

CHAPTER «MEDICAL SCIENCES»

PARTICIPATION OF HOMOCYSTEINE IN THE REGULATION OF CALCIUM-PHOSPHORUS METABOLISM AND CARDIOVASCULAR FUNCTION IN CHILDREN LIVING IN AREAS AFFECTED BY THE CHERNOBYL NUCLEAR POWER PLANT ACCIDENT

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DOI: <https://doi.org/10.30525/978-9934-26-602-7-14>

Abstract. The Chernobyl Exclusion Zone (ChEZ) still remains a source of long-lived radioactive elements, the spread of which beyond its boundaries occurs mainly during forest fires. In this regard, the victims of radiation exposure are, first of all, residents of settlements located nearby. In 2015, during the implementation of the European Commission project "Health and Ecological Programmes around the Chernobyl Exclusion Zone: Development, training and coordination of health-related projects" and the regional council of Rhone-Alpes (France) project, the phenomenon of an increase in the concentration of homocysteine (H_{cy}) in the blood of most children living near the ChEZ, above the physiological level, was first identified. The studies conducted at the same time made it possible to establish a connection between hyperhomocysteinemia and genetic polymorphisms of the folate cycle (FC) and environmental impacts, in particular, with forest fires in the ChEZ. It is also known that in adults hyperhomocysteinemia is often accompanied by osteoporosis and impaired cardiovascular function. Taking these facts into account, *the aim of this study* was to assess the participation of H_{cy} in the regulation

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of calcium-phosphorus metabolism and the functioning of the cardiovascular system, with the incorporation of ^{137}Cs into the body, in children living in areas affected by the Chernobyl accident. *Research methods.* The results of genetic, laboratory and instrumental testing of 956 children (444 boys and 512 girls) aged 12-18 years from Ivankivsky and Polissky districts of the Kyiv region, conducted in Ukraine within the framework of the projects of the European Commission and the Rhone-Alpes Regional Council (France), were used. In this case, the specific activity of ^{137}Cs was determined in the body of each child. The relationship between the analyzed indicators was estimated using the Spearman rank correlation coefficient (r_{xy}). *Results.* The correlation analysis was used to study the relationships between the levels of H_{cy} , parathyroid hormone (PTH), total calcium (Ca), ionized calcium (Ca^{2+}), inorganic phosphorus (P), the level of physical development of children (according to the Rohrer weight-height index), systolic, diastolic and pulse arterial pressure indicators taking into account their genetic status of FC and the content of ^{137}Cs in the body. It was shown that the incorporation of ^{137}Cs into the body of children is one of the causes of energy deficiency in the cells of vital organs, leading to a decrease in the intensity of anabolic processes, interrelated disorders of H_{cy} methylation, calcium-phosphorus metabolism and the functioning of the cardiovascular system. The inverse correlation between the values of the specific activity of ^{137}Cs in the body and the serum Ca indicators in groups of children aged 12 and 13 years indicates a violation of mineral metabolism in the developing organism under conditions of radiation exposure. Cellular energy deficiency induced by the effect of incorporated ^{137}Cs , as well as mutations of the FC genes, is the cause of the disruption of the H_{cy} methylation process, the concentration of which in the blood increases, in some cases exceeding the physiological level. The state of hyperhomocysteinemia contributes to an increase in the concentration of Ca^{2+} in the blood, including due to the effect of H_{cy} on bone tissue cells. Hormonal control of calcium-phosphorus metabolism in children living in the area affected by the Chernobyl accident depends on the state of the FC genome and the H_{cy} level in the blood. Direct correlation between H_{cy} and Ca^{2+} is most pronounced in the subgroup of children carrying the T/TMTHFR:677 genotype. At the same time, the effect of PTH on Ca^{2+} metabolism decreases, as evidenced by the absence of a correlation between Ca^{2+} and PTH. In the case of homozygotes of the

GMTR:2756 allele in the genome, H_{cy} blocks the process of PTH formation. By increasing the concentration of Ca in the blood, H_{cy} affects phosphate metabolism. Persistent, genetically determined (homozygotes of the GMTR:2756 and TMTHFR:677 risk alleles) hyperhomocysteinemia can cause an increase in the Ca level in the blood, impaired PTH synthesis and P retention in the body. As a result, calcium-phosphate complexes are formed in the blood and deposited in soft tissues and blood vessel walls. Children with the absence of homozygotes of the GMTR:2756 and TMTHFR:677 risk alleles in the genome have a compensatory mechanism associated with the stimulating effect of P on the process of PTH formation, which allows the body to excrete excess P through the kidneys with urine. The effect of incorporated ^{137}Cs on the state of the cardiovascular system of children living near the ChEZ is confirmed by the method of correlation analysis. The pathogenesis of the development of calcium-phosphorus metabolism disorders and cardiovascular system activity in hyperhomocysteinemia (H_{cy} content in the blood is more than $10.0 \mu\text{mol/l}$) with various variants of FC genotypes is presented in detail. *Conclusions.* Hyperhomocysteinemia, affecting calcium-phosphorus metabolism, under certain conditions, is an integral part of the adaptive response of the body aimed at normalizing metabolic processes in the cardiovascular system when exposed to incorporated radionuclides ^{137}Cs . At the same time, with an unfavorable combination of endogenous (FC genes) and exogenous (radiation exposure) factors, hyperhomocysteinemia is an element of the pathological process affecting the heart and blood vessels.

1. Introduction

The accident at the Chernobyl nuclear power plant (ChNPP) in April 1986 resulted in the release of a huge amount of radioactive elements into the atmosphere [1, p. 12; 2, p. 22].

The humanitarian consequences of this planetary-scale catastrophe have been felt for many years [2, p. 205].

Forest trees and soil on the territory of the ChEZ are currently a source of long-lived radioactive elements, the spread of which beyond its borders occurs mainly during forest fires [3, p. 10].

In this regard, the victims of radiation exposure are, first of all, residents of settlements located close to it.

The projects of the European Commission "Health and Ecological Programmes around the Chernobyl Exclusion Zone: Development, training and coordination of health-related projects" and the Regional Council of Rhone-Alpes (France), implemented in Ukraine in 2013-2017, made it possible to carry out clinical, laboratory and instrumental examination, with the determination of the content of ^{137}Cs in the body, of most children living in the Ivankivsky and Polissky districts of the Kyiv region [4, p. 11, 12].

