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ГЕНЕТИКА ФОЛАТНОГО ЦИКЛУ, РІВЕНЬ ГОМОЦИСТЕЇНУ, ГОРМОНІВ ЩИТОПОДІБНОЇ ЗАЛОЗИ ТА ГІПОФІЗА У КРОВИ ДІТЕЙ ІЗ РАЙОНІВ, ЯКІ МЕЖУЮТЬ З ЧОРНОБИЛЬСЬКОЮ ЗОНОЮ ВІДЧУЖЕННЯ

FOLATE CYCLE GENETICS, BLOOD HOMOCYSTEINE, THYROID AND PITUITARY HORMONES IN CHILDREN FROM DISTRICTS BORDERING THE CHERNOBYL EXCLUSION ZONE

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The implementation of projects of the European Commission «Health and Ecological Programmes around the Chornobyl Exclusion Zone: Development, Training and Coordination of Health-Related Projects» and that of the Regional Council of Rhфne-Alpes (France) enabled to examine the state of health of most children from districts bordering the Chornobyl exclusion zone. At the same time, hyperhomocysteinemia was first found in 73.2% of the examined children aged 12-17 years old from Ivankivskyi district and in 79.8% of the examined children of the same age from Poliskyi district [1].

Hyperhomocysteinemia or elevation above the physiological level in a blood concentration of a sulfur-containing amino acid homocysteine signals that there is an unfavourable state of metabolism in a body. In adults, it may be combined with a number of severe conditions leading to disability and mortality [2-7]. Given the importance of this issue for medical science and practical health care, it is necessary to investigate the causes of this phenomenon. In particular, genetic changes in the folate

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Метою роботи *було визначення взаємозв'язку між станом генетичного апарату фолатного циклу, змістом гомоцистеїну, гормонів щитоподібної залози та аденогіпофіза у крови дітей із Іванківського і Поліського районів Київської області, які межують з Чорнобильською зоною відчуження (ЧЗВ).*

Методи. *Імунохімічний, генетичний, статистичний.*

Результати. *У 158 дітей із Поліського району та 178 дітей із Іванківського визначався вміст у крови гомоцистеїну (H_{cy}), тиреотропного гормону гіпофіза (ТТГ), вільного трийодтироніну (T_3), вільного тироксину (T_4), також оцінювався стан генетичної системи фолатного циклу (ФЦ). Середній вік обстежених склав (15,2 ± 0,9) років (95% ДІ 15,0-15,4 років). З урахуванням генотипів ФЦ було сформовано генетичні підгрупи, засновані на 100% представництві одного конкретного генотипу. Лабораторне обстеження проведено двічі: у квітні і грудні 2015 року (до і після пожеж у ЧЗВ). Встановлено, що у загальній групі дітей, а також у більшості аналізованих генетичних підгруп рівень H_{cy} і гормонів щитоподібної залози (ЩЗ) у дітей із Іванківського району був достовірно вищим, ніж у дітей із Поліського. При цьому у загальній групі, а також у більшості генетичних підгруп дітей із Іванківського району між H_{cy} і ТТГ виявлено прямий кореляційний зв'язок, який був відсутнім у дітей із Поліського району. Рівень H_{cy} у крови дітей обох районів був достовірно вищим у підгрупі, що містить тільки гомозиготні варіанти алелі Т генетичного поліморфізму MTHFR:677 порівняно з підгрупами, що містять нейтральні алелі цього ж поліморфізму. При цьому були відсутні відмінності щодо ТТГ, T_3 і T_4.*

Висновки. *Проведений аналіз дозволив встановити синхронну реакцію метаболічних циклів, що забезпечують обмін H_{cy} і гормонів ЩЗ в організмі підлітків незалежно від генотипів ФЦ. Кореляційний аналіз, а також результати статистичного аналізу свідчать про те, що підвищення рівня H_{cy} у крови дітей індукувало синтез ТТГ і T_3. Отримані результати свідчать про тісний зв'язок між гормоногенезом ЩЗ і обміном сірковмісних амінокислот метіоніну і H_{cy}. Найбільш імовірною причиною підвищення рівня H_{cy} і внаслідок цього гормонів гіпофізарно-тиреоїдної вісі у крови дітей із районів, що межують з ЧЗВ, є пожежі лісу, який містить довгоіснуючі радіоактивні елементи.*

