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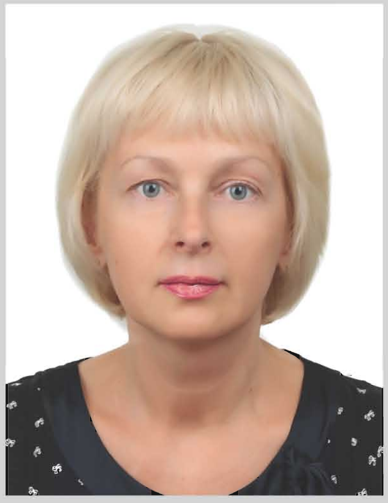
CHILDHOOD LEUKEMIA AFTER THE LOW-DOSE RADIATION EXPOSURE



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Childhood leukemia risks after the low-dose exposure from different sources of ionizing radiation are analyzed. Correlations between the leukemia risks and age of irradiated children, radiation exposure dose, and term of exposure are represented.

Leukemia incidence levels about one third among all childhood cancers [3, 19] and acute leukemia (AL) is the most frequent disease. Among all risk factors (environmental, genetic, and infectious ones) only the ionizing radiation (IR) is significantly linked to childhood AL, with no such strong and stable correlation for another risk factors [3, 21, 39, 40, 46]. Numerous studies found out the leukemia risk in irradiated children been higher and realized earlier compared with adults [4, 10, 21, 36, 39, 40, 41, 46, 47, 49]. Despite absence of threshold [6, 48, 50], the leukemia risk depends on age of irradiated individual, radiation exposure dose, and term of exposure [3, 26, 27].

The absolute and relative leukemia risks in exposed to IR depend on leukemia type [36]. The highest excess absolute risk (EAR) was defined for acute myeloid leukemia (AML) (at 1.1 cases per 10^4 PY Sv) with its decline for chronic myelogenous leukemia (CML), and acute lymphoblastic leukemia (ALL) (at 0.9, and at 0.6 cases per 10^4 PY Sv, respectively) [9]. The highest excess relative risk (ERR) was found for ALL at 9.1, for CML at 6.2, and for AML at 3.3 per Sv.

The aftermath of low-dose exposure of childhood populations is still urgent nowadays. A large amount of conducted studies on childhood leukemia risks revealed an ambiguous data. Mixed results were received in children exposed to diagnostic X-ray, i.e. a significant increase of risk for pre B-ALL (OR=3.2; 95% confidence interval (CI) 1.5–7.2), and for those exposed at the age over 5 years (OR=3.8; 95% CI 1.1–13.3). The ALL risk was not confirmed (OR=1.2; 95% CI 1.0–1.6) [24, 42].

The elevated risk for childhood leukemia was found in some studies on low-dose exposure [4, 7, 8, 17, 29]. The leukemia risk was increased in child inhabitants of contaminated areas exposed *in utero* [35]. But these results have not been confirmed in a similar study in Germany [43], in Belarus [16], and in Ukraine [30]. So, the *in utero* exposure needs further research with taking into account the discrepancies of performed studies including the European Childhood Leukemia — Lymphoma Incidence Study (ECLIS) [5].

Linear dose — response models of leukemia risk in the low-dose range (<100 mGy) are based on leukemia mortality among the Japanese atomic bomb survivors [6, 48, 50]. ERR for children increases after a minimum latent period of 2 years, rising to a maximum of approximately 50 Gy^{-1} about 7 years after exposure. UNSCEAR 2000 and US NRC 2006 publications confirmed the increase of childhood leukemia ERR within 2 to 5 years upon irradiation. Risk of leukemia mortality is moderately increased in exposed children under ten years old, and considerably decreased in the 10–19 age group [9, 41]. EAR for exposed at a young age sharply declines with time during the next 10–20 years upon irradiation [9]. At 25 years after exposure the ERR declines reaching the value of approximately 2 [36, 48, 50].

The childhood leukemia risks linked to low-dose irradiation after the Chornobyl nuclear power plant (ChNPP) accident were analyzed in a large number of studies [28]. Methodological differences of studies included the dose estimation, data sources, and follow-up periods. Dose estimation was based on the UNSCEAR recommendations and included both external and internal dose values (1988). Design of the most of studies was the same and included the pre-accident (1980–1985) and post-accident (since 1986) analysis of leukemia rates [1, 12–15, 25, 34, 35, 37, 44]. Only in one study in Ukraine [30] the post-accident leukemia rates were compared for the population of contaminated and non-contaminated territories.

Some studies on the Chornobyl catastrophe consequences revealed an increased childhood leukemia risk. In German studies [25, 43] the relative risk (RR) was significantly higher in infants (RR=1.48; 95% CI 1.02–2.15). Preliminary results in USA study [23] showed the potential increase in childhood leukemia rate but these data require a rigorous assessment due to the very low level of Chornobyl exposure. Turkish study [12] revealed the higher number of ALL cases in post-accident period compared with pre-accident period with no incidence rate estimation. According to the study results [35] the leukemia incidence rate in exposed infants was significantly increased (RR=2.6; 95% CI 1.4–5.1), though being not in elder children (RR=1.11; 95% CI 0.8–1.5).

In a case-control study [30, 31] were analyzed the leukemia rates in population of contaminated territories (Rivne, Zhytomyr, Chernihiv, and Cherkasy regions) *vs* non-contaminated areas, thus the pre-accident incident rates were not estimated. The 246 childhood leukemia cases 0–5 years of age at the time of the Chornobyl accident and 492 randomly selected controls matched by age, sex, and type of settlement were included to the analysis. Four dose-range groups were selected, namely 0–2.9 mGy, 3–9.9 mGy, 10–99.9 mGy, and 100–313.3 mGy. The risk of leukemia was significantly increased among exposed to radiation doses higher than 10 mGy (2.4; 95% CI 1.4–4.0; p=0.01); among males (2.8; 95% CI 1.4–5.5; p=0.01); among AL cases diagnosed since 1987 till 1992 (2.5; 95% CI 1.2–5.1; p=0.05), and particularly among AML cases (5.8; 95% CI 1.4–24.6; p=0.05). A significant association between leukemia risk and radiation dose to the bone marrow is however difficult to interpret due to some problems in selection and comparability of controls in this study [5].