One of the areas of the European Commission project was the assessment of contamination of the Ivankivsky district with ^{137}Cs and ^{90}Sr radionuclides 30 years after the Chernobyl accident [4, p. 120, 121], which allows for an effective analysis of the impact of the radiation factor on the health of local residents.

The influence of ^{137}Cs on the physical development, the state of the cardiovascular and hematopoietic systems of children living near the ChEZ was established [4, p. 17; 4, p. 19].

Metabolic changes in the bodies of these children associated with the exchange of sulfur-containing amino acids, hormones of the thyroid and adrenal glands, and minerals were identified.

Particular attention was paid to the increase in the content of the sulfur-containing amino acid homocysteine (H_{cy}) in the blood of most of the examined children, which plays an important role in metabolic processes in the body [5, p. 29].

Statistical analysis of the obtained information made it possible to establish a connection between hyperhomocysteinemia and genetic polymorphisms of FC [6, p. 160] and environmental impacts, in particular, with forest fires in the ChEZ [3, p. 25].

At the same time, the participation of H_{cy} in the regulation of thyroid hormone metabolism was determined [7, p. 63].

The information obtained about the relationship between H_{cy} and calcium-phosphorus metabolism in the bodies of the examined children [8, p. 92; 9, p. 55] requires careful scientific analysis, taking into account the fact that in adults hyperhomocysteinemia is often accompanied by osteoporosis, and therefore it is considered a predictor of bone fractures [10, p. 2045].

Numerous studies have established a link between H_{cy} and cardiovascular diseases [11, p. 8, 9].

The aim of this study was to assess the participation of H_{cy} in the regulation of calcium-phosphorus metabolism and the functioning of the cardiovascular system, with the incorporation of ^{137}Cs into the body, in children living in areas affected by the Chernobyl accident.

2. Material and methods

To conduct an analytical study, the indicators of genetic, laboratory and instrumental testing of 956 children (444 boys and 512 girls) were used, conducted in Ukraine within the framework of projects of the European Commission and the regional council of Rhone-Alpes (France). In this case, the specific activity of ^{137}Cs was determined in the body of each child.

The examination of children was carried out in compliance with the rules of bioethics and was agreed upon with the parents. At the time of the examination, the children lived in the Polissky and Ivankivsky districts of the Kyiv region, near the ChEZ, in the territory, the soil of which contained radioactive elements ^{137}Cs and ^{90}Sr [4, p. 120, 121; 12, p. 54, 55].

For the purpose of laboratory and genetic examination of children aged 12-18 years who attended school, blood was taken from the cubital vein in the morning on an empty stomach.

The obtained blood samples were examined in a laboratory certified in accordance with European quality standards.

In the blood of the examined children, H_{cy} , PTH, Ca, Ca^{2+} , P were determined.

H_{cy} in the blood was determined using the immunochemical method with chemiluminescent detection (ECLIA). Analyzer and test system: Architect 1000 (ABBOT Diagnostics (USA)).

The state of hyperhomocysteinemia in the examined children was recorded when the concentration of H_{cy} in the blood exceeded the level of $10.0 \mu\text{mol/l}$.

PTH was determined using an immunochemical method with electrochemiluminescent detection (ECLIA). Analyzer and test system: Cobas 6000, Roche Diagnostics (Switzerland).

Determination of Ca was carried out by a spectrometric method on an automatic biochemical analyzer Flexor E (manufacturer Vital

Scientific, Netherlands), using reagents from Point Scientific, Inc. (USA). Wavelength 650 nm.

Determination of Ca^{2+} was carried out using an ion-selective method. Analyzer and test system: AVL 9180; Roche Diagnostics (Switzerland).

Determination of P was carried out by a spectrometric method on an automatic biochemical analyzer Flexor E (manufacturer Vital Scientific, Netherlands), using reagents from Point Scientific, Inc. (USA). Wavelength 340 nm.

Reference values for PTH – 15.0-65.0 pg/ml, Ca – 2.1-2.55 mmol/l, Ca^{2+} – 1.16-1.32 mmol/l, P – 0.90-1.65 mmol/l.

During the genetic study of the folate cycle (FC), the allelic variants C677T and A1298C of the MTHFR gene (association with the enzyme methylenetetrahydrofolate reductase), A2756G of the MTR gene (association with the enzyme B_{12} -dependent methionine synthase), A66G of the MTRR gene (association with the enzyme methionine synthase reductase) were determined. In this case, the method was used: PCR in Real-time mode.

To assess the physical development (PD) of children, the Rohrer weight-height index (IR) was used, the quotient of body weight in kilograms divided by body length in meters cubed [13, p. 15].

When measuring the weight and body length of children, unified anthropometric methods were used [14, p. 31].

In accordance with the IR values, three groups were identified during the examination of children in the Polissky and Ivankivsky districts:

- 1 – disharmonious (low) PD, $\text{IR} < 10.7 \text{ kg/m}^3$;
- 2 – harmonious PD, IR in the range ≤ 13.7 and $\geq 10.7 \text{ kg/m}^3$;
- 3 – disharmonious (high) PD, $\text{IR} > 13.7 \text{ kg/m}^3$;

Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were determined automatically using a patient monitor (RM 9000, Penton Ltd.). In this case, pulse pressure (PP) was calculated – the difference between systolic and diastolic blood pressure.

Determination of the specific activity of ^{137}Cs in the body of children was carried out on a 3-detector human radiation spectrometer "SICH-AKP-3" (OOO NPP "ATOMKOMPLEKSPRIBOR", Ukraine) for 10 minutes.

For automatic processing of spectra and calculation of the specific activity of radioactive elements, the software of the "AKWin" device was used.

Statistical processing of the obtained results was carried out using the IBM SPSS Statistics 22 program (USA). For the analyzed indicators, the median (Me), interquartile range (IQR), minimum and maximum parameter values, percentiles were calculated. A hypothesis about the type of distributions was tested (Kolmogorov-Smirnov criterion).

The statistical significance of the indicators was assessed by determining the significance level p using a statistical program.

The relationship between the analyzed indicators was determined using the Spearman rank correlation coefficient (r_{xy}). The strength of the correlation was assessed using the traditional scale: weak – from 0 to 0.299; average – from 0.3 to 0.699; strong – from 0.7 to 1.0.

3. Research results and their discussion

The specific activity of ^{137}Cs in the body of the examined children was recorded in the group of boys in the range of 0.78 – 95.11 Bq/kg, in the group of girls – 1.06 – 26.96 Bq/kg.