Ключові слова: гомоцистеїн, фолатний цикл, генетичні підгрупи, гормони щитоподібної залози і гіпофіза, підлітки, радіоактивно забруднені території.

cycle [8, 9] and thyroid diseases [10] are pointed out as causes of hyperhomocysteinemia. In this regard, it is important to identify a relationship between the state of folate cycle genetic apparatus and blood levels of homocysteine, thyroid and pituitary hormones in children living in districts bordering the Chornobyl exclusion zone. At the same time, one should take into account the effect of an external environmental factor associated with the Chornobyl exclusion zone on the body of children.

The purpose of the current research was to identify interrelations between the state of folate cycle genetic apparatus and blood levels of homocysteine, thyroid and adenohypophysis hormones in children from Ivankivskyi and Poliskyi districts, Kyiv region, bordering the Chornobyl exclusion zone.

Material and methods. The research was carried out in Poliskyi and Ivankivskyi districts, Kyiv region, whose territories are contaminated with radionuclides as a result of the accident at the Chornobyl nuclear power plant (a ^{137}Cs soil contamination density is <2 Ci/sq.km [11]). The age of the children at the time of the examination was (15.2 ± 0.9) years old (95% CI 15.0-15.4 years old).

158 children from Poliskyi district and 178 children from Ivankivskyi district underwent laboratory examination. At the same time, we assessed blood levels of homocysteine (H_{cy}), pituitary thyroid stimulating hormone (TSH), free triiodothyronine (T_3), free thyroxine (T_4) and the state of the genetic system of the folate cycle (FC).

The examined children had blood drawn from the ulnar vein after fasting in the morning to carry out the above studies. At the time of blood draws, all of them attended school. Blood from the children of Poliskyi district was drawn on 02.04.2015, from children of Ivankivskyi district on 18.12.2015.

The blood samples were analysed at a laboratory certified under quality standards with a financial support of the Regional Council of Rhône-Alpes (France) and were agreed with the parents.

TSH, T_3 and T_4 were determined using an electrochemiluminescent immunoassay (ECLIA) method. Analyser and test kit: Cobas 6000, Roche Diagnostics (Switzerland).

The blood H_{cy} concentration was measured using a chemiluminescent immunoassay (CLIA) method. Analyzer and test kit: Architect 1000 (ABBOT Diagnostics (USA)). The blood Hcy level in children of more than 10 µmol/L was defined as hyperhomocysteinemia.

The following allelic variants were identified during genetic analysis of folate cycle: C677T and A1298C of the MTHFR gene (synthesis of the methylenetetrahydrofolate reductase enzyme), A2756G of the MTR gene (synthesis of the B_{12}-dependent methionine synthase enzyme) and A66G of the MTRR gene (synthesis of the methionine synthase reductase enzyme). A real-time PCR method was used. Analyser and test kit: DT-96 detecting thermocycler, DNA-Technology (Russia).

Taking into account the folate cycle genotypes, genetic subgroups were formed based on 100% representation of one specific genotype (table 1).

The statistical processing of the findings was performed using the IBM SPSS Statistics 22 software (USA). The arithmetic mean (M), standard error of mean (m), confidence interval for the mean value (95% CI), median (Me), interquartile range (IQR), minimum and maximum parameter values and percentiles were calculated for the variables analysed.

