# CHAPTER «MEDICAL SCIENCES»

## GENETIC REGULATION OF THE METABOLISM OF METHIONINE, HOMOCYSTEINE AND VITAMINS B9, B12 IN CHILDREN LIVING NEAR THE CHERNOBYL EXCLUSION ZONE

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**Abstract.** In 2015, the majority of children living near the Chernobyl exclusion zone had an elevated level of homocysteine in the blood, however, at the same time, the level of serum vitamins $B_9$ and $B_{12}$ was determined within the reference values. Considering that B vitamins are cofactors of the folate cycle enzymes that regulate the metabolism of the sulfur-containing amino acids methionine and homocysteine, it was important to determine the causes of this phenomenon. **The purpose of this study** was to identify correlations between vitamins $B_{12}$, $B_9$ and homocysteine, as well as vitamin $B_6$, taking into account the genetic factor, in a group of children living under constant radiation exposure associated with the Chernobyl nuclear power plant accident. **Research methods.** The results of laboratory and instrumental examination of 178 children aged 12-17 from the Ivankovsky district of the Kyiv region were used. Immunochemical, genetic, spectrometric and statistical research methods were used. **Results.** Correlation analysis was used to study the relationship between the levels of homocysteine, $B_{12}$, $B_9$, $B_6$ in the blood of children, taking into account their genetic status of folate cycle and the content of $^{137}Cs$ in the body. An elevated level of homocysteine (more than 10.0 μmol/l) was detected in 73.0 % of the examined patients. The causes

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of hyperhomocysteinemia in children living near the Chernobyl exclusion zone are mutations in the folate cycle genes, insufficient content of vitamins $B_9$ and $B_{12}$ in the body, as well as the impact of an environmental factor associated with the Chernobyl nuclear power plant accident. The pathogenesis of the development of hyperhomocysteinemia in various variants of folate cycle genotypes is presented in detail. **Conclusions.** In assessing vitamins $B_9$ and $B_{12}$ status in children living near the Chernobyl exclusion zone, one should take into account not only their blood values but also that of homocysteine and vitamin $B_6$, the specific activity of radionuclides in the body and the state of the genetic apparatus of the folate cycle. Despite the fact that homocysteine impaired remethylation processes occurred in most children living near the Chernobyl exclusion zone, the correction of their metabolism with vitamins $B_9$ and $B_{12}$ should be carried out individually, taking into account the state of the genes that control the folate cycle.

## 1. Introduction

The metabolism of sulfur-containing amino acids methionine (Met) and homocysteine ($H_{cy}$) is closely related to vitamins $B_9$ and $B_{12}$.

Met under the action of adenosine triphosphate (ATP) converts into adenosylmethionine (SAM), and becomes a donor of methyl groups for a wide range of hormonal, lipid and protein metabolism reactions. During these reactions, adenosylhomocysteine ($SAH_{cy}$) is formed, which, in high concentrations, impairs the processes of cellular methylation, being an inhibitor of SAM-dependent methyltransferases, including DNA methyltransferase [1, p. 674].

$SAH_{cy}$ under the action of $SAH_{cy}$-hydrolase undergoes hydrolysis with the formation of $H_{cy}$ and adenosine.

Vitamin $B_{12}$ in the form of methylcobalamin is a cofactor of cytosolic methionine synthase (MTR), which ensures the process of $H_{cy}$ methylation and the internal cycle of Met formation [1, p. 674].

Vitamin $B_9$ in the form of separate compounds transports methyl groups for MTR [2, p. 252]. At the same time, methylenetetrahydrofolate reductase (MTHFR) is an important link, and it ensures the conversion of 5,10-methylenetetrahydrofolate ($CH_2$ – THF) to methyltetrahydrofolate ($CH_3$ – THF).

$CH_3$-THF is the only active form of vitamin $B_9$ circulating in the blood. It enters cells by endocytosis, with the participation of specific folate receptors, and easily leaves them [3, p. 2404].

