blood level of homocysteine – a product of the metabolism of the essential amino acid methionine – exceeds the physiological threshold in more than 75.0% of children aged 12-17 years old in districts located near the Chornobyl nuclear power plant (Ivankivsky and Polessky districts) [1].

This effect associated with the abnormal functioning of the folate cycle (FC) is based on both genetic changes and the environmental impact on a growing organism caused by the accident at the Chornobyl nuclear power plant [2].

The abnormal functioning of the folate cycle in adults is known to be the basis for the development of cancers, in particular, breast cancer [3-5], which incidence in Kyiv region is the highest among all the regions of Ukraine and increases annually (fig. 1) [8-12].

Special attention in the etiology of breast cancer is given to carriers of the T risk allele of the MTHFR:677 genetic polymorphism [13, 14].

Taking this into account, the aim of this study was to make an assessment of the prevalence of this allele in a group of girls from Ivankivsky and Polіsky districts located near the Chornobyl exclusion zone. In addition, we assessed variants of combined carriership of the T allele with risk alleles of other genetic polymorphisms regulating the FC.

Material and methods. The group under analysis included 251 girls aged 8-17 years old. All the children had blood drawn from the ulnar vein after fasting in the morning in order to carry out genetic analysis.

Results. Genetic predisposition to breast cancer was assessed by the MTHFR:677T allele frequency. A total of 142 girls (56.6%) were carriers of the T allele, 25 girls (10.0%) were homozygous TT carriers, and 60 girls (23.9%) were compound heterozygous 677CT/1298AC MTHFR allele carriers.

Conclusions. The presence of genetic changes in the folate cycle results in a significant decrease in methylenetetrahydrofolate reductase activity and, correspondingly, an increase in homocysteine level in the blood, creating conditions for the development of oncological diseases. Taking into account the high level of genetic susceptibility, in conjunction with the continuous influence of radionuclides and their decay products on the body, it is necessary to identify a group at risk for developing oncological diseases of the mammary gland.

Key words: folate cycle, risk allele, breast cancer, girls, contaminated territories.

The aim of this paper was to assess the prevalence of the T risk allele of the MTHFR:677 genetic polymorphism in a group of girls from Ivankivsky and Polisky districts located near the Chornobyl exclusion zone. In addition, we assessed variants of combined carrierrship of the T allele with risk alleles of other genetic polymorphisms regulating the folate cycle.

Research methods. Immunoolchemical, statistical.

Results. Genetic predisposition to breast cancer risk was analyzed in a group of 251 adolescent girls. Carrierrship of the T allele of the MTHFR:C677T polymorphism was found in 142 children (56.6%), while the homozygous T/T variant was found in 25 girls, or in 10.0% of cases. Compound heterozygosity for the 677CT/1298AC alleles of the MTHFR gene was recorded in 60 individuals, or in 23.9% of cases.

Conclusions. The revealed genetic changes in the folate cycle lead to a significant decrease in the activity of methylenetetrahydrofolate reductase, and, accordingly, to an increase in the level of homocysteine in the blood, creating conditions for the occurrence of breast cancer.

Given the high level of genetic predisposition, taking into account the constant impact on the body of radioactive elements and their decay products, the occurrence, as a consequence, of serious metabolic disorders, it is necessary to identify the breast cancer risk group of children.

Keywords: folate cycle, risk alleles, breast cancer, adolescent girls, radiation contaminated areas.
The carriership of the MTHFR:C677T polymorphism T allele was observed in 142 girls (56.6%), while the T/T homozygous variant was found in 25 girls or in 10.0% of cases (table 2). This genotype variant leads to a significant decrease in the activity of methylenetetrahydrofolate reductase and, accordingly, an increase in blood homocysteine levels [15].

It is placed on the same level as the TT genotype of the same polymorphism in terms of the degree of inhibition of the methylenetetrahydrofolate reductase enzyme activity, and accordingly, the degree of increase in the blood level of homocysteine [17].