The distribution hypothesis was tested (a Kolmogorov-Smirnov test). All the studied parameters did not conform to the normal distribution law, thus, a non-parametric Mann-Whitney U test was used to compare values. The statistical significance of variables was assessed by determining a significance level for p with the help of the statistical software programme. The Student's t-test was used to compare relative values. The critical level of significance for the null hypothesis (p) was set at 0.05. Associations between H_{cy}, TSH, T_3 and T_4 values were identified with the help of the Spearman's rank correlation coefficient (rxy). The strength of an association was assessed according to a typical scale: weak – 0 to 0.299; moderate – 0.3 to 0.699; strong – 0.7 to 1.0.

Results and their discussion. The level of H_{cy} and thyroid hormones (T_3 and T_4) was statistically significantly higher in children from Ivankivskyi district than in those from Poliskyi district in a total group of children (tables 2-4).

The H_{cy} level was statistically significantly higher in the blood of children from Ivankivskyi district comprising genetic subgroups 1, 2, 4, 5, 7, 8, 11, 12 than in that of children from Poliskyi district from similar subgroups (tables 2-4).

Table 1

Subgroups of children with a specific folate cycle genotype

Subgroup	Genotype	Number of children in subgroups	
		Poliskyi district	Ivankivskyi district
1	A/A MTR:2756	104	106
2	A/G MTR:2756	45	61
3	G/G MTR:2756	9	11
4	A/A MTHFR:1298	82	89
5	A/CMTHFR:1298	60	80
6	C/C MTHFR:1298	16	9
7	C/C MTHFR:677	79	80
8	C/T MTHFR:677	60	83
9	T/T MTHFR:677	19	15
10	A/AMTRR:66	32	27
11	A/G MTRR:66	72	93
12	G/G MTRR:66	54	58
Total group		158	178

The level of thyroid hormones was higher in genetic subgroups 1, 5, 7, 8, 11, 12 of children from Ivankivskyi district than in similar subgroups of children from Poliskyi district. At the same time, this related to two hormones simultaneously (T_3 and T_4) in the subgroups 1, 5, 11, 12, and concerned only T_3 in the subgroup 7 and only T_4 in the subgroup 8.

Thus, a higher level of H_{cy} and thyroid hormones was simultaneously recorded in children from Ivankivskyi district compared to those from Poliskyi district in most of the analysed subgroups.

There were no differences between values of T_3 and T_4 with the existing differences in the blood concentration of H_{cy} in the subgroups 2 and 4 of children from Ivankivskyi and Poliskyi districts (tables 2-4).

There were no differences both in relation to H_{cy} and both thyroid hormones between children from the above districts in the subgroups 3, 6, 9 and 10 (tables 2-4).

The TSH blood level did not differ statistically in the children from Poliskyi and Ivankivskyi districts in all subgroups except a subgroup 12 with the main G/G MTRR:66 genotype.

The H_{cy} blood level was statistically significantly higher in the subgroup 9 containing only homozygous variants of the MTHFR:677 genetic polymorphism T allele compared to subgroups containing neutral C alleles of the same polymorphism – subgroups 7 and 8 both in the children from Poliskyi district and those from Ivankivskyi district (table 5). At the same time, there were no differences in relation to TSH, T_3 and T_4.

A direct association was found between Hcy and TSH in a total group as well as in most genetic subgroups from Ivankivskyi district (table 6). A direct association was also recorded between H_{cy} and T_3, but in a smaller number of subgroups.

The H_{cy}-TSH and H_{cy}-T_3 associations were identified simultaneously in the subgroup 4 (table 6). There was no association between H_{cy} and T_4 in the total group and in separate genetic subgroups.

There was no direct association between H_{cy} и TSH in the total group of children and all analysed subgroups of children from Poliskyi district. A direct association was observed between H_{cy} and T_3 in the subgroups 1 and 12 (table 7). № association was found between H_{cy} and T_4.

The MTHFR:677 genetic polymorphism T allele was almost uniformly present in all subgroups of children from Poliskyi and Ivankivskyi districts formed on the basis of the MTR:A2756G, MTHFR:A1298C (A/A, A/C genotypes), MTRR:A66G genetic polymorphisms (table 8).