Abnormal functioning of the enzymes of the folate cycle (FC) leads to an increase in the level of $H_{cy}$ in the blood (hyperhomocysteinemia). Elevated blood levels of $H_{cy}$ in adults are associated with the development of cancers and cardiovascular diseases [4, p. 80; 5, p. 212; 6, p. 44; 7, p. 76]. Mutations in the folate cycle genes, as well as inadequate status of vitamins $B_9$ and $B_{12}$ [8, c. 25684] can be the causes of hyperhomocysteinemia.

Deep $B_{12}$-folic deficiency leads to the development of severe pathological conditions, of which macrocytic megaloblastic anemia is the most well-known [9, c. 202].

There is information that hyperhomocysteinemia occurs in approximately 5.0 % of the population [10, p. 1]. However, an increased level of $H_{cy}$ in the blood was recorded in 2015 in the majority of children living near the Chernobyl exclusion zone. At the same time, the level of serum vitamins $B_9$ and $B_{12}$ was determined within the reference values [11, p. 29].

From a scientific and practical point of view, it is important to determine the causes of this phenomenon, both internal, related to the state of the genetic apparatus, and external, affecting the developing body.

**The purpose of this study** was to identify correlations between vitamins $B_{12}$, $B_9$ and $H_{cy}$, as well as vitamin $B_6$ (pyridoxine), taking into account the genetic factor, in a group of children living under constant radiation exposure associated with the Chernobyl nuclear power plant accident.

## 2. Material and methods

Results of laboratory and instrumental examination of 178 children living near the Chernobyl exclusion zone were used. The average age of the children at the time of examination was 13.6 ± 0.1 years (95 % CI 13.4 – 13.8 years).

The examined children attended school and had no complaints about their health at the time of blood draw. The blood samples were analyzed at a laboratory certified under international quality standards with the agreement of parents.

A chemiluminescent immunoassay method was used when determining blood levels of $H_{cy}$, vitamins $B_9$ and $B_{12}$.

Blood vitamin $B_6$ in children was determined using high performance liquid chromatography [12, p. 45–46].

The following allelic variants of genetic polymorphisms were identified during genetic analysis of the FC: C677T MTHFR (synthesis of MTHFR), A2756G MTR (synthesis of MTR) and A66G MTRR (synthesis of the methionine synthase reductase enzyme). A real-time PCR method was used [12, p. 46].

The reference range for vitamin $B_9$ (folacin) in the blood of children was 4.6 – 18.7 ng/mL, for vitamin $B_{12}$ (holotranscobalamin, or active vitamin $B_{12}$) – 191.0 – 663.0 pg/mL, vitamin $B_6$ – 8.7 – 27.2 μg/L.

$^{137}Cs$ specific activity in children was measured using a three-detector spectrometer manufactured by AtomKompleksPribor (Ukraine).

The statistical processing of the results obtained was performed using the IBM SPSS Statistics 22 software (USA).

Associations between blood levels of $H_{cy}$, vitamins $B_9$, $B_{12}$ and $B_6$ were identified with the help of the Spearman's rank correlation coefficient ($r_{xy}$).

Correlations were determined between $H_{cy}$, vitamins $B_9$, $B_{12}$, $B_6$ and the genetic risk index (Risk) for the MTHFR:C677T genetic polymorphism, taking into account the following conditions: 0 – Genotype 677CC – no risk; 1 – Genotype 677ST – low risk; 2 – Genotype 677TT – high risk.

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.

## 3. Results and discussion

In the total group of children (178 people), the level of $H_{cy}$ over 10.0 μmol/L was reported in 73.0 % of cases, while the level of vitamin $B_9 < 4.6$ ng/mL was found in 20.8 % of cases, and the level of vitamin $B_{12} < 191.0$ pg/mL was observed only in 6.2 % of cases (Table 1).

$^{137}Cs$ was detected in the body of all examined children. However, the specific activity of this radionuclide over 5 Bq/kg of body weight in the examined group of children was registered – in 14.4 % of cases (in the range from 6.64 to 90.71 Bq/kg) [11, p. 28].

The $H_{cy} – B_9$ and $H_{cy} – B_{12}$ inverse correlations, as well as, $B_9 – B_{12}$ direct correlation were reported in this group (Figure 1).