The blood Ca level in boys and girls in individual age groups had no statistical differences, while the blood P level in boys aged 13, 14 and 15 years was significantly higher than in girls from similar groups (Table 1, 2).

At the same time, the blood Ca level of children from all age groups had no significant differences, while the blood P level of children aged 12-13 years was higher than in the blood of children aged 14-18 years (Table 1).

In all analyzed age groups (12-18 years), the proportion of cases with blood Ca level > 2.55 mmol/l was significantly more than the proportion of cases with blood Ca level in the range of 2.1-2.55 mmol/l (Table 3).

A blood Ca level below 2.10 mmol/l was recorded in one girl aged 13 years (Table 3).

The proportion of cases with blood P levels in the range of 0.90-1.65 mmol/l was greater than the proportion of cases with blood P levels < 0.90 mmol/l in groups of children aged 12-13 years (Table 4).

Table 1

**Statistical characteristics in groups of children
from areas affected by the Chernobyl accident**

N ¹	Group name	Age (years)	N ²	Ca, mmol/l		P, mmol/l	
				Me	IQR	Me	IQR
1	Boys	12	88	2.635	2.550 - 2.690	1.095	0.920 - 1.373
2	Girls	12	98	2.630	2.490 - 2.710	1.080	0.860 - 1.250
3	Boys	13	101	2.620	2.510 - 2.735	1.150	0.940 - 1.400
4	Girls	13	102	2.615	2.495 - 2.720	0.935	0.748 - 1.170
5	Boys	14	109	2.650	2.465 - 2.760	1.080	0.885 - 1.270
6	Girls	14	94	2.610	2.470 - 2.743	0.830	0.675 - 1.063
7	Boys	15	70	2.645	2.478 - 2.770	0.950	0.750 - 1.133
8	Girls	15	104	2.610	2.503 - 2.708	0.775	0.630 - 0.878
9	Boys	16	54	2.640	2.510 - 2.730	0.790	0.518 - 0.973
10	Girls	16	75	2.620	2.520 - 2.700	0.800	0.610 - 1.020
11	Boys	17-18	22	2.630	2.535 - 2.715	0.725	0.473 - 0.900
12	Girls	17-18	39	2.600	2.490 - 2.680	0.700	0.570 - 0.910

Note: N¹ – group number; N² – number of children in the group; Me – median, IQR – interquartile range; Ca – calcium; P – phosphorus.

Table 2

**Results of statistically significant differences when comparing
the P values in the blood of the examined boys and girls**

Comparison groups	Number of comparison groups	Average rank	U-criterion value, significance level p
3	101	120.68	U = 3264.500 p = 0.0001
4	102	83.50	
5	109	124.50	U = 2670.000 p = 0.0001
6	94	75.90	
7	70	106.99	U = 2276.000 p = 0.0001
8	104	74.38	

Table 3

**Statistical indicators reflecting the content of Ca
in the blood of children**

N ¹	N ²	Blood Ca level					
		> 2.55 mmol/l		2.1 - 2.55 mmol/l		< 2.10 mmol/l	
		Abs.	%	Abs.	%	Abs.	%
1	88	63	71.6	25	28.4	0	0
2	98	67	68.4	31	31.6	0	0
3	101	64	63.4	37	36.6	0	0
4	102	62	60.8	39	38.2	1	1.0
5	109	65	59.6	44	40.4	0	0
6	94	57	60.6	37	39.4	0	0
7	70	48	68.6	22	31.4	0	0
8	104	70	67.3	34	32.7	0	0
9	54	40	74.1	14	25.9	0	0
10	75	47	62.7	28	37.3	0	0
11	22	15	68.2	7	31.8	0	0
12	39	24	61.5	15	38.5	0	0

Note: N¹ is the group number; N² is the number of children in the group.

Table 4

**Statistical indicators reflecting the content of P in the blood of
examined children**

N ¹	N ²	Blood P level					
		> 1.65 mmol/l		0.90 - 1.65 mmol/l		< 0.90 mmol/l	
		Abs.	%	Abs.	%	Abs.	%
1	88	6	6.8	63	71.6	19	21.6
2	98	4	4.1	67	68.4	27	27.5
3	101	5	5.0	74	73.3	22	21.7
4	102	1	1.0	56	54.9	45	44.1
5	109	2	1.8	78	71.6	29	26.6
6	94	0	0	42	44.7	52	55.3
7	70	1	1.4	41	58.6	28	40.0
8	104	0	0	23	22.1	81	77.9
9	54	0	0	17	31.5	37	68.5
10	75	0	0	29	38.7	46	61.3
11	22	0	0	5	22.7	17	77.3
12	39	1	2.6	11	28.2	27	69.2

Note: N¹ is the group number; N² is the number of children in the group.

However, in groups of girls aged 14-18 years and in groups of boys aged 16-18 years, the proportion of cases with blood P levels < 0.90 mmol/l began to prevail over the proportion of cases with blood P levels in the range of 0.90-1.65 mmol/l (Table 4).

Blood P levels above 1.65 mmol/l were recorded in 20 of 956 children (2.1%). These were mainly children aged 12-13 years (Table 4).

IR values were determined in the group of boys in the range from 9.0 to 30.2 kg/m³, in the group of girls in the range from 8.5 to 23.0 kg/m³.

At the same time, there were no statistical differences between the age groups, while in the groups of girls aged 14.15 and 17-18 years, the IR values were more than in similar groups of boys (Tables 5, 6).