Analysis of childhood leukemia incidence in Belarus after the ChNPP accident for the 1980–2004 period [22] revealed a significant transient increase in the childhood leukemia incidence for cases 0–14 years old at the time of diagnosis for the 1986–1992 period: standardized incidence ratio (SIR)=1.13 (95% CI 1.02–1.26), ERR=7.8% per 1 mSv (95% CI 1.0–15.4), EAR=30.1 cases per 10^4 PY Sv (95% CI 3.9–59.2), attributive risk (AR)=11.7% (95% CI 1.5–23). After 1992 the leukemia incidence decreased to under the pre-accident level.

Further analysis of Belarus data (1980–2008) revealed a statistically significant 33%-increase of the leukemia incidence in children exposed in 1987 (RR=1.33; p=0.004), especially in children less than one year old (RR=2.68; p=0.0004), another increase occurred in 1990–1992 [18]. A highly significant increase in childhood leukemia (+16.5%) and infant leukemia (+95%) was found when the rates since 1987 till 1992 were compared with former studies [11, 15] and statements in the UNSCEAR reports (2000, 2008) that rejected the incidence increase of childhood leukemia in Belarus after the Chornobyl accident [18].

Some of conducted studies on low-doses exposure have not confirmed an increase in the childhood leukemia risk [20] including investigations of Chornobyl accident aftermath [25, 40, 43]. As for the ECLIS report [32, 33, 38] there were no convincing data of the excess in childhood leukemia rates in contaminated areas. After the five year post-accident period a small increase in rates but not in the childhood leukemia risk was found out in Ukraine [37], in Belarus [14], in Finland [1], in Sweden [13], and in Greece [35]. In the study [13] were analysed the 888 cases 0–15 years old 6.5 years after the accident. The RR for AL was 0.9 (95% CI 0.6–1.4) in highly contaminated areas (>10 kBq/m^2) *vs* the same areas before the accident, for the ALL cases aged under 5 years at diagnosis the RR was 1.5 (0.8 to 2.6). When comparing the highly contaminated areas with low contaminated ones the RR was 0.9 (0.7 to 1.3), for ALL cases under 5 years old the RR was 1.2 (0.8 to 1.9). A dose-response analysis in the Swedish study showed no correlation between the degree of contamination and the incidence of childhood leukemia [44]. In the study [40] wasn't revealed a significant association between the risk of childhood leukemia and Chornobyl irradiation in children 0–14 years of age. In the Hungarian population-based study [45] the 2204 cases diagnosed since 1973 till 2002 were analyzed. In the period of the hypothesized impact of the Chornobyl accident the incidence rate was elevated by 2.5%, but not significantly (95% CI −8.1%; +14.3%; p=0.663). The age-standardized incidence, age distribution, gender ratio, and magnitude of increasing trend of childhood leukemia incidence were similar to that in other European countries.

No univocal results on childhood leukemia rates were received through the studies in Ukraine, Belarus, and Russia. There wasn't revealed any excess of leukemia among children aged 0–19 in contaminated oblasts in Ukraine when compared to the pre-accident (1980–1985) and post-accident (1986–1996) period [2]. Childhood leukemia risks were not increased in the earlier study in Belarus [15]. Further analyses with the estimation of soil contamination density found a non-significant risk increase (RR=1.26; 95% CI 0.76–2.10) in the highly contaminated territories of Belarus [16]. Some other national studies in Belarus [11] defined no increase in childhood leukemia rates. In a population-based case — control study [7] were analyzed the 421 leukemia cases (114 ones from Belarus, 268 from Ukraine, and 39 from Russia) diagnosed since April 26, 1986 till December 31, 2000 in contaminated regions among children who were in utero or under 6 years of age at the time of the ChNPP accident. The accumulated absorbed radiation dose to the bone marrow was estimated for each subject. The mean dose was higher among cases (10.8 mGy) *vs* controls (6.3 mGy). Mean doses were similar in Belarus and Russia with little difference between cases and controls, in Ukraine the mean dose for cases was substantially higher (10.1 mGy) than for controls (3.5 mGy). The conclusion is that there was no convincing evidence of an increased risk of childhood leukemia due to the Chornobyl exposure [7].

Summarizing all above-mentioned methodological differences between the reviewed studies it is unavailable to precise exactly the childhood leukemia incidence after the ChNPP accident. So this problem needs further concern and research.

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Лейкемія у дітей після опромінення малими дозами іонізуючого випромінювання

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Резюме. Проаналізовано ризики лейкемії у дітей після опромінення малими дозами від різних джерел іонізуючого випромінювання. Представлено взаємозв'язок між ризиками лейкемії та віком опромінених дітей, дозою іонізуючого випромінювання, тривалістю опромінення.

Ключові слова: дитяче населення, ризики лейкемії, іонізуюче випромінювання.

Лейкемия у детей после облучения малыми дозами ионизирующего излучения

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Резюме. Проанализированы риски лейкемии у детей после облучения малыми дозами от различных источников ионизирующего излучения. Представлена взаимосвязь между рисками лейкемии и возрастом облученных детей, дозой ионизирующего излучения, длительностью облучения.

Ключові слова: детское население, риски лейкемии, ионизирующее излучение.