Table 1

**The proportion of cases with values different from the reference range in the genetic groups of children from Ivankovsky district**

| Group | No. | Number of cases in a group | | | | | | Number of cases in the subgroup with $H_{cy}$ level > 10 µmol/L | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | $H_{cy}$ > 10 µmol/L | | $B_9$ < 4.6 ng/mL | | $B_{12}$ < 191.0 pg/mL | | $B_9$ < 4.6 ng/mL | | $B_{12}$ < 191.0 pg/mL | |
| | | n | % | n | % | n | % | n | % | n | % |
| 1 | 178 | 130 | 73.0 | 29 | 16.3 | 9 | 5.1 | 27 | 20.8 | 8 | 6.2 |
| 2 | 45 | 33 | 73.3 | 4 | 8.9 | 3 | 6.7 | 3 | 9.1 | 2 | 6.1 |
| 3 | 72 | 52 | 72.2 | 15 | 20.8 | 4 | 5.6 | 14 | 26.9 | 4 | 7.7 |
| 4 | 11 | 5 | 45.5 | 1 | 9.1 | 0 | 0 | 1 | 20.0 | 0 | 0 |
| 5 | 98 | 74 | 75.5 | 19 | 19.4 | 3 | 3.1 | 19 | 25.7 | 3 | 4.1 |
| 6 | 15 | 12 | 80.0 | 7 | 46.7 | 1 | 6.7 | 7 | 58.3 | 1 | 8.3 |

Note. No. – number of cases in a group. Numbering of groups according to the main genetic polymorphisms: «1» – Total; «2» – A/A MTR:2756-C/C MTHFR:677; «3» – risk allele G MTR:2756; «4» – G/G MTR:2756; «5» – risk allele T MTHFR:677; «6» – T/T MTHFR:677.

However, in separate groups of children, composed taking into account separate FC genotypes, there were significant differences in the correlation relationships of the analyzed metabolic variables.

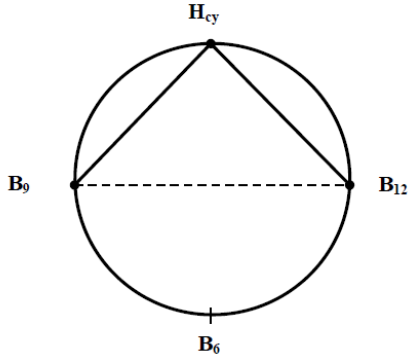


**Figure 1. Correlations between metabolic parameters in the general group of children**

$H_{cy}$ levels over 10.0 µmol/l were found in 73.3 % of cases in the group with a combination of homozygous variants of neutral alleles of A/A MTR:2756 and C/C MTHFR:677 polymorphisms (25.3 % of the total number of children). At the same time, there was no deficiency of vitamins $B_9$ and $B_{12}$ in the body of most children taking into account the reference values of the laboratory (Table 1).

An inverse association was found between $H_{cy}$ values and that of vitamin $B_{12}$. Vitamins $B_9$ and $B_{12}$ are directly

associated (Figure 2). Thus, the level of $H_{cy}$ depends on vitamin $B_{12}$ under conditions of genetic well-being of the main FC enzymes MTHFR and MTR. Insufficient levels of this vitamin in the body leads to hyperhomocysteinemia. In turn, the activity of MTHFR, and hence the production of the active form of vitamin $B_9$ – $CH_3$-THF, will directly depend on levels of vitamin $B_{12}$ in the body.

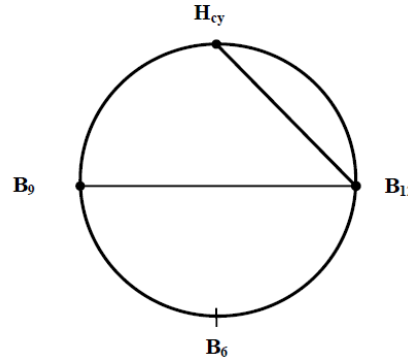


**Figure 2. Correlations between metabolic parameters in the group of children with a combination of A/A MTR:2756 and C/C MTHFR:677 polymorphisms**

In this case, insufficient intake of vitamins may be the cause of hyperhomocysteinemia. However, in most children of this group, the level of vitamins in the blood was within the reference range.

