                          |                           |

3
Comparing the content of eicosapentaenoic acid, the age of individuals was found to be significant in all age groups. The content of AR is significantly higher than PR. The proportion of people with its deficiency decreased in SAR from 23.2% to 15.60% in PR and from 11.2% to 9.50% in AR, respectively. At the same time, in both regions, the age-related increase in α-linolenic acid was accompanied by a decrease in the proportion of people with its deficit – in SAR from 17.5% to 5.80%, and in AR – from 6.60% to 3.10%, respectively, whereas the proportion of individuals with its excessive content, on the contrary, was found to be increasing to 15.80% in SAR and 26.40% in AR.

Regardless of the region of residence, the content of eicosapentaenoic acid was found increasing from 22-35 to 46-60 years, especially in AR individuals, combined with a decrease in the occurrence of deficient states from 23.2% to 15.60% in PR and from 11.2% to 9.50% AR, respectively. At the same time, in contrast to SAR, there were individuals with excessive content of eicosapentaenoic acid, their number increasing from 5.0% to 12.30% in age groups 22-35 to 46-60. However, most prominent age-related, statistically significant changes were observed in individuals of the AR. Comparing the similar age groups of SAR and AR, it was found that the content of eicosapentaenoic acid in AR individuals was significantly higher than in PR in all age groups of mature age.

Regardless of the region, the age-related increase in glucose levels, their abnormally high values being frequent in the Arctic region, is associated with the increase in the content of essential ω-3 PUFAs.
which is verified by the big number of direct correlations between glucose and omega-3 PUFAs C18: 3n3, C205n3, C226n3), as compared with SAR residents (C226n3).

Thus, in practically healthy mature northerners (aged 22-35, 36-45 and 46-60), the increase in blood of ω-3 PUFA was observed due to the increase in linoleic, docosahexaenoic and eicosapentaenoic acids – more pronounced in the Arctic region (AR). Despite the increase with age of essential PUFAs in the blood, the largest lability in their content was found in residents of the AR aged 36-45 and 46-60, with a pronounced imbalance towards either lower than normal or higher than normal values in AR residents and only towards lower than normal values in SAR residents of all age groups.

In our opinion, the identified patterns are associated with an increase in actual nutrition, especially among the AR residents, of the proportion of carbohydrates while preserving the proportion of lipids, which increases the risk of developing the somatic diseases uncommon among the AR residents.

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5
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