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E.D. Okhlopkova, L.I. Konstantinova, A.A. Grigorieva, S.D. Efremova, L.D. Olesova, A.I. Yakovleva, S.I. Sofronova, T.E. Popova, A.N. Romanova

CONTENT OF HORMONES IN THE POPULATION OF SOUTH YAKUTIA WORKING IN AN AREA WITH NATURAL RADIATION

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A study of the level of hormones in the blood serum was carried out in 173 residents of the Aldan region aged from 22 to 75 years, of which 65 (39.8%) were men and 108 (60.2%) women, the average age was 44.0 (35. 0; 52.0) years. In the working population, there is functional tension of the pituitary-thyroid link, characterized by a higher frequency of occurrence of thyroid hormone levels below the normal T3total. in 27.2%, T3f. in 19.3% and T4f. in 11.6% of people, more pronounced in women. Increased concentrations of thyroid hormones T3f., T4f. and T4tot. observed with age, T3total and T4total in people with an increased body mass index. The presence of increased levels of antibodies to thyroid peroxidase in 18 (10.4%) people indicates a strained immune system, therefore it is recommended to include endocrinological examinations in periodic medical examinations

Keywords: radon, endocrine system, thyroid hormones, cortisol, South Yakutia.

Introduction. The largest uranium ore deposit in Russia is located in the Aldan region. The study and development of the territories of the Central Aldan gold-uranium mining region, in which the Elkon gold-uranium, Lebedinsky and Kuranakh gold mining nodes are identified, with the extraction of minerals has led to the emergence of centers of radioactive contamination (uranium ore dumps, mine workings). The ecological and geological assessment of the area is characterized as satisfactory for 53.5% of its territory, tense for 39.6% and crisis for 6.9%.

The maximum values of the exposure dose rate of gamma radiation in some areas are 1600-2150 μR/h (micro-roentgen per hour), the specific effective activity of natural radionuclides is 20441-23640 Bq/kg, and the uranium content is 1637-1888·10-4 mg/ kg2, which exceeds the background levels by almost 1000 times [12]. In the mountain taiga landscapes of the region, radiation varies from 30 to 50 μR/hour (in Central Yakutia the normal radiation background is 15 μR/hour) and contamination of wild plants (moss, berries and mushrooms) with natural radionuclides uranium - 238 and radium - 226 is noted [5 ,13]. Regular consumption of forest products with a high content of radionuclides can result in higher doses of internal radiation in individual citizens [8].

In the air of 46 premises located on the territory of the Aldan region, an excess of sanitary standards for radon content was noted (Rn222-429±86 Bq/m3) [14].

Radon is a radioactive gas and is a carcinogen; its radioactive particles, when accumulated in the body, can negatively affect human health, damage the DNA structure of cells, cause pathological processes, lung cancer, hormonal changes and increase mortality [1; 17]. It has been established that in the settlements of the Aldan mining region there has been a steady trend of deterioration in the health of the population [13].

The impact of climatic and environmental factors among residents of the North is accompanied by tension in adaptation processes, which is particularly manifested in the activation of the pituitary-thyroid system [9]. Thyroid hormones (T4 and T3) play an important role in maintaining the homeostasis of the internal environment, the normal functioning of all organs and systems (growth, development of the body, energy supply to organs and tissues, myocardial contractility, intestinal motility, etc.) [4]. Changes in the levels of thyroid hormones can disrupt the functioning of most organs and systems (musculoskeletal, cardiovascular and nervous systems, gastrointestinal tract) [2].

Therefore, for the timely development and implementation of measures for the prevention of chronic non-infectious diseases, the study of the state of the pituitary-thyroid system in residents living in areas with natural radiation is relevant.

The purpose of the study was to assess the level of thyroid hormones and cortisol in residents of the Aldan region.

Materials and methods. The study involved 173 residents from the city of Aldan and the city of Tommot, Aldan district, aged from 22 to 75 years, the average age was 44.0 (35.0; 52.0) years, of which 65 were men (39.8%) and women - 108 (60.2%), average age - 45.0 (35.0; 53.0) years, and 42.0 (36.0; 51.0) years, respectively. The study was carried out within the framework of the research work at the Federal State Budgetary Scientific Institution "Yakut Scientific Center for Medical Problems" "Regional characteristics of biochemical, immunological and morphological parameters in the indigenous and newcomer population of the Republic of Sakha (Yakutia) in health and pathology" (FGWU-2022-0014) and