On the territory affected by the accident at the Chernobyl nuclear power plant, and in particular, near the Chernobyl exclusion zone, one of the factors that can have a significant impact on the metabolism are radioactive elements that enter the body of children and adults with food, air and water.

An increase in the blood level of $H_{cy}$ was recorded in 79.8 % of cases in a group of adolescent children from Polessky district after forest fires in the Chernobyl exclusion zone. An increase in the $H_{cy}$ level was observed in 87.9 % of cases in the A/A MTR:2756 – C/C MTHFR:677 genetic subgroup [13, p. 26].

Mutation of the gene responsible for the synthesis of MTR, expressed as the G risk allele of the MTR:2756 polymorphism, was found in 40.5 % of cases. In this group, there was no direct association $B_9$ _ $B_{12}$ which suggests an abnormal coordination in the functioning of the main enzyme systems of the FC. At the same time, an inverse association appeared between vitamins $B_{12}$ and $B_6$ (Figure 3).

In this group, the blood level of $H_{cy}$ more than 10 μmol/l was measured in 72.2 % of cases, the blood concentration of vitamins $B_9$ and $B_{12}$ less than the reference level was present in 26.9 % and 7.7 % of cases, respectively (Table 1).

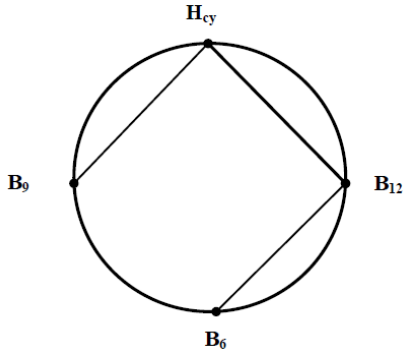


**Figure 3. Correlations between metabolic parameters in the group of children – carriers of the G allele of MTR:2756 polymorphism**

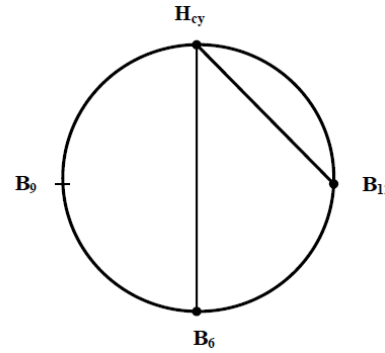


**Figure 4. Correlations between metabolic parameters in the group of children with the G/G genotype MTR:2756**

There were strong associations: an inverse one between $H_{cy}$ and vitamin $B_{12}$ and a direct one – between $H_{cy}$ and vitamin $B_6$ in the group that included only the homozygous variant G/G MTR:2756 (6.2 % of cases). There was no association between $H_{cy}$ and vitamin $B_9$ (Figure 4).

At the same time, the relative number of cases of hyperhomocysteinemia is less (45.5 %), and only in one child the level of vitamin $B_9$ was below the reference range (Table 1).

Strong associations $H_{cy} – B_6$, $B_{12} – B_6$, $H_{cy} – B_{12}$ were determined in the group of children with a combination of G/G MTR:2756 and A/G MTRR:66 genotypes (Table 2). The blood level of $H_{cy}$ over 10 μmol/L was found in 3 cases (60.0 %) in this group, consisting of 5 children (2.8 %). Analyzed vitamin values, with the exception of one (vitamin $B_{12}$ level = 853.4 pg/mL), were within the reference range set by the laboratory.

A pronounced genetic defect led to abnormal functioning of MTR, and therefore, cobalamin was poorly used, or, in general, was not used at all in the reaction of transferring the methyl group from the $CH_3$-THF molecule to a $H_{cy}$ one.