In the group of girls under study, compound heterozygosity for the MTHFR gene 677 CT/1298 AC alleles was found in 60 girls or in 23.9% of cases, while the carriership of the 677 MTHFR polymorphism TT homozygous variant was observed in 25 girls, or in 10.0% of cases. Thus, there is genetically determined predisposition to the abnormal functioning of the FC and the increase in the blood homocysteine level in 85 girls or in 33.9% of cases in the studied population of children (table 3).

Heterozygous associations of the MTHFR:C677T and MTRR: A66G, as well as MTHFR:C677T and MTRR:A66G polymorphisms were noticed to be an internal factor contributing to the occurrence of severe diseases, including congenital defects [17, 18].

In the group of girls under study, the compound heterozygosity of the MTHFR:677CT/ MTRR:66AG polymorphisms was observed in 61 girls, or in 24.3% of cases, the compound heterozygosity of the MTR: 2756AG/MTHFR:66AG polymorphisms was found in 37 girls, or in 14.7% of cases (table 3). Attention should be given to the compound heterozygosity of the MTR: 2756AG/MTHFR:677CT polymorphisms in 35 girls, or in 13.9 of cases, because there occurs a combined disruption of the functioning of the main enzyme systems of the FC. In this case, the environmental effect in the form of radiation will be a provoking factor. The combinations of a homozygous variant of one polymorphism and a heterozygous variant of another one were observed less frequently, while the combinations of homozygous variants of risk alleles of these polymorphisms were not found at all (table 3).

Thus, we should acknowledge that the girls of the examined group from the districts bordering the Chornobyl exclusion zone have a high level of genetic predisposition to cancer, including breast cancer.

Hyperhomocysteinemia, a condition when the level of homocysteine in the blood exceeds the physiological threshold is a manifestation of dysfunction of the genetic system that controls the folate cycle. This condition in children of Ivankovsky and Polessky districts was especially evident after forest fires in the Chornobyl exclusion zone [19].

In particular, the blood concentration of homocysteine above 10 µmol/L was reported in 89 out of 137 examined girls from these districts (65.0%) after the 2015 forest fires [20].

At the same time, hyperhomocysteinemia was not associated with the number of the folate cycle genetic polymorphisms under study, despite the carriership of several variants of the latter by the majority of girls in the group under analysis. In addition, there was a clear direct association between the blood homocysteine level and the severity of the genetic risk associated with a genetic polymorphism responsible for the synthesis of methylenetetrahydrofolate reductase – the main enzyme of the FC (table 4) [20].

In order to carry out correlation studies that determine an association between blood Hcy levels and genetic abnormalities in the FC, in a number of

<table>
<thead>
<tr>
<th>Gene, polymorphism</th>
<th>Genotype variants</th>
<th>Abs. number</th>
<th>%</th>
<th>Abs. number</th>
<th>%</th>
<th>Abs. number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>MTHFR:C677T</td>
<td>«Neutral» allele</td>
<td>109</td>
<td>43.4</td>
<td>117</td>
<td>46.6</td>
<td>25</td>
<td>10.0</td>
</tr>
<tr>
<td></td>
<td>«Risk» allele</td>
<td>122</td>
<td>48.6</td>
<td>110</td>
<td>43.8</td>
<td>19</td>
<td>7.6</td>
</tr>
<tr>
<td>MTHFR:A1298C</td>
<td>«Neutral» allele</td>
<td>195</td>
<td>62.5</td>
<td>80</td>
<td>31.9</td>
<td>14</td>
<td>5.6</td>
</tr>
<tr>
<td></td>
<td>«Risk» allele</td>
<td>122</td>
<td>48.6</td>
<td>110</td>
<td>43.8</td>
<td>19</td>
<td>7.6</td>
</tr>
<tr>
<td>MTRR:A66G</td>
<td>«Neutral» allele</td>
<td>45</td>
<td>17.9</td>
<td>120</td>
<td>47.8</td>
<td>86</td>
<td>34.3</td>
</tr>
<tr>
<td></td>
<td>«Risk» allele</td>
<td>195</td>
<td>62.5</td>
<td>80</td>
<td>31.9</td>
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<td>5.6</td>
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</tbody>
</table>
cases under consideration, the MTHFR C677T genotypes under analysis were assessed using a point system (0-2) depending on how they affect Hcy formation – R genetic risk scores: «0» – 677CC genotype – no risk; «1» – 677CT genotype – low risk; «2» – 677TT genotype – high risk [15].