Yakut Scientific Center of Complex Medical Problems: **OKHLOPKOVA Elena Dmitrievna** – Ph.D. in Biology , senior researcher, Federal State Budgetary Institution YSC CMP, elena_ohlopkova@mail.ru; **GRIGORYEVA Anastasia Anatolyevna** – junior researcher at the Federal State Budgetary Scientific Institution YSC CMP, nastiagrigoryeva@gmail.com; **KONSTANTINOVA Lena Ivanovna** – Ph.D. in Biology, research fellow at the Federal State Budgetary Institution YSC CMP, konstanta.l@mail.ru; **EFREMOVA Svetlana Dmitrievna** – junior researcher at the Federal State Budgetary Scientific Institution YSC KMP, esd64@mail.ru; **OLESOVA Lyubov Dygynovna** – Ph.D. in Biology, senior research scientist-supervisor. lab., at the Federal State Budgetary Scientific Institution YSC CMP, oles59@mail.ru; **YAKOVLEVA Alexandra Ivanovna** – research fellow at the Federal State Budgetary Scientific Institution YSC CMP, sashyak@mail.ru; **SOFRONOVA Sargylana Ivanovna** – Ph.D., chief researcher, head of the science division of the Federal State Budgetary Scientific Institution YSC CMP, sara2208@mail.ru; **POPOVA Tatyana Egorovna** – MD, Deputy Director of Research, Federal State Budgetary Scientific Institution YSC CMP, tata2504@yandex.ru; **ROMANOVA Anna Nikolaevna** – MD, Director, Federal State Budgetary Scientific Institution YSC CMP, ranik@mail.ru

the research work of the Academy of Sciences of the Republic of Sakha (Yakutia) "Evaluation levels of exposure of the population of the Aldan region due to natural sources of exposure and recommendations for carrying out protective measures to reduce them." The study was carried out with the informed consent of the subjects and was approved by the decision of the Local Ethics Committee at the Federal State Budgetary Institution "YSC KMP".

Blood sampling from all subjects was carried out in the morning (8-11 a.m.) on an empty stomach from the ulnar vein into a vacutainer with a coagulation activator, in a state of relative muscle rest.

Analysis of the levels of thyroid hormones (triiodothyronine-T3free, T3total, thyroxine-T4total, T4free), thyroid-stimulating hormone (TSH), thyroglobulin (TG), antibodies to thyroglobulin (anti-TG), antibodies to thyroid peroxidase (anti-TPO) and cortisol was carried out in blood serum by enzyme-linked immunosorbent assay (ELISA) on a Uniplan photometer using standard Vector Best kits (Russia), according to the manufacturer's instructions.

Body mass index (BMI) was calculated using the formula: BMI (kg/m²) = body weight (kg)/height (m²) [11].

Statistical processing of the data was carried out using the IBM SPSS Statistics 23 application package. Standard methods of variation statistics were used: calculation of average values (M), error of the average (m). The normality of distribution was checked by the Kolmogorov-Smirnov method. In the case of a normal distribution of quantitative indicators, the t-Student test was used to evaluate statistical hypotheses, and in the case of deviation from the normal distribution, the Mann-Whitney U test was used. The assessment of relationships between variables was carried out using the paired correlation method using Pearson (for metric variables) and Spearman criteria (for variables measured on a rank scale), where r is the correlation coefficient, p is the significance of the result.

Results and discussion. An analysis of the hormone levels in the residents of Aldan and Tommot in the pituitary-thyroid system showed that the average hormone level in the examined residents of the Aldan region varied within the reference values and did not have significant differences by gender (Table 1).

However, the levels of T3tot., T3st. were shifted to the lower limit of normal, which may be a criterion for a decrease in thyroid reserves. In residents of the North, the tension in the functional state of the pituitary-thyroid system can be contributed to by a natural lack of iodine, which is characteristic of the population of Siberia [7]. Inhibition of the functional activity of the thyroid gland (increased concentration of thyroid-stimulating hormone, decreased level of thyroxine, triiodothyronine), according to literature data, was noted among the population of patients with nodular goiter who were exposed to radiation in the past. [6].

Quantity T3tot. is often indicative of questionable results of T3 light tests, which are carried out to determine thyroid dysfunction in humans. The level of free hormones is less than 0.1% of their total amount, but it is the free fraction of hormones that is the most biologically active and it is this fraction that provides all the effects of thyroid hormones. The main point of application for triiodothyronine is DNA in combination with its receptors in the cell nucleus. Here, T3 activates transcription, synthesis of RNA and enzyme proteins involved in the body's most important metabolic reactions, including under stress; with its direct and irreplaceable participation, the processes of cell proliferation and differentiation occur [9].