Table 5

**Statistical indicators of physical development and circulatory system
of children from areas affected by the Chernobyl accident**

N	IR		SBP, mmHg		DBP, mmHg		PP	
	Me	IQR	Me	IQR	Me	IQR	Me	IQR
1	12.200	11.300-13.875	123.00	116.25-129.75	71.00	64.00-78.00	50.50	43.25-61.75
2	12.500	11.400-13.900	124.00	116.00-133.25	70.00	61.75-78.00	55.00	47.00-63.25
3	11.900	10.850-13.200	124.00	116.00-133.50	67.00	60.00-75.50	57.00	49.00-67.00
4	12.300	11.075-13.800	125.00	119.75-134.00	71.00	66.00-77.00	54.50	46.75-63.00
5	11.900	11.050-12.900	127.00	116.00-136.00	68.00	62.00-74.50	58.00	49.50-72.00
6	12.600	11.300-14.275	128.00	119.00-138.25	71.00	65.00-80.25	58.00	48.75-67.00
7	12.150	11.000-13.150	130.00	121.00-141.00	70.00	62.75-75.25	61.00	53.00-68.50
8	12.900	12.025-14.125	131.00	122.00-139.75	73.00	64.00-80.00	59.00	51.00-67.00
9	12.350	11.475-13.225	132.00	127.75-139.00	69.00	64.00- 73.25	65.00	57.00-73.25
10	12.200	11.400-14.000	128.00	120.00-135.00	71.00	62.00-76.00	59.00	52.00-67.00
11	12.250	10.875-13.175	127.50	118.75-147.25	67.00	56.00-73.25	67.00	56.50-72.25
12	13.100	12.200-15.400	121.00	116.00-135.00	66.00	58.00-74.00	57.00	50.00-71.00

Note: N – group number; Me – median, IQR – interquartile range; IR – Rohrer index; SBP – systolic blood pressure; DBP – diastolic blood pressure; PP – pulse pressure.

Table 6

**Results of statistically significant differences
when comparing IR indicators in groups of boys and girls**

Comparison groups	Number of comparison groups	Average rank	U-criterion value, significance level p
5	109	93.29	U = 4173.500 p = 0.023
6	94	112.10	
7	70	72.16	U = 2566.500 p = 0.001
8	104	97.82	
11	22	23.95	U = 274.000 p = 0.020
12	39	34.97	

There were no significant differences in the values of the indicators characterizing the state of the cardiovascular system between the studied age groups of children: SBP, DBP, PP.

The DBP values in the groups of girls aged 13 and 14 years were more than in the similar groups of boys, while in the group of boys aged 16 years the SBP values were more than in the similar group of girls (Table 7).

Table 7

**Results of statistically significant differences when comparing DBP
and SBP indicators in groups of boys and girls**

Comparison groups	Comparison indicator	Number of comparison groups	Average rank	U-criterion value, significance level p
3	DBP	101	92.96	U = 4237.500 p = 0.029
4		102	110.96	
5	DBP	109	91.83	U = 4014.000 p = 0.008
6		94	113.80	
9	SBP	54	73.77	U = 1551.500 p = 0.024
10		75	58.69	

An inverse correlation between ^{137}Cs and Ca was established in the group of boys aged 12 and 13 years, and in the group of girls aged 13 years (Table 8).

An inverse correlation was also recorded between the values of ^{137}Cs and SBP, ^{137}Cs and IR in most age groups (Table 8).

Table 8

**Results of correlation analysis in groups of boys and girls
from areas affected by the Chernobyl accident**

N	Correlation coefficient	Correlations				
		¹³⁷ Cs-Ca	¹³⁷ Cs-SBP	¹³⁷ Cs- DBP	¹³⁷ Cs- PP	¹³⁷ Cs-IR
1	Spearman's	-0.277**	-0.375**	-0.072	-0.362**	-0.564**
	Sign. (2-tailed), p	0.009	0.0001	0.507	0.001	0.0001
	N	88	88	88	88	88
2	Spearman's	-0.068	-0.321**	-0.073	-0.283**	-0.591**
	Sign. (2-tailed), p	0.503	0.001	0.473	0.005	0.0001
	N	98	98	98	98	98
3	Spearman's	-0.216*	-0.390**	-0.266**	-0.171	-0.485**
	Sign. (2-tailed), p	0.030	0.0001	0.007	0.087	0.0001
	N	101	101	101	101	101
4	Spearman's	-0.218*	0.070	-0.013	-0.028	-0.578**
	Sign. (2-tailed), p	0.028	0.482	0.894	0.777	0.0001
	N	102	102	102	102	102
5	Spearman's	-0.020	-0.324**	0.006	-0.292**	-0.300**
	Sign. (2-tailed), p	0.839	0.001	0.947	0.002	0.002
	N	109	109	109	109	109
6	Spearman's	-0.194	-0.218*	-0.022	-0.167	-0.647**
	Sign. (2-tailed), p	0.061	0.034	0.834	0.107	0.0001
	N	94	94	94	94	94
7	Spearman's	-0.172	-0.317**	0.010	-0.382**	-0.430**
	Sign. (2-tailed), p	0.155	0.007	0.935	0.001	0.0001
	N	70	70	70	70	70
8	Spearman's	0.024	-0.255**	-0.040	-0.216*	-0.524**
	Sign. (2-tailed), p	0.812	0.009	0.690	0.028	0.0001
	N	104	104	104	104	104
9	Spearman's	-0.072	-0.304*	-0.184	-0.129	-0.338*
	Sign. (2-tailed), p	0.605	0.025	0.182	0.351	0.012
	N	54	54	54	54	54
10	Spearman's	-0.022	-0.110	-0.055	-0.026	-0.349**
	Sign. (2-tailed), p	0.851	0.349	0.640	0.827	0.002
	N	75	75	75	75	75
11	Spearman's	-0.348	-0.108	-0.106	-0.212	-0.190
	Sign. (2-tailed), p	0.113	0.632	0.637	0.343	0.398
	N	22	22	22	22	22
12	Spearman's	0.115	-0.067	-0.137	-0.005	-0.400*
	Sign. (2-tailed), p	0.485	0.687	0.405	0.977	0.012
	N	39	39	39	39	39

Note. * – correlation is significant at the 0.05 level (two-sided); ** – correlation is significant at the 0.01 level (two-sided); N – group number; SBP – systolic blood pressure; DBP – diastolic blood pressure; PP – pulse pressure; IR – Rohrer index; Ca – calcium; P – phosphorus.

In several groups, direct correlations were determined between the indicators characterizing the circulatory system and the physical development of children (IR) (Table 9).