The strongest association was reported ith the homozogous variant of the MTHFR: 677 Т/T risk allele [15]. At the same time, the external environmental factor in the form of radionuclides and wood combustion products contributed to a decrease in the activity of this enzyme by blocking energy processes in the cell [19].

**Conclusions**

1. In the population of girls living in districts bordering the Chornobyl exclusion zone, a predisposition to abnormal functioning of the folate cycle and an increase in the blood level of homocysteine associated with the MTHFR:677 genetic polymorphism Т allele was identified in 56.6% of cases. A homozygous variant of the Т allele carriage was reported in 10.0% of cases, the compound heterozygosity for the 677CT/1298AC alleles of the MTHFR gene was observed in 23.9% of cases.

2. The compound heterozygosity of the MTHFR:677CT/MTRR:66AG, MTR:2756AG/MTR:66AG and MTHFR:677CT/MTR:2756AG polymorphisms observed in 24.3%, 14.7% and 13.9% of cases respectively also contributes to the abnormal homocysteine metabolism.

3. The genetic changes in the folate cycle that were found provide conditions for the occurrence of cancers, including breast cancer.

4. Taking into account the high level of a genetic predisposition and constant effect of radioactive elements and their decay products on the organism, and as a result, the occurrence of serious metabolic disorders, it is necessary to identify a children’s breast cancer risk group.

**Literature**


2. Bandazhevsky Yu.I., Dubovaya N.F. The State of Folate Metabolism and its Link...
Цель работы была оценка встречаемости аллелей риска T генетического полиморфизма МТФР:677T в группе девочек из Иванковского и Полесского районов, расположенных вблизи Чернобыльской зоны отчуждения, и вариантов сочетанного носительства аллелей T с аллелями риска других генетических полиморфизмов, контролирующих фолатный цикл.

Методы исследования.
Иммунохимический, статистический.

Результаты. Генетическая предрасположенность к риску возникновения рака молочной железы проанализирована в группе, состоящей из 251 девочек-подростков. Выявлено носительство аллелей T поли-морфизма МТФР:C677T у 142 детей (56,6%), при этом гомозиготный вариант T/T встречался у 25 девочек, или в 10,0% случаев. У 60 лиц, или в 23,9% случаев, регистрировалась компаунд-гетерозиготность по аллелям 677CT/1298AC гена МТФР.

Выводы. Выявленные генетические изменения фолатного цикла приводят к значительному снижению активности метилтетрагидрофолатредуктазы и, соответственно, увеличению содержания гомоцистена в крови, создавая условия для возникновения онкологических заболеваний молочной железы.

Учитывая высокий уровень генетической предрасположенности, а также постоянное воздействие на организм радиоактивных элементов и продуктов их распада, возникает необходимость выделять группу риска детей в отношении возникновения онкологических заболеваний молочной железы.

Ключевые слова: фолатный цикл, аллели риска, рак молочной железы, девочки-подростки, радиоактивно загрязненные территории.


ЗАКОНОМІРНОСТІ ФОРМУВАННЯ ЗАХВОРЮВАНЬ ПЕЧІНКИ У ПОСТРАЖДАЛИХ ВНАСЛІДКОВ АВАРІЇ НА ЧОРНОБИЛЬСЬКІЙ АЕС

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ПАТТЕРNS OF LIVER DISEASE FORMATION IN VICTIMS OF THE CHORNOBYL NUCLEAR POWER PLANT ACCIDENT

non-alcoholic fatty liver disease (NAFLD) is a problem not only of modern hepatology, but also has a global importance for the state of human health, which is both due to the broad reach and the consequences of the progression of this pathology – the development of the liver cirrhosis, hepatocellular carcinoma, liver-cell deficiency [1].

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