In this regard, the role of the above allele can not be considered as the main reason for a higher blood level of H_{cy} in children from Ivankivskyi district compared to those from Poliskyi district.

The findings show synergism in values of H_{cy}, T_3 and T_4 in the blood of children from the groups of adolescents under study from the districts bordering the Chornobyl exclusion zone.

Higher levels of Hcy were found in most genetic subgroups of children from Ivankivskyi district compared to those from Poliskyi district. At the same time, more higher levels of thyroid hormones were recorded in 75.0% of cases.

№ genetic subgroups were found in which there were differences between hormone levels

Table 2

Statistical characteristics of values of H_{cy}, TSH, T_3 and T_4 in genetic subgroups of children from Poliskyi district

Subgroup	H_{cy}, µmol/L		TSH, mIU/mL		T_3, pg/ml		T_4, ng/dl	
	Me	IQR	Me	IQR	Me	IQR	Me	IQR
1	10.26	8,39-13.56	1.82	1.39-2.43	4.04	3.79-4.59	1.19	1.09-1.29
2	9.37	7.75-10.95	1.94	1.51-2.65	4.24	3.84-4.68	1.15	1.06-1.25
3	11.13	10.17-12.32	2.10	1.19-2.41	4.37	3.53-5.63	1.04	0.98-1.32
4	10.14	7.99-13.04	1.89	1.29-2.55	4.11	3.79-4.69	1.18	1.06-1.28
5	10.19	9.01-13.19	1.82	1.47-2.37	4.02	3.71-4.57	1.17	1.08-1.28
6	10.31	8.00 -12.69	1.93	1.62-3.22	4.18	3.92-4.64	1.20	1.10-1.35
7	9.44	7.93-11.16	1.80	1.34-2.39	4.09	3.82-4.55	1.20	1.09-1.29
8	10.24	8.42-13.18	1.82	1.42-2.55	4.02	3.75-4.68	1.15	1.04-1.25
9	14.47	10.15-22.78	2.26	1.50-3.14	4.38	3.68-5.02	1.23	1.05-1.29
10	9.26	8.03-13.13	1.92	1.67-2.36	4.20	3.85-4.69	1.21	1.12-1.34
11	10.08	7.98-11.99	1.60	1.26-2.40	4.07	3.68-4.66	1.17	1.04-1.28
12	10.81	9.13-14.18	2.27	1.43-2.82	4.08	3.84-4.53	1.17	1.09-1.28
Total group	10.17	8.30 –13.10	1.86	1.41-2.48	4.10	3.79-4.62	1.18	1.07-1.28

Table 3

Statistical characteristics of values of H_{cy}, TSH, T_3 and T_4 in genetic subgroups of children from Ivankivskyi district

Subgroup	H_{cy}, µmol/L		TSH, mIU/mL		T_3, pg/ml		T_4, ng/dl	
	Me	IQR	Me	IQR	Me	IQR	Me	IQR
1	11.93	9.73-13.76	1.86	1.33-2.57	4.37	3.99-4.74	1.26	1.14-1.32
2	11.57	10.23-13.33	1.72	1.30-2.22	4.41	4.00-4.81	1.21	1.09-1.30
3	9.46	8.49-11.58	1.79	1.20-1.93	4.59	3.96-4.65	1.23	1.13-1.33
4	11.53	9.64-14.22	1.85	1.29-2.43	4.35	3.88-4.75	1.22	1.12-1.31
5	11.91	10.42-13.30	1.77	1.31-2.36	4.43	4.06-4.79	1.25	1.17-1.32
6	9.09	7.91-12.56	1.93	1.45-2.73	4.38	4.05-4.91	1.13	1.00-1.19
7	11.36	9.38-12.97	1.76	1.30-2.29	4.44	4.08-4.81	1.24	1.12-1.31
8	11.61	9.86-13.31	1.83	1.30-2.22	4.33	3.99-4.66	1.23	1.14-1.30
9	16.59	12.10-26.71	2.47	1.43-3.13	4.12	3.84-4.88	1.20	1.14-1.29
10	10.86	9.19-13.23	1.79	1.39-2.77	4.41	3.96-4.60	1.25	1.14-1.33
11	11.58	9.46-13.22	1.79	1.31-2.57	4.42	4.01-4.81	1.22	1.12-1.30
12	12.13	10.74-14.49	1.83	1.27-2.24	4.33	3.99-4.77	1.27	1.15-1.31
Total group	11.62	9.69 -13.39	1.80	1.30-2.42	4.40	3.99-4.75	1.23	1.14-1.31