The state of hyperhomocysteinemia which occurred, with a simultaneous decrease in the content of vitamin $B_{12}$ in the blood activated a cycle of trans-

Table 2

**Associations between $H_{cy}$ and vitamins $B_9$, $B_{12}$, $B_6$ in the group of children with a combination of A/G MTRR:66 and G/G MTR:2756 genotypes**

| Parameter | Correlation coefficient, Significance, p | Parameter | | | |
|---|---|---|---|---|---|
| | | $B_6$ | $B_9$ | $B_{12}$ | $H_{cy}$ |
| $B_6$ | Spearman's ($r_{xy}$) | 1.000 | -.600 | -.900* | 1.000** |
| | Sign. (2-tailed) | . | .285 | .037 | . |
| | N | 5 | 5 | 5 | 5 |
| $B_9$ | Spearman's ($r_{xy}$) | -.600 | 1.000 | .800 | -.600 |
| | Sign. (2-tailed) | .285 | . | .104 | .285 |
| | N | 5 | 5 | 5 | 5 |
| $B_{12}$ | Spearman's ($r_{xy}$) | -.900* | .800 | 1.000 | -.900* |
| | Sign. (2-tailed) | .037 | .104 | . | .037 |
| | N | 5 | 5 | 5 | 5 |
| $H_{cy}$ | Spearman's ($r_{xy}$) | 1.000** | -.600 | -.900* | 1.000 |
| | Sign. (2-tailed) | . | .285 | .037 | . |
| | N | 5 | 5 | 5 | 5 |

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

sulfuration reactions in which vitamin $B_6$ is a cofactor of cystathionine β-synthase (CBS), which catalyzes condensation of the amino acids $H_{cy}$ and serine, with the formation of cystathionine (Cyst).

Under the action of cystathionine γ-lyase, Cyst is converted into cysteine (Cys), which is involved in the synthesis of direct anticoagulants – heparin, heparan sulfate and chondroitin sulfate and the formation of glutathione, which protects cells from oxidative stress [14, p. 1712].

Mutation of the methionine synthase reductase gene in the form of the A/G MTRR:66 genetic polymorphism, prevented the restoration of MTR activity resulting in a clearer association between MTR and CBS.

The CBS activator is SAM, the main source of methyl groups in methylation reactions and an allosteric inhibitor of MTHFR [15, p. 217].

There is information that the CBS enzyme is absent in the cells of the central nervous system, myocardium, endothelial cells of the vascular wall, and therefore, excessive $H_{cy}$ is not utilized through the trans-sulfuration

reaction [16, p. 2]. In this case, $H_{cy}$ utilization occurs using only the FC, and therefore, these cells are more vulnerable in the presence of hyperhomocysteinemia.

In the group of children with the risk allele T of the genetic polymorphism MTHFR:677 (55.1 % of cases), medium-strength relationships were recorded: direct $B_9 – B_{12}$ and inverse ones $H_{cy} – B_{12}$ and $H_{cy} – B_9$ (Figure 5).

In this group, the level of $H_{cy}$ in the blood over 10 μmol/L was determined in 75.5 % of cases, while $B_9$ level was less than 4.6 ng/mL in 1/4 of the persons, and the level of vitamin $B_{12}$ was less than 191.0 pg/mL only in 4.1 % of cases (Table 1).

In the presence of a homozygous variant of the T allele of the MTHFR:677 polymorphism (8.4 % of cases), there was a moderate $H_{cy} – B_9$ association, there were no $H_{cy} – B_{12}$ and $B_9 – B_{12}$ associations (Figure 6), the level of $H_{cy}$ in the blood of children, as well as the proportion of cases of hyperhomocysteinemia (Table 1), were the largest of all genetic groups [17, p. 12, 13].

The severity of the genetic risk of the MTHFR:C677T polymorphism was directly related to $H_{cy}$, and, inversely, to vitamin $B_9$ (Table 3).

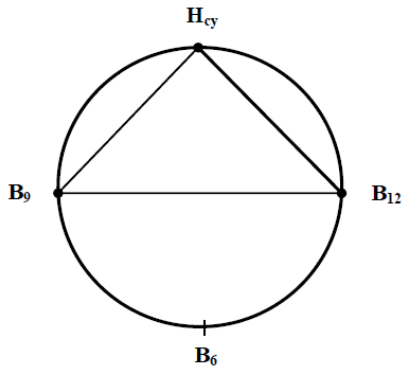


**Figure 5. Correlations between metabolic parameters in the group of children – carriers of the T allele of the MTHFR:677 polymorphism**