Thyroxine is the main thyroid hormone and is produced only by thyroid cells. T4general is a total indicator of bound and free fractions of thyroxine. Most of T4 is in a state bound to transport proteins and is biologically inactive. All the main functions are performed by T4, circulating in the plasma in free form: it increases basal metabolism, supports energy metabolism, stimulates and normalizes processes in the central nervous system,

Table 1

Indicators of hormone levels in residents of the Aldan region

Indicator	Average value (M±m)		
	Total n=173	Men n=65	Women n=108
T3tot.(1.3-3.0 n/mol/l)	1.6±0.45	1.55±0.05	1.64±0.07
T3free (4-8.6 pmol/l)	4.82±0.104	5.04±0.16	4.54±0.14
T4total (52-155 nmol/l)	103.36±2.26	101.39±2.96	106.44±2.97
T4free (10.3-24.5 pmol/l)	15.13±0.28	15.29±0.37	14.66±0.45
TG (<50ng/ml)	7.16±1.11	5.81±1.85	9.13±1.69
TSH (0.4-5 mIU/l)	2.19±0.18	1.98±0.14	2.42±0.32
Anti-TG (up to 100IU/ml)	8.15±1.23	6.77±1.52	9.39±1.87
Anti-TPO (up to 30 U/ml)	15.63±3.56	11.62±5.12	18.07±4.81
Cortisol(190-690 nmol/l)	388.86±13.10	422.57±23.23	352.31±16.45 p=0.019

Table 2

Hormone levels depending on age

Indicator	Age group		
	1 group n=93	2 group n=64	3 group n=16
T3tot.(1.3-3.0 n/mol/l)	1.56±0.47	1.67±0.10	1.44±0.05
T3free (4-8.6 pmol/l)	4.51±0.13	5.03±0.19 p_{1-2}=0.037	4.69±0.20
T4tot. (52-155 nmol/l)	99.26±2.44	108.52±3.76	121.86±7.38 p_{1-3}=0.012 p_{2-3}=0.075
T4free (10.3-24.5 pmol/l)	14.50±0.34	15.25±0.60	16.81±0.54 p_{1-3}=0.012
TG (<50ng/ml)	7.06±1.49	8.63±2.35	6.49±1.33
TSH (0.4-5 mIU/l)	1.89±0.10	2.73±0.47 p_{1-2}=0.022	2.03±0.30
Anti-TG (up to 100IU/ml)	6.79±1.24	8.74±2.33	14.83±6.76
Anti-TPO (up to 30 U/ml)	12.73±4.60	20.84±6.52	12.49±10.12
Cortisol(190-690 nmol/l)	360.69±19.1	386.79±21.58	448.00 ±44.24

Note: 1-young (20-44 years old); 2-middle age (45-59 years); 3-elderly (60-74 years old)

and promotes bone tissue renewal. The effect of thyroid hormones on various parts of endocrine regulation depends on their concentration: in physiological doses they have an anabolic effect, in large doses they have a catabolic effect [16].

Thyroid-stimulating hormone is synthesized by the anterior pituitary gland and is the main regulator of the thyroid gland. TSH stimulates the synthesis of T3 and T4 by thyroid cells and their release into the blood. The synthesis and secretion of TSH is stimulated by thyroliberin, a hypothalamic peptide that is produced when the level of thyroid hormones in the bloodstream is low. Elevated levels of T3 and T4 suppress TSH secretion through a classical negative feedback mechanism [10]. This mechanism maintains a constant level of thyroid hormones, as well as metabolic stability. When connections between the thyroid gland, hypothalamus and pituitary gland are disrupted, the functioning of the endocrine glands is disrupted. Situations arise when, with high levels of T3 and T4, thyroid-stimulating hormone continues to increase.

The average TSH concentration varied within normal limits, elevated levels of TSH and TG were noted in 2 (1.2%) and 5 (2.9%) people, respectively, while elevated anti-TG levels of more than 100 IU/l were not detected. (Table 4), which is a favorable sign for the diagnosis and treatment of malignant neoplasms of the thyroid gland.

It has been proven that elevated TSH levels are associated with a higher risk of developing well-differentiated thyroid cancer and its more aggressive clinical course, manifested by a higher frequency of advanced stages of the tumor. A long-term increase in TSH stimulates the growth of residual thyroid tissue and tumor foci [3;18].