Table 9

Results of correlation analysis in groups of boys and girls from areas affected by the Chernobyl accident

N	Correlation coefficient	Correlations					
		Ca-SBP	Ca-DBP	Ca-PP	IR-SBP	IR-DBP	IR-PP
1	Spearman's	0.199	-0.024	0.253*	0.395**	0.216*	0.271*
	Sign. (2-tailed), p	0.063	0.828	0.017	0.0001	0.044	0.011
	N	88	88	88	88	88	88
2	Spearman's	0.240*	0.288**	-0.031	0.352**	0.136	0.307**
	Sign. (2-tailed), p	0.017	0.004	0.760	0.0001	0.182	0.002
	N	98	98	98	98	98	98
3	Spearman's	0.118	0.130	0.032	0.319**	0.157	0.208*
	Sign. (2-tailed), p	0.241	0.196	0.753	0.001	0.117	0.037
	N	101	101	101	101	101	101
4	Spearman's	0.089	0.109	0.077	0.125	0.070	0.102
	Sign. (2-tailed), p	0.375	0.276	0.440	0.210	0.483	0.307
	N	102	102	102	102	102	102
5	Spearman's	0.192*	0.124	0.143	0.168	-0.013	0.218*
	Sign. (2-tailed), p	0.046	0.198	0.139	0.081	0.890	0.023
	N	109	109	109	109	109	109
6	Spearman's	0.090	0.046	0.005	0.194	-0.130	0.282**
	Sign. (2-tailed), p	0.390	0.662	0.964	0.060	0.212	0.006
	N	94	94	94	94	94	94
7	Spearman's	0.009	-0.214	0.164	0.242*	0.062	0.224
	Sign. (2-tailed), p	0.940	0.075	0.175	0.043	0.612	0.062
	N	70	70	70	70	70	70
8	Spearman's	0.168	0.035	0.108	0.232*	0.010	0.281**
	Sign. (2-tailed), p	0.088	0.726	0.276	0.018	0.923	0.004
	N	104	104	104	104	104	104
9	Spearman's	0.062	0.164	-0.104	0.164	0.110	0.040
	Sign. (2-tailed), p	0.656	0.237	0.453	0.237	0.428	0.773
	N	54	54	54	54	54	54
10	Spearman's	0.242*	0.124	0.116	0.121	-0.045	0.114
	Sign. (2-tailed), p	0.036	0.288	0.323	0.301	0.701	0.329
	N	75	75	75	75	75	75
11	Spearman's	-0.065	-0.208	0.297	0.310	0.091	0.145
	Sign. (2-tailed), p	0.773	0.353	0.180	0.161	0.689	0.521
	N	22	22	22	22	22	22
12	Spearman's	0.194	-0.205	0.284	0.375*	0.283	0.093
	Sign. (2-tailed), p	0.236	0.211	0.079	0.019	0.081	0.572
	N	39	39	39	39	39	39

Note. * – correlation is significant at the 0.05 level (two-sided); ** – correlation is significant at the 0.01 level (two-sided); N – group number; SBP – systolic blood pressure; DBP – diastolic blood pressure; PP – pulse pressure; IR – Rohrer index; Ca – calcium; P – phosphorus.

A direct correlation between the indicators reflecting the content of Ca and P in the blood was found in groups of boys aged 13 and 14 years and girls aged 12 and 13 years (Table 10).

In the group of 12-year-old girls, direct correlations of Ca-IR, Ca-SBP, and Ca-DBP were revealed (Table 9, 10). In this group, weakly expressed inverse correlations of P-IR and P-SBP were determined (Table 10).

A direct correlation of Ca-SBP was also recorded in the group of 14-year-old boys and 16-year-old girls (Table 9).

Table 10

**Results of correlation analysis in groups of boys and girls
from areas affected by the Chernobyl accident**

N	Correlation coefficient	Correlations					
		Ca-IR	Ca-P	P-IR	P-SBP	P-DBP	P-PP
1	Spearman's	0.161	0.124	-0.125	-0.104	-0.084	-0.013
	Sign. (2-tailed), p	0.133	0.248	0.247	0.334	0.434	0.907
	N	88	88	88	88	88	88
2	Spearman's	0.274**	0.231*	-0.204*	-0.210*	-0.100	-0.168
	Sign. (2-tailed), p	0.006	0.022	0.044	0.038	0.328	0.099
	N	98	98	98	98	98	98
3	Spearman's	0.079	0.296**	-0.035	-0.158	-0.007	-0.128
	Sign. (2-tailed), p	0.431	0.003	0.729	0.116	0.947	0.201
	N	101	101	101	101	101	101
4	Spearman's	0.049	0.313**	-0.118	-0.034	-0.041	0.003
	Sign. (2-tailed), p	0.628	0.001	0.239	0.736	0.682	0.975
	N	102	102	102	102	102	102
5	Spearman's	0.116	0.269**	-0.051	-0.083	0.055	-0.125
	Sign. (2-tailed), p	0.228	0.005	0.602	0.394	0.569	0.194
	N	109	109	109	109	109	109
6	Spearman's	0.156	0.100	-0.248*	-0.049	-0.033	-0.025
	Sign. (2-tailed), p	0.132	0.338	0.016	0.636	0.751	0.813
	N	94	94	94	94	94	94
7	Spearman's	0.033	0.042	-0.036	-0.064	-0.070	-0.026
	Sign. (2-tailed), p	0.788	0.729	0.766	0.598	0.567	0.832
	N	70	70	70	70	70	70
8	Spearman's	-0.048	-0.013	-0.198*	-0.226*	-0.113	-0.136
	Sign. (2-tailed), p	0.629	0.894	0.044	0.021	0.254	0.169
	N	104	104	104	104	104	104
9	Spearman's	0.097	0.065	0.001	-0.032	0.028	-0.106
	Sign. (2-tailed), p	0.485	0.643	0.992	0.820	0.843	0.444
	N	54	54	54	54	54	54
10	Spearman's	0.144	0.222	-0.219	-0.176	-0.142	-0.047
	Sign. (2-tailed), p	0.219	0.056	0.059	0.131	0.226	0.689
	N	75	75	75	75	75	75
11	Spearman's	-0.042	-0.052	-0.432*	0.013	-0.250	0.166
	Sign. (2-tailed), p	0.854	0.817	0.045	0.955	0.262	0.459
	N	22	22	22	22	22	22

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12	Spearman's	0.117	-0.009	-0.401*	-0.286	-0.383*	0.107
	Sign. (2-tailed), p	0.477	0.956	0.011	0.077	0.016	0.515
	N	39	39	39	39	39	39

Note. * – correlation is significant at the 0.05 level (two-sided); ** – correlation is significant at the 0.01 level (two-sided); N – group number; IR – Rohrer index; Ca – calcium; P – phosphorus; SBP – systolic blood pressure.

In the genetic subgroups of boys, compared with similar subgroups of girls, the proportion of hyperhomocysteinemia cases was more (Table 11).

This was most pronounced in the subgroups with the G/G MTR:2756 and T/T MTHFR:677 genotypes (Table 11).