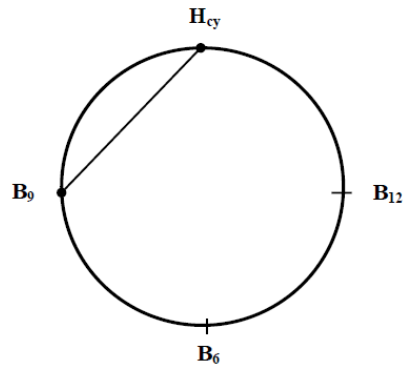


**Figure 6. Correlations between metabolic parameters in the group of children with the T/T genotype MTHFR:677**

The presence of the T allele of the MTHFR:677 polymorphism in the genome predisposed to lower levels of vitamin $B_9$ in the blood in comparison with the C/C MTHFR:677genotype [18, p. 252; 19, p. 29].

However, in this case, there was no activation of the trans-sulfuration cycle, as evidenced by the absence of $H_{cy} – B_6$ and $B_{12} – B_6$ associations.

In this group, the largest proportion of cases of folate deficiency was recorded (Table 1), which was associated with a decrease in the formation and circulation of $CH_3$-THF in the blood.

Table 3

**Correlations of $H_{cy}$, $B_{6,}$ $B_9$, $B_{12}$ and genetic risk index (Risk) of MTHFR:C677T polymorphism in the total group of children**

| Parameter | Correlation coefficient | Parameter | | | |
|---|---|---|---|---|---|
| | | $H_{cy}$ | $B_6$ | $B_9$ | $B_{12}$ |
| Risk MTHFR:C677T | Spearman's ($r_{xy}$) | 0.201** | 0.060 | -0.218** | -0.005 |
| | Sign. (2-tailed), p | 0.007 | 0.428 | 0.004 | 0.952 |
| | N | 178 | 178 | 178 | 178 |

Note. * – Correlation is significant at the 0.05 level (2-tailed). ** – Correlation is significant at the 0.01 level (2-tailed). Risk MTHFR:C677T: CC, CT, TT.

Thus, damage to the gene responsible for the synthesis of the MTHFR enzyme caused a more pronounced increase in the blood level of $H_{cy}$ compared to the G/G MTR:2756 mutation, which impairs the synthesis of MTR, since, in the second case, the adaptive mechanisms of $H_{cy}$ utilization in the form of trans-sulfuration reactions were activated.

Metabolic correction, in this case, should take place with the use of foods and medicines containing $CH_3$-THF, since the body is not able to properly methylate THF on its own.

In some cases, a methylated form of cobalamin is used, although most children do not have vitamin $B_{12}$ deficiency.

The analysis performed showed a role of endogenous (genetic) and exogenous (environmental) factors in the occurrence of impaired metabolism of $H_{cy}$ and Met in the body of children living in areas affected by the Chernobyl nuclear power plant accident.

Mutations in the FC genes are the cause of impaired physiological relationships between components of the enzyme system, in which vitamins

$B_9$ and $B_{12}$ are actively involved. The blood level of vitamins, as well as the nature of their associations between themselves and of vitamin $B_6$ and $H_{cy}$, reflects the activity of enzymes.

In particular, in the homozygous variant of the risk allele T of the MTHFR:677 polymorphism, the genetic factor plays a leading role in the disruption of $H_{cy}$ remethylation processes by reducing the formation of the active form of folic acid, $CH_3$ _ THF.

There are gene-related adaptive mechanisms of metabolism that allow to reduce the negative impact on a developing body of high $H_{cy}$ concentrations.

The most pronounced blocking of the $H_{cy}$ remethylation process occurred in the group with the G/G MTR:2756 genotype, while the number of children with hyperhomocysteinemia here is the smallest of all the analyzed groups. This is due to the fact that the $H_{cy}$ utilization process involves a cycle of trans-sulfuration reactions in which vitamin $B_6$ is a coenzyme of CBS.

However, in the majority of children permanently residing in areas contaminated with radioactive elements as a result of the accident at the Chernobyl nuclear power plant, an increase in the $H_{cy}$ level in the blood, and hence the impairment of processes of its remethylation occurred regardless of the state of the genes that control the FC [20, p. 138].

The constant presence of $^{137}Cs$, its decay products, as well as other long-lived radioactive agents in a child's body blocks metabolic processes in the cells of vital organs. The energy deficit originating from it is the cause of a decrease in the activity of FC enzymes and, consequently, of an increase in $H_{cy}$ levels in the blood.