FOLATE CYCLE GENETICS, LEVEL OF HOMOCYSTEINE, THYROID AND PITUITARY HORMONES IN THE BLOOD AMONG THE CHILDREN FROM THE DISTRICTS BORDERING THE CHORNOBYL EXCLUSION ZONE

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Objective: *The aim of the study was to identify interrelations between the state of folate cycle genetic apparatus and blood levels of homocysteine, thyroid and adenohypophysis hormones in the blood among the children from Ivankivskyi and Poliskyi districts, Kyiv region, bordering the Chornobyl exclusion zone (ChEZ).*
Methods: *Immunochemical, genetic, statistical ones.*
Results: *We measured blood levels of homocysteine (H_{cy}), pituitary thyroid-stimulating hormone (TSH), free triiodothyronine (T_3), free thyroxine (T_4) in 158 children from Poliskyi district and 178 children from Ivankivskyi district and assessed the state of a genetic system of the folate cycle (FC). The average age of the examined was (15.2 ± 0.9) years old (95% CI 15.0-15.4 years old). Taking into account the FC genotypes, genetic subgroups were formed, they were based on 100% representation of one specific genotype. The laboratory examination was carried out twice: in April and December 2015 (before and after the fires in the ChEZ). It was found out that in the total group of the children, as well as in most of analyzed genetic subgroups, the level of H_{cy} and thyroid hormones (TG) in the children from Ivankivskyi district was statistically significantly higher than in those from Poliskyi district. At the same time, a direct association between Hcy and TSH was observed in the total group, as well as in most of the genetic subgroups of children from Ivankivskyi district, and this ssociation was absent in the children from Poliskyi district. The blood level of H_{cy} both in the children from Poliskyi district and in the children from Ivankivskyi district was statistically significantly higher in the subgroup containing only homozygous variants of the T allele of the MTHFR:677 genetic polymorphism in comparison with the subgroups containing neutral C alleles of the same polymorphism. At the same time, there were no differences for TSH, T_3 and T_4.*
Conclusions: *The analysis enabled to establish a synchronous reaction of metabolic cycles ensuring the metabolism of H_{cy} and thyroid hormones in the adolescents, regardless of the FC genotypes. Correlation analysis, as well as the results of statistical analysis, indicate that an increase in the level of H_{cy} in the blood of children induced the synthesis of TSH and T_3. The results show a close relationship between thyroid hormone genesis and the metabolism of methionine sulfur-containing amino acids and H_{cy}. A forest fire, containing long-lived radioactive elements, is the most likely reason for the increase of H_{cy} level and, as a result, the hormones of the pituitary-thyroid axis in the blood of the children living in the districts, bordering the ChEZ.*
Keywords: homocysteine, folate cycle, thyroid and pituitary hormones, adolescents, radiation contaminated areas.

and there were no differences between H_{cy} levels.

The high blood level of H_{cy} in children from Ivankovsky district allowed to confirm synchronization of reactions of metabolism of H_{cy} and thyroid and pituitary hormones using a correlation analysis.

An increase in the H_{cy} level was found to induce the synthesis of TSH and T_3 in the body of children living under conditions of radiation exposure associated with the Chornobyl nuclear power plant accident.

The absence of significant statistical differences in the levels of H_{cy}, TSH, T_3 and T_4 was recorded in the subgroup 9 where there are homozygous variants of the MTHFR:677 genetic polymorphism T risk allele which results in high blood Hcy levels regardless of environmental exposure.