Thyroglobulin is a protein that is produced by the follicles of the thyroid gland. TG contains iodine, from which two main hormones are subsequently synthesized - thyroxine and triiodothyronine. Normally, the thyroid gland produces a small amount of TG. A significant increase in the level of TG in the blood is observed during tumor processes in the thyroid gland, so this indicator in some cases can serve as a tumor marker. Determination of serum TG biomarkers together with anti-TG is the only clinically recommended method for timely diagnosis of relapse of thyroid malignancies and treatment monitoring [3]. In benign diseases characterized by dysfunction of the thyroid gland (inflammation of the thyroid tissue - thyroiditis, Graves' disease or Basedow's disease, Hashimoto's thy-

Table 3

Hormone levels depending on body mass index

Indicator	Body mass index				
	1 group n=48	2 group n=62	3 group n=36	4 group n=14	5 group n=6
T3tot.(1.3-3.0 n/mol/l)	1.48±0.04	1.62±0.11	1.60±0.07	1.92±0.11 p_{1-4}=0.026	1.63±0.17
T3free (4-8.6 pmol/l)	4.35±0.19	4.86±0.18	5.15±0.23 1-3=0.033	4.57±0.48	4.46±0.32
T4tot. (52-155 nmol/l)	98.40±3.40	100.93±3.56	114.37±4.22 p_{1-3}=0.010 p_{2-3}=0.036	113.27±9.85	108.94±11.89
T4free (10.3-24.5 pmol/l)	14.19±0.47	15.48±0.61	15.78±0.52	12.39±0.97 p_{2-4}=0.025 p_{3-4}=0.011	15.36±1.55
TG (<50ng/ml)	6.23±2.59	7.82±1.96	5.01±1.47	16.75±6.95 p_{1-4}=0.025 p_{3-4}=0.019	15.18±6.18
TSH (0.4-5 mIU/l)	1.93±0.15	2.39±0.41	2.12±0.23	2.95±1.40	2.45±0.24
Cortisol (190-690 nmol/l)	363.62±26.46	381.94±23.09	426.62±30.33	341.13±29.87	308.72±60.1

Notes: 1-normal weight, BMI < 25; 2-overweight, BMI 25–29.9; 3-obesity I degree, BMI 30–34.9; 4-class II obesity, BMI 35–39.9; 5—grade III obesity, BMI >40.

Table 4

Frequency of hormonal imbalances in men and women in Aldan region, n/%

Indicator	Total	gender		Pearson chi-square	df	p
		Men	Women			
T3tot.(1.3-3.0 n/mol/l)						
1	47/27.2	20/30.8	27/25.0	1.231	2	0.540
2	125/72.3	45/69.2	80/74.1			
3	1/0.6	-	1/0.9			
T3free (4-8.6 pmol/l)						
1	33/19.1	8/12.3	25/23.1	5.121	2	0.077
2	139/80.3	57/87.7	82/75.9			
3	1/0.6	-	1/0.9			
T4tot. (52-155 nmol/l)						
1	-	-	-	0.929	1	0.335
2	164/94.8	63/96.9	101/93.5			
3	9/5.2	2/3.1	7/6.5			
T4free (10.3-24.5 pmol/l)						
1	20/11.6	4/6.2	16/14.8	3.584	2	0.167
2	152/87.9	61/93.8	91/84.4			
3	1/0.6	-	1/0.6			
TG (<50ng/ml)						
1		-	-	0.663	1	0.416
2	169/97.1	64/98.5	104/96.3			
3	5/2.9	1/1.5	4/3.7			
TSH (0.4-5 mIU/l)						
1	-	-	-	1.207	1	0.272
2	171/98.8	65/100	106/98.1			
3	2/1.2	-	2/1.9			
Anti-TPO (up to 30 U/ml)						
1	-	-	-	1.474	1	0.225
2	155/89.6	60/92.3	95/88.0			
3	18/10.4	5/7.7	13/12.0			
Anti-TG (up to 100IU/ml)						
2	173/100	64/100	109/100			

Note: 1-level below normal; Level 2 is normal; 3-level above normal.

roiditis), the TG level can also increase, and the disease can be accompanied by a decrease (hypothyroidism) or an increase (hyperthyroidism, thyrotoxicosis) in thyroid function. TG synthesis is under the control of TSH.