In this regard, when considering specific cases of hyperhomocysteinemia, it is necessary to take into account blood $B_9$ and $B_{12}$ levels, the state of the FC genes and $^{137}Cs$ specific activity in the body.

The findings suggest that there is a necessity to use an integrated approach in assessing $B_{12}$ and $B_9$ status in children living in areas affected by the Chernobyl nuclear power plant accident. In addition to the measurement of blood levels of these vitamins, it is obligatory to measure $H_{cy}$ and vitamin $B_6$ levels. At the same time, it is necessary to use information on the associations of the analyzed indicators in a particular genetic group.

## 4. Conclusions and prospects for further development

1. 30 years after the accident at the Chernobyl nuclear power plant, in a group of children aged 12-17 years old in the Ivankovsky district, a power plant, blood levels of $H_{cy}$ > 10 μmol/l were recorded in 73.0 % of cases, while the values were below the reference range, were determined for vitamin $B_9$ – in 16.3 % of cases, for vitamin $B_{12}$ – in 5.1 % of cases.

2. The causes of hyperhomocysteinemia in children living near the Chernobyl exclusion zone are mutations in the FC genes, insufficient content of vitamins $B_9$ and $B_{12}$ in the body, as well as the impact of an environmental factor associated with the accident at the Chernobyl nuclear power plant.

3. Inverse associations of $H_{cy}$ with vitamins $B_9$ and $B_{12}$ in the group of children with a predominance of hyperhomocysteinemia cases suggest a functional deficiency of these vitamins, despite the fact that the values of the latter do not go beyond the reference level.

4. The state of hyperhomocysteinemia in children living near the Chernobyl exclusion zone may be associated with impaired MTR function as a result of exposure to an environmental factor of a radiation nature.

5. Vitamin $B_{12}$ is a key element in the process of $H_{cy}$ remethylation with the formation of methionine in individuals with no risk alleles of genetic polymorphisms that have the greatest negative effect on the activity of the main enzymes of the folate cycle MTHFR and MTR, and also, with a favorable effect of environmental factors on the body. In this case, vitamin $B_{12}$ can be an effective tool to prevent the onset of a state of hyperhomocysteinemia.

6. In the group of children with the G risk allele of the MTR:2756 polymorphism, no direct correlation between vitamins $B_9$ and $B_{12}$ was determined, which means that there was no connection between the MTHFR and MTR enzymes. At the same time, a decrease in the content of active forms of vitamin $B_{12}$ in the blood and a simultaneous increase in the content of $H_{cy}$ had a stimulating effect on the cycle of trans-sulfurization reactions, with the participation of vitamin $B_6$ as a cofactor of the CBS enzyme, which is responsible for the formation of cystathionine from $H_{cy}$ and serine.

7. The decrease in $H_{cy}$ blood levels in children with the G/G MTHFR:677 genotype, which blocks the activity of MTR, is associated with the activation of an adaptive mechanism in the form of a cycle of trans-sulfuration reactions.

8. In the group of children with a homozygous variant of the T allele of the MTHFR:677 polymorphism, compared with other genetic groups, the state of hyperhomocysteinemia is more pronounced, with the greatest decrease in the level of folic acid in the blood. Metabolic correction, in this case, should occur with the use of foods and drugs containing $CH_3$-THF.

9. In assessing vitamins $B_9$ and $B_{12}$ status in children living near the Chernobyl exclusion zone, one should take into account not only their blood values but also that of $H_{cy}$ and vitamin $B_6$, the specific activity of radionuclides in the body and the state of the genetic apparatus of the FC.

10. The metabolism correction in children living in areas affected by the Chernobyl nuclear power plant accident should be based on measures to prevent the effects of human internal and external exposure to radioactive elements.

11. Despite the fact that $H_{cy}$ impaired remethylation processes occurred in most children living near the Chernobyl exclusion zone, the correction of their metabolism with vitamins $B_9$ and $B_{12}$ should be carried out individually, taking into account the state of the genes that control the FC.

**Conflict of interests.** The authors declare no conflict of interest.

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