Table 11

The proportion of cases of hyperhomocysteinemia in genetic subgroups of children in the Polissky district

Genetic subgroup	Boys			Girls		
	N	N ¹		N	N ¹	
		Abs.	%		Abs.	%
A/A MTR:2756	49	35	71.43	55	23	41.82
A/G MTR:2756	24	10	41.67	21	8	38.10
G/G MTR:2756	5	5	100	4	3	75.00
A/A MTHFR:1298	36	22	61.11	46	20	43.48
A/C MTHFR:1298	34	23	67.65	26	10	38.46
C/C MTHFR:1298	8	5	62.50	8	4	50.00
C/C MTHFR:677	39	20	51.28	40	14	35.00
C/T MTHFR:677	29	20	68.97	31	15	48.39
T/T MTHFR:677	10	10	100	9	5	55.56
A/A MTRR:66	16	8	50.00	16	4	25.00
A/G MTRR:66	35	19	54.29	37	18	48.65
G/G MTRR:66	27	23	85.19	27	12	44.44
All genotypes	78	50	64.10	80	34	42.50

Note: N – number of cases in the subgroup; N¹ – number of cases of hyperhomocysteinemia ($H_{cy} > 10.0 \mu\text{mol/l}$).

Direct correlations of H_{cy} -Ca²⁺ and P-PTH were recorded in the general group and a number of genetic subgroups (Table 12) [8, p. 90, 91; 9, p. 55].

Table 12

**Results of correlation analysis in genetic subgroups
of children Polissky district**

Genetic subgroup	Correlation coefficient	Correlations		
		H _{cy} -Ca ²⁺	H _{cy} -PTH	P-PTH
A/A MTR:2756	Spearman's	0.319**	0.025	0.482**
	Sign. (2-tailed), p	0.001	0.800	0.0001
	N	104	104	104
A/G MTR:2756	Spearman's	0.362*	-0.048	-0.234
	Sign. (2-tailed), p	0.014	0.755	0.121
	N	45	45	45
G/G MTR:2756	Spearman's	0.201	-0.767*	0.150
	Sign. (2-tailed), p	0.604	0.016	0.700
	N	9	9	9
A/A MTHFR:1298	Spearman's	0.462**	-0.020	0.280*
	Sign. (2-tailed), p	0.0001	0.858	0.011
	N	82	82	82
A/C MTHFR:1298	Spearman's	0.216	0.126	0.283*
	Sign. (2-tailed), p	0.097	0.338	0.029
	N	60	60	60
C/C MTHFR:1298	Spearman's	-0.192	-0.389	0.519*
	Sign. (2-tailed), p	0.476	0.137	0.039
	N	16	16	16
C/C MTHFR:677	Spearman's	0.169	-0.099	0.411**
	Sign. (2-tailed), p	0.136	0.386	0.0001
	N	79	79	79
C/T MTHFR:677	Spearman's	0.399**	0.073	0.115
	Sign. (2-tailed), p	0.002	0.580	0.380
	N	60	60	60
T/T MTHFR:677	Spearman's	0.619**	0.326	0.394
	Sign. (2-tailed), p	0.005	0.173	0.095
	N	19	19	19
A/A MTRR:66	Spearman's	0.403*	0.123	0.405**
	Sign. (2-tailed), p	0.022	0.502	0.021
	N	32	32	32
A/G MTRR:66	Spearman's	0.319**	0.074	0.260*
	Sign. (2-tailed), p	0.006	0.537	0.027
	N	72	72	72
G/G MTRR:66	Spearman's	0.276*	-0.067	0.270*
	Sign. (2-tailed), p	0.044	0.633	0.049
	N	54	54	54
General group	Spearman's	0.314**	0.013	0.301**
	Sign. (2-tailed), p	0.0001	0.869	0.0001
	N	158	158	158

Note. * – correlation is significant at the 0.05 level (two-sided); ** – correlation is significant at the 0.01 level (two-sided); H_{cy} – homocysteine; PTH – parathyroid hormone; ²⁺Ca – ionized calcium; P – phosphorus.

The most pronounced correlation between H_{cy} and Ca^{2+} was determined in the subgroup with the main genotype T/TMTHFR:677. In this case, there was no correlation between P-PTH (Table 12).

The most pronounced direct correlation between P-PTH was recorded in the subgroups with the main genotypes A/AMTR:2756, C/CMTHFR:1298 and C/C MTHFR:677 (Table 12).

In all analyzed genetic subgroups, there was no correlation between Ca^{2+} and PTH.

The correlation between H_{cy} and PTH was recorded only in the subgroup with the main genotype G/G MTR:2756, where it was inversely directed (Table 12). Thus, the residence of children near the ChEZ, in the territory affected by the Chernobyl accident, leads to the penetration of ^{137}Cs into their bodies.

This is due to the consumption of wild berries and mushrooms, as well as vegetable and berry crops grown on soils containing radioactive elements.

Constant fires of radioactive forests in the ChEZ [3, p. 10] increase the penetration of ^{137}Cs into the bodies of local residents.

The incorporation of ^{137}Cs into vital organs and systems of children [15, p. 489] has a negative effect on anabolic processes, reducing the energy potential of the body.

This may be associated with damage to mitochondria and a decrease in ATP formation, in particular in cardiomyocytes, as evidenced by an increase in the activity of aspartate aminotransferase (AST) in the blood serum of children living in areas affected by the Chernobyl accident (Table 13) [4, p. 29].

Table 13

The proportion of cases of exceeding reference values of transaminase activity and the de Ritis coefficient in a group of children

Age, years	Number of children	AST > 34.0 U/l		ALT > 36.0 U/l		AST > 34.0 U/l - AST/ALT > 2.0	
		Abs.	%	Abs.	%	Abs.	%
12-18	649	176	27.1 ± 1.8	7	1.08 ± 0.4	123	18.95 ± 1.5

Note: AST – aspartate aminotransferase ; ALT – alanine aminotransferase; AST/ALT – de Ritis coefficient.

The decrease in the intensity of synthetic processes is reflected by the inverse correlation between ^{137}Cs and IR, recorded in 11 of 12 age groups.

At the same time, calcium-phosphorus metabolism changes.

If the penetration of Ca^{2+} into the cell does not require energy expenditure, then its removal from the cell (about 30% of intracellular Ca^{2+}) is carried out by Ca^{2+} -ATPase, localized on the plasma membrane (PMCA), and receiving the main energy from adenosine triphosphate (ATP) hydrolysis [16, p. 383].