Table 4

Results of statistical differences in variables of children from Poliskyi and Ivankivskyi districts

Subgroup	H_{cy}, µmol/L		TSH, mIU/mL		T_3, pg/ml		T_4, ng/dl	
	Mann-Whitney U test	Significance level, p	Mann-Whitney U test	Significance level, p	Mann-Whitney U test	Significance level, p	Mann-Whitney U test	Significance level, p
1	4384.000	0.010	5444.500	0.878	4215.500	0.003	4447.500	0.016
2	721.500	0.0001	1151.000	0.157	1122.500	0.110	1101.500	0.083
3	35.000	0.271	39.000	0.425	44.000	0.676	38.000	0.382
4	2659.500	0.002	3558.500	0.780	3163.500	0.133	3038.000	0.059
5	1769.500	0.008	2215.000	0.436	1659.500	0.002	1709.000	0.004
6	68.000	0.821	64.000	0.651	58.000	0.428	48.500	0.183
7	2068.500	0.0001	3013.500	0.614	2183.500	0.001	2857.500	0.297
8	1917.000	0.019	2357.500	0.588	2012.500	0.051	1651.000	0.001
9	134.000	0.768	141.500	0.972	137.000	0.849	137.000	0.849
10	314.500	0.074	396.000	0.584	431.000	0.988	396.000	0.584
11	2405.500	0.002	3042.500	0.315	2486.500	0.005	2661.500	0.024
12	1201.500	0.034	1206.500	0.036	1176.000	0.023	1199.000	0.033
Total group	10450.500	0.0001	13319.000	0.403	11115.000	0.001	11461.500	0.003

The results obtained make it possible to state about external environmental effects on the body of children living near the Chornobyl exclusion zone during the period between two blood draws.

The most probable environmental factor causing significant metabolic diseases in the body of most children living in settlements located near the Chornobyl exclusion zone should be considered fires of forests, which have accumulated a huge amount of long-lived radioactive elements over the 30 post-Chornobyl years [12, 13].

A fire of forest and meadow vegetation occurred on an area of 10127 ha in the Chornobyl exclusion zone on April 26-29, 2015. Therefore the maximum density of territory contamination in low-fire areas in some quarters of the Lubianskyi forestry was 1040 kBq/sq.m – ^{137}Cs; 368 kBq/sq.m – ^{90}Sr; 11.4 kBq/sq.m – $^{238-240}Pu$ and 14.4 kBq/sq.m – ^{241}Am [14].

Experimental research has established a negative effect of ^{137}Cs and ^{90}Sr radionuclides contained in oats consumed by laboratory animals on the metabolism of methionine, and thus its daughter product, homocysteine [15].

The burning of trees is also accompanied by the release into the environment of fine particles 0.1-2.5 µm in size (PM2.5), including black carbon, capable of penetrating the respiratory tract, reaching the bronchioles and alveoli [16], causing metabolic disturbances in the cardiovascular system [17]. A positive association is known between black, as well as organic carbon and blood levels of H_{cy} in older men. At the same time, no associations were recorded between the level of H_{cy} and PM2.5 [18].

The data obtained show a synchronous increase in the levels of H_{cy} and thyroid hormones in the body of children of most genetic subgroups after forest fires in the Chornobyl exclusion zone in 2015.