Antithyroglobulin antibodies (anti-TG) are specific immunoglobulins directed against the precursor of thyroid hormones. They are a specific marker of autoimmune thyroid diseases (Graves disease, Hashimoto's thyroiditis). The cells of the thyroid gland are collected in follicles, in which a protein specific only to this organ accumulates - thyroglobulin, which contains iodine. Subsequently, thyroid cells produce thyroxine and triiodothyronine from it. Sometimes thyroglobulin becomes a target for the immune system: antibodies (anti-TG) begin to be produced against it - the reason for this process is still precisely unknown. As a result, the normal synthesis of thyroid hormones from this protein is significantly disrupted: in some cases it decreases, in others it increases.

Correlation analysis showed a direct connection between the levels of T3free, T4free., T4tot. with age (r=0.190; p=0.012), (r=0.227; p=0.003), (r=0.202; p=0.007) and T3tot., T4tot. with body mass index (r=0.168; p=0.031), (r=0.216; p=0.005)

Depending on age, the subjects were divided into 3 groups: 1 - young (20-44 years), 2 - middle age (45-59 years), 3 - elderly (60-74 years). An increase in hormone levels was noted in the 2nd age group: T3 free by 10.3% (p=0.037) and TSH and 30.7% (p=0.022) compared with the 1st (Table 2), in the 3rd age group T4total. and T4 free by 18.54% and 10.9% in comparison with the 1st and 2nd age groups, respectively (Table 2).

Depending on body mass index, the subjects were divided into 5 groups: 1-normal weight, BMI < 25, 2-overweight, BMI 25–29.9, 3-I degree obesity, BMI 30–34.9, 4-obesity II degree, BMI 35–39.9, 5-obesity III degree, BMI >40. The average content of hormones in blood serum in all groups varied within the reference values. However, in persons of the 3rd group there is a slight increase in the concentration of some hormones: T3f. by 19.8%, T4tot. by 13.7% compared to group 1 and T4tot. by 11.7%, compared with group 2 (Table 3).

In the 4th group, an increase in T3total was noted. by 22.9%, TG by 62.8% in comparison with the 1st group and TG by 70% in comparison with the 3rd group. Level T4f. in this group with II degree obesity was the lowest, in comparison with the 2nd, 3rd groups by 20 and 21.5%, respectively (Table 3).

Analysis of the frequency of occurrence of hormonal disorders showed that the most pronounced deviations in the content of T3total. (reduced in 47 people (27.2%)), T3f. (reduced in 33 people (19.1%)), T4f. (decreased in 20 (11.5%)), anti-TPO (increased in 18 (11.5%)) (Table 4).

The frequency of disorders according to gender distribution did not have statistically significant differences, however, the increase in the frequency of occurrence of hormonal changes was more pronounced in women (Table 4). The number of indicators below generally accepted norms was noted T3total. in 20 (30.8%) men and 27 (25.0%) women, T3f. in 8 (12.3%) men and 25 (23.1%) women, T4f. in 4 (6.2%) men and 16 (14.7%) women. An elevated level was determined by T4tot. in 2 (3.1%) men and 7 (6.4%) women, T3 St free. and T4 free. – in 1 (0.9%) woman, TG – in 1 (1.5%) man and 4 (3.7%) women, TSH in only 2 (1.9%) women and anti-TPO in 5 (7.7%) men and 13 (12%) women (Table 4).

Antibodies to thyroid peroxidase are protein compounds whose action is directed against the enzymes responsible for the formation of the active form of iodine necessary for the synthesis of thyroid hormones. If anti-TPO is elevated, this is a marker of the presence of autoimmune thyroid diseases in the body. As a result of immune failure, a deficiency of thyroid hormones may develop.

The level of the stress hormone cortisol corresponded to the reference values, but in the group of men it was slightly higher by 16.6% (p = 0.019) (Table 1), which may be due to an increase in psycho-emotional stress. Cortisol concentrations also tended to increase with age (Table 2). In residents of northern latitudes, there was a twofold increase in the level of the stress hormone cortisol and psycho-emotional stress by 19.4%, compared with healthy residents of middle latitudes [15].

Thus, in the Aldan region, residents of the cities of Aldan and Tommot show changes in the content of thyroid hormones, which is characterized by a higher frequency of occurrence of low T3total levels. at (27.2%), T3free at (19.3%) and T4free at (11.6%), more clearly manifested in women. Increased concentration of hormones T3f., T4f. and T4total, observed with age. An increase in T3total and T4total levels is observed in people with an increased body mass index. The presence of elevated levels of antibodies to thyroid peroxidase in 18 (10.4%) people indicates a strained immune system, therefore it is recommended to include endocrinological examinations in periodic medical examinations.

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