The transition of Ca^{2+} from the cytosol to the sarcoplasmic reticulum is carried out with the participation of sarco(endo)plasmic Ca^{2+} ATPase (SERCA) [16, p. 383; 17, p. 261].

In this case, the energy of ATP synthesized by mitochondria is also expended.

Mitochondria participate in the regulation of intracellular Ca^{2+} concentration, being its spatial buffer. At the same time, the continuous supply of Ca^{2+} to mitochondria will maintain mitochondrial dehydrogenases in an active state. Activation of dehydrogenases stimulates mitochondrial respiration and an increase in ATP production [18, p. 58].

Ca^{2+} enters mitochondria from the endoplasmic reticulum in a certain amount, the excess of which can lead to damage to these organelles [19, p. 3].

Ca^{2+} is a biologically active form of Ca and its concentration in the blood is strictly controlled by PTH, calcitriol (the active form of vitamin D3) and calcitonin [20, p. 2].

The potential of cell membranes, especially the nervous system and the heart, directly depends on the concentration of extracellular Ca^{2+} [21, p. 346]. Incorporation of ^{137}Cs into the body disrupts the transmembrane transition of Ca^{2+} and promotes its intracellular retention. This process is reflected in the inverse correlation between the specific activity of ^{137}Cs and the concentration of serum Ca, recorded in groups of children aged 12 and 13 years.

However, the level of Ca in the blood of most of the examined children exceeded the value of 2.55 mmol/l, established as the upper limit of the physiological range.

We associate this with a violation of H_{cy} methylation and the occurrence of hyperhomocysteinemia.

With an increase in the level of H_{cy} in the blood, there is an increase in the concentration of serum Ca^{2+} , as evidenced by the direct correlation between H_{cy} and Ca^{2+} in most of the analyzed genetic subgroups.

Thus, H_{cy} interferes with the process of regulation of intracellular Ca^{2+} .

In this case, the participation of PTH is reduced or completely excluded.

The genetic factor plays an important role in the regulation of calcium-phosphorus metabolism.

The correlation relationship H_{cy} - Ca^{2+} is most pronounced in the subgroup with the main genotype T/TMTHFR:677, with the highest, of all genetic subgroups, level of H_{cy} in the blood and the proportion of cases of hyperhomocysteinemia.

This confirms the participation of methylenetetrahydrofolate reductase FC in the processes of intra-intercellular Ca^{2+} exchange.

H_{cy} , when its concentration in the blood increases, affects bone tissue cells, resulting in an increase in Ca^{2+} in the blood.

In vitro experiments have proven the ability of H_{cy} to directly stimulate the formation and activity of osteoclasts. Mild and moderate hyperhomocysteinemia enhances bone resorption and contributes to the development of osteoporosis [22, p. 1008, 1009].

However, H_{cy} is able to moderately stimulate the primary activity of human osteoblasts [23, p. 1208].

PTH regulates Ca homeostasis and stimulates bone remodeling by directly affecting osteoblasts and osteocytes and by indirectly affecting osteoclasts. Thus, PTH stimulates both bone resorption and bone formation [24, p. 2].

In hyperhomocysteinemia, PTH does not control the Ca level in the blood.

In the general group and individual genetic subgroups, no correlations were found between the parameters reflecting the content of Ca^{2+} and PTH in the blood. Also, no correlations were found between the parameters characterizing the content of H_{cy} and P in the blood.

An increase in the Ca^{2+} content in the blood in hyperhomocysteinemia leads to a decrease in PTH production and an increase in the concentration of serum P.

In the subgroup with the main genotype T/TMTHFR:677, the PTH content in the blood was the lowest, compared with most other subgroups (Table 14) [8, p. 88].

Table 14

**Statistical characteristics in genetic subgroups
of children Polissky district**

Genetic subgroup	H _{cy} , μmol/l		PTH, pg/ml		Ca ²⁺ , mmol/l	
	Me	IQR	Me	IQR	Me	IQR
A/A MTR:2756	10.26	8.39-13.56	35.00	26.03-44.40	1.26	1.22-1.31
A/G MTR:2756	9.37	7.75-10.95	34.20	28.60-41.90	1.24	1.21-1.30
G/G MTR:2756	11.13	10.17-12.32	35.60	30.65-48.80	1.24	1.21-1.31
A/A MTHFR:1298	10.14	7.99-13.04	34.85	29.18-42.15	1.26	1.21- 1.30
A/C MTHFR:1298	10.19	9.01-13.19	35.00	25.18-44.40	1.26	1.22-1.31
C/C MTHFR:1298	10.31	7.99-12.69	36.40	24.75-45.93	1.24	1.21-1.28
C/C MTHFR:677	9.44	7.93-11.16	34.30	28.40-41.80	1.24	1.21-1.31
C/T MTHFR:677	10.24	8.42- 13.18	35.60	28.73-45.60	1.26	1.21-1.30
T/T MTHFR:677	14.47	10.15-22.78	31.20	24.60-36.10	1.26	1.24-1.29
A/A MTRR:66	9.26	8.03-13.13	36.10	29.33-50.78	1.26	1.22-1.31
A/G MTRR:66	10.08	7.98-11.99	35.90	29.50-44.95	1.26	1.22-1.30
G/G MTRR:66	10.81	9.13-14.18	30.75	24.56-37.50	1.24	1.21-1.29
General group	10.17	8.30-13.10	35.00	28.20-43.58	1.25	1.21-1.30

Note: Me – median, IQR – interquartile range; H_{cy} – homocysteine; PTH – parathyroid hormone; Ca²⁺ – ionized calcium.

In the case of the homozygous variant of the G allele of the MTR: A2756G polymorphism, H_{cy} had a direct suppressive effect on the formation of PTH, as evidenced by the inverse correlation of H_{cy}-PTH.

Thus, with hyperhomocysteinemia, there is an increase in the concentration of Ca in the blood and a delay in the elimination of P from the body.

This condition is dangerous for the body, and therefore, reactions occur in it aimed at establishing the physiological concentration of these macronutrients.

With an increase in the level of Ca²⁺ in the cells of the renal tubules, its reabsorption is inhibited and excretion in the urine increases [20, p. 2].

The direct correlation between P and PTH indicates a stimulating effect of P on the process of PTH formation, which allows the body to excrete excess P through the kidneys with urine.

The ability of P to directly influence the processes of PTH formation in hypercalcemia has also been noted by other authors [25, p. 2144].