Table 5

Statistically significant differences when comparing blood Hcy values in children of subgroups № 9[1] and № 7[2], № 9[1] and № 8[2] from Poliskyi and Ivankivskyi districts

Variables	Poliskyi district				Ivankivskyi district			
	Subgroups 9 and 7		Subgroups 9 and 8		Subgroups 9 and 7		Subgroups 9 and 8	
	n	H_{cy}	n	H_{cy}	n	Hcy	n	H_{cy}
Average rank[1]	19	71.11	19	52.63	15	68.27	15	66.77
Average rank[2]	79	44.30	60	36.00	80	44.20	83	46.38
Mann-Whitney U test	340.00		330.00		296.00		363.50	
Asymptotic significance (2-tailed), p	0.0001		0.006		0.002		0.011	

Table 6

Results of correlation analysis between values of H_{cy} and T_3, H_{cy} and TSH in genetic subgroups of children of Ivankivskyi districts

Sub-group	Genotype	Correlation coefficient	Parameters: H_{cy}, µmol/L; T_3, pg/ml	Parameters: H_{cy}, µmol/L; TSH, mIU/mL
2	A/G MTR:2756	Spearman's	0.129	0.278*
		p	0.321	0.030
		N	61	61
4	A/A MTHFR:1298	Spearman's	0.299**	0.288**
		p	0.004	0.006
		N	89	89
6	C/C MTHFR:1298	Spearman's	0.617	0.733*
		p	0.077	0.025
		N	9	9
7	C/C MTHFR:677	Spearman's	0.256*	0.023
		p	0.022	0.838
		N	80	80
8	C/T MTHFR:677	Spearman's	0.075	0.278*
		p	0.498	0.011
		N	83	83
10	A/A MTRR:66	Spearman's	0.502**	0.108
		p	0.008	0.592
		N	27	27
11	A/G MTRR:66	Spearman's	0.053	0.303**
		p	0.612	0.003
		N	93	93
Total group		Spearman's	0.157*	0.206**
		p	0.037	0.006
		N	178	178

*Note: * – correlation is significant at the <0.05 level (2-tailed).*
*** – correlation is significant at the <0.01 level (2-tailed).*

Conclusions

Laboratory examination of children from districts bordering the Chornobyl exclusion zone in April and December 2015 enabled to establish a synchronous reaction of metabolic cycles supporting the metabolism of H_{cy} and thyroid hormones in a developing body, irrespective of folate cycle genotypes.

The conducted correlation analysis, as well as the results of statistical analysis, show that an increase in the level of H_{cy} in the blood of children induced the synthesis of TSH and T_3.

The absence of differences in levels of H_{cy}, TSH, T_3 and T_4 between similar subgroups of children from Ivankivskyi and Poliskyi districts that include 100% carriership of the T/T MTHFR:677 genotype is associated with the T risk allele causing high blood levels of H_{cy} regardless of environmental exposure.

The results obtained show a close relationship between thy-

ГЕНЕТИКА ФОЛАТНОГО ЦИКЛА, УРОВЕНЬ ГОМОЦИСТЕИНА, ГОРМОНОВ ЩИТОВИДНОЙ ЖЕЛЕЗЫ И ГИПОФИЗА В КРОВИ ДЕТЕЙ ИЗ РАЙОНОВ, ГРАНИЧАЩИХ С ЧЕРНОБЫЛЬСКОЙ ЗОНОЙ ОТЧУЖДЕНИЯ

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Цель работы*: определение взаимосвязи между состоянием генетического аппарата фолатного цикла, содержанием гомоцистеина, гормонов щитовидной железы и аденогипофиза в крови детей из Иванковского и Полесского районов Киевской области, граничащих с Чернобыльской зоной отчуждения (ЧЗО).*

