

# Infant Mortality among Offspring of Individuals Living in the Radioactively Contaminated Techa River Area, Southern Urals

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Massive discharge of liquid radioactive wastes into the Techa River in 1949-1956 by the industrial complex Mayak for production of plutonium for weapon resulted in protracted internal and external radiation exposure of the population living along the river. The Techa River Offspring Cohort comprises individuals born after December 31, 1949, whose one or both parents were exposed in the Techa riverside villages. The study group includes 7,897 individuals. About 40% of the Techa River Offspring Cohort members born in 1950-1956 could be exposed *in utero* and after birth. The mean dose estimates based on the Techa River Dosimetry System 2000 were: 0.07 Gy for parental gonads, 0.01 Gy for fetus and 0.02 Gy for postnatal exposure of bone marrow. Over 46 years of follow-up from 1950-1995, 916 subjects died and the cause of death was known in 93% of them. Out of 916 subjects dead, 456 (53%) died under 1 year of age, mainly due to respiratory tract diseases (38% of all infant deaths), infections (27%) and perinatal disorders (13%). It has been shown that the baseline infant mortality rate depends on gender, ethnicity and birth year. Radiation risk analysis was based on a simple parametric linear excess relative risk model with adjustment for gender, ethnicity and birth year. There was no evidence of increasing infant mortality risk with parental gonadal dose. The infant mortality rate significantly depended on fetal dose and dose to bone marrow received during the first year of life with a 3% increase in risk per 1 cGy of intrauterine and postnatal doses.

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## Introduction

The overexposures in the residents of the Techa riverside villages in the Southern Urals resulted from the operations of the Mayak Production Association (Mayak PA), an industrial complex for production of plutonium for weapon. Because of the flaws in the technological processes of reprocessing and storage of radioactive waste at the Mayak PA, a considerable amount of radioactive wastes were released into the Techa River in the period from 1949 through 1956, causing a prolonged combined (external and internal) radiation exposure of the riverside communities.<sup>1,2</sup> To provide medical care and follow-up of the exposed population, the Urals Research Center for Radiation Medicine (URCRM, former Branch 4 of the Biophysics Institute) was established. As a result of the URCRM activities for about five decades, a wealth of original information on the environmental situation and health status of the people exposed in the Techa

River area has been collected.

The purpose of the present study is to estimate the infant death rates for a 45-year period of follow-up of the offspring of Techa riverside residents exposed to a protracted influence of radiation taking into account exposure of parental gonads before conception of the child, exposure over the period of intrauterine development and after birth, as well as to study the influence of non-radiation risk factors on the infant mortality.

## Subjects and Methods

### *Techa River Offspring Cohort definition and follow-up activities*

The study is focused on the cohort of the first-generation offspring of exposed parents, the so called Techa River Offspring Cohort (TROC). The TROC comprises individuals born after December 31,

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1949 whose one or both parents lived in any of the Techa riverside villages in the period from January 1, 1950 through December 31, 1960.<sup>3</sup> Currently, the TROC includes only offspring born in the five districts of the Chelyabinsk region in which birth certificates have been collected on a regular basis. The initial size of this cohort was 11,155 individuals. Nearly 3,000 offspring had no assessments of exposure doses and were temporally excluded from the study. Finally, the study cohort used for radiation risk analyses amounts to 7,897 members. Table 1 shows the gender, ethnicity, and birth year characteristics of the study TROC.

Men account for 51% of the study group. The TROC includes two ethnic groups: Slavs, mostly Russians and, Tartars and Bashkirs; they differ in life style, religion, dietary habits, etc. The proportion of Tartars and Bashkirs in the TROC amounts to 56%. Over half the offspring (56%) were born during the first decade, i.e., in the period from 1950 through 1959. About 40% of the cohort members were born during the period of massive releases (1950-1956). The decrease in the number of newborn offspring with period of follow-up can be associated with the decreasing number of parents of reproductive age.

As of the end of 1995, 5,998 (76%) of the TROC members were alive; 1,067 (13%) individuals were dead and death certificate was available for 87% of them; and 832 (11%) individuals were lost to follow-up, but their vital status was known until the end of 1995. Out of 1,067 death cases, 916 were registered among non-migrants in the catchment area.

The information on death cases was obtained from death certificates collected by the URCRM for over 50-year follow-up of the exposed population. Death certificates kept at the regional Civil Registrar's Office (ZAGS) have been systematically copied for the total population of Krasnoarmeisky and Kunashaksky raions (districts) through which the Techa flows, and for residents of villages in Argaiashsky, Sosnovsky and Kaslinsky raions to which large groups of residents were evacuated from contaminated areas. These

five raions of Chelyabinsk region form the catchment area for the TROC mortality rate analysis. The death certificates were used for creating a computer file of death cases and causes of death. The file also included passport information, i.e. family name, first name, patronymic, date and place of birth, which enabled identifying death cases among exposed people and their offspring. Death cases identified among exposed persons or their offspring were entered into the exposed-population death registry.<sup>2</sup> Causes of death were coded according to the ICD-9.<sup>4</sup>

#### *Exposure conditions and dose assessment*

From 1949 through 1956, a total of  $76 \times 10^6$  m<sup>3</sup> of radioactive wastes with total combined activity of  $10^{17}$  Bq (2.75 MCi) for  $\beta$ -radiators were released into the Techa River. Approximately 98% of the total activity were released from 1950 through 1951. The composition of releases included 20.4% of <sup>89</sup>Sr and <sup>90</sup>Sr, 12.2% of <sup>137</sup>Cs, 26.8% of rare-earth elements, 25.9% of <sup>103</sup>Ru and <sup>106</sup>Ru, and 13.6% of <sup>95</sup>Zr and <sup