This compensatory mechanism was determined in subgroups of children with the absence of risk alleles GMTR:2756 and TMTHFR:677 in the genome.

The absence of a stimulating effect of P on the process of PTH synthesis in subgroups that include these risk alleles creates conditions for the formation of calcium-phosphate complexes in the blood with their deposition in soft tissues and the walls of blood vessels. Ca^{2+} and P are linked by a single homeostatic mechanism in which PTH, calcitriol and fibroblast growth factor 23 (FGF23) take an active part [25, p. 443, 444; 26, p. 3986-3988].

Our studies indicate an active role of FC in this process.

An increase in the H_{cy} level in the blood, caused by mutations of the FC genes and environmental radiation exposure, leads to a violation of calcium-phosphorus homeostasis in the developing child's body.

Short-term hyperhomocysteinemia and the associated increase in the Ca level in the blood can be attributed to elements of the adaptation process in the body, which is in unfavorable environmental conditions.

Long-term hyperhomocysteinemia induced by genetic defects of FC and environmental exposure is an element of the pathological process.

Violation of calcium-phosphorus metabolism during the incorporation of ^{137}Cs affects the cardiovascular system of children living near the ChEZ.

An inverse correlation was established between the specific activity of ^{137}Cs and the SBP values in groups of children aged 12-16 years (Table 8).

This is due to damage to the mitochondria of cardiomyocytes, as evidenced by the direct correlation between the specific active ^{137}Cs and AST activity in the blood of the examined children from the Ivankivsky and Polissky districts (Table 15) [4, p. 31, 32].

Table 15

Results of the analysis of correlations between the values of specific activity of ^{137}Cs and the activity of serum AST in a group of children

Age, years	Correlation coefficient	Correlations	
		^{137}Cs (Bq/kg) - AST, U/l	^{137}Cs (Bq/kg) - AST/ALT
12-18	Spearman's	0.207**	0.187**
	Sign. (2-tailed), p	0.0001	0.0001
	N	649	649

Note. ** – correlation is significant at the 0.01 level (two-sided). AST – aspartate aminotransferase ; ALT – alanine aminotransferase; AST/ALT – de Ritis coefficient.

The resulting deficit of ATP energy carriers leads to a decrease in the contractility of the myocardium and a decrease in SBP. This is confirmed by the inverse correlation between AST and SBP ($r_{xy} = -0.122$, $p = 0.001$, $n = 803$).

Violation of intra/intercellular Ca^{2+} exchange associated with damage to mitochondria and, in connection with this, a decrease in ATP formation, has a negative effect on the processes of contraction and relaxation of the heart muscle.

A reflection of this process is the inverse correlation relationship $^{137}\text{Cs} - \text{Ca}$.

Thus, with an increase in the incorporation of ^{137}Cs into the child's body, there is a decrease in SBP.

An increase in the Ca level in the blood under the influence of H_{cy} contributes to an increase in the contractility of the myocardium, as evidenced by the direct correlations of Ca-SBP in groups No. 2, 5 and 10 (Table 9).

Thus, H_{cy} , with an increase in its level in the blood, influencing calcium-phosphorus metabolism, participates, under certain conditions, in the formation of adaptive reactions of the body aimed at normalizing metabolic processes in the cardiovascular system of the child's body.

However, with a combination of environmental radiation exposure and homozygotes of risk alleles of genetic polymorphisms of FC, the resulting hyperhomocysteinemia is an element of the pathological process affecting the heart and blood vessels.

Conclusions

The incorporation of ^{137}Cs into the body of children living in areas affected by the Chernobyl accident is one of the causes of energy deficiency in the cells of vital organs, leading to a decrease in the intensity of anabolic processes, interrelated disturbances in H_{cy} methylation, calcium-phosphorus metabolism and the functioning of the cardiovascular system.

The inverse correlation between the values of the specific activity of ^{137}Cs in the body and the serum Ca levels in groups of children aged 12 and 13 years indicates a disturbance of mineral metabolism in the developing body under conditions of radiation exposure.

This is due to a decrease in the functioning of mitochondria exposed to the effects of incorporated radionuclides ^{137}Cs .

Cellular energy deficiency induced by the effect of incorporated ^{137}Cs , as well as mutations of the FC genes, is the cause of the disruption of the H_{cy} methylation process, the concentration of which in the blood increases, exceeding, in some cases, the physiological level.

Hormonal control of calcium-phosphorus metabolism in children living in the area affected by the Chernobyl accident depends on the state of the FC genome and the level of H_{cy} in the blood.

The direct correlation between H_{cy} and Ca^{2+} is most pronounced in the subgroup of children carrying the T/TMTHFR:677 genotype.

At the same time, the influence of PTH on Ca^{2+} metabolism decreases, as evidenced by the absence of a correlation between Ca^{2+} and PTH.

In the case of homozygotes of the GMTR:2756 allele in the genome, H_{cy} blocks the process of PTH formation.

By increasing the concentration of Ca in the blood, H_{cy} affects phosphate metabolism.

Persistent, genetically determined hyperhomocysteinemia can cause an increase in the level of Ca in the blood, disruption of PTH synthesis and retention of P in the body. As a result, calcium-phosphate complexes are formed in the blood with their deposition in soft tissues and the walls of blood vessels.

In this regard, children who are carriers of homozygotes of the GMTR:2756 and TMTHFR:677 alleles should be included in the risk group.

In children with the absence of homozygotes of the GMTR:2756 and TMTHFR:677 alleles in their genome, a compensatory mechanism functions, associated with the stimulating effect of P on the process of PTH formation, which allows the body to remove excess P through the kidneys with urine.

The inverse correlation between ^{137}Cs and SBP in a group of children living in areas affected by the Chernobyl accident reflects the effect of incorporated ^{137}Cs on the state of their cardiovascular system.

In cardiomyocytes, at the same time, suppression of cellular energy and disruption of calcium-phosphorus metabolism occur, leading to a decrease in the contractility of the heart muscle.

Hyperhomocysteinemia, affecting calcium-phosphorus metabolism, under certain conditions, is an integral part of the adaptive response of the body aimed at normalizing metabolic processes in the cardiovascular system when exposed to incorporated radionuclides ^{137}Cs .

At the same time, with an unfavorable combination of endogenous (FC genes) and exogenous (radiation exposure) factors, hyperhomocysteinemia is an element of the pathological process affecting the heart and blood vessels.

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

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