Методы исследования. *Иммунохимический, генетический, статистический.*

Результаты. *У 158 детей из Полесского района и 178 детей из Иванковского определялось содержание в крови гомоцистеина (H_{cy}), тиреотропного гормона гипофиза (ТТГ), свободного трийодтиронина (T_3), свободного тироксина (T_4), также оценивалось состояние генетической системы фолатного цикла (ФЦ). Средний возраст обследованных составил (15,2 ± 0,9) лет (95% ДИ 15,0-15,4 лет). С учетом генотипов ФЦ были сформированы генетические подгруппы, основанные на 100% представительстве одного конкретного генотипа. Лабораторное обследование проведено дважды: в апреле и декабре 2015 года (до и после пожаров в ЧЗО). Установлено, что в общей группе детей, а также большинстве анализируемых генетических подгрупп уровень H_{cy} и гормонов щитовидной железы (ЩЖ) у детей из Иванковского района был достоверно выше, чем у детей из Полесского района. При этом в общей группе, а также в большинстве генетических подгрупп детей из Иванковского района между H_{cy} и ТТГ выявлена прямая корреляционная связь, отсутствующая у детей из Полесского района. Уровень H_{cy} в крови у детей из этих районов был достоверно выше в подгруппе, содержащей только гомозиготные варианты аллели Т генетического полиморфизма MTHFR:677, по сравнению с подгруппами, содержащими нейтральные аллели С этого же полиморфизма. При этом отсутствовали различия в отношении ТТГ, T_3 и T_4*

Выводы. *Проведенный анализ позволил установить синхронную реакцию метаболических циклов, обеспечивающих обмен H_{cy} и гормонов ЩЖ в организме подростков, независимо от генотипов ФЦ. Корреляционный анализ, а также результаты статистического анализа свидетельствуют о том, что повышение уровня H_{cy} в крови детей индуцировало синтез ТТГ и T_3. Полученные результаты говорят о тесной связи между гормоногенезом ЩЖ и обменом серосодержащих аминокислот метионина и гомоцистеина. Наиболее вероятной причиной повышения уровня H_{cy} и вследствие этого гормонов гипофизарно-тиреоидной оси в крови детей, проживающих в районах, граничащих с ЧЗО, стали пожары леса, содержащего долгоживущие радиоактивные элементы.*

Ключевые слова: гомоцистеин, фолатный цикл, гормоны щитовидной железы и гипофиза, подростки, радиоактивно загрязненные территории.

roid gland hormonogenesis and metabolism of sulfur-containing amino acids – methionine and H_{cy}.

Fires of forests that contain long-lived radioactive elements are the most likely reason for an increase in the H_{cy} level and as a result pituitary-thyroid axis hormones in the blood of children living in districts bordering the Chornobyl exclusion zone.

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Table 7

Results of correlation analysis between values of H_{cy} and T_3, H_{cy} and TSH in genetic subgroups of children of Poliskyi districts

Subgroup	Genotype	Correlation coefficient	Parameters		Parameters	
			H_{cy}, μmol/L	T_3, pg/ml	H_{cy} μmol/L	TSH, mIU/mL
1	A/A MTR:2756	Spearman's	0.204*		0.010	
		p	0.038		0.917	
		N	104		104	
12	G/G MTRR:66	Spearman's	0.424**		0.195	
		p	0.001		0.158	
		N	54		54	
Total group		Spearman's	0.130		-0.002	
		p	0.102		0.984	
		N	158		158	

*Note: * – correlation is significant at the <0.05 level (2-tailed).*
*** – correlation is significant at the <0.01 level (2-tailed).*

Table 8

Proportion of cases of carriership of MTHFR:C677T polymorphism T allele in genetic subgroups of children from Ivankivskyi and Poliskyi districts

Sub-group	Genotype	Number of cases of carriership of MTHFR:C677T polymorphism T allele in subgroups of children			
		Ivankivskyi district		Poliskyi district	
		Abs.	%	Abs.	%
1	A/A MTR:2756	61	57.55	50	48.08
2	A/G MTR:2756	32	52.46	24	53.33
3	G/G MTR:2756	5	45.45	5	55.56
4	A/A MTHFR:1298	60	67.42	54	65.85
5	A/C MTHFR:1298	38	47.50	25	41.67
6	C/C MTHFR:1298	0	0	0	0
7	C/C MTHFR:677	0	0	0	0
8	C/T MTHFR:677	83	100	60	100
9	T/T MTHFR:677	15	100	19	100
10	A/A MTRR:66	14	51.85	14	43.75
11	A/G MTRR:66	53	56.99	37	51.39
12	G/G MTRR:66	31	53.45	28	51.85
Total group		98	55.06	79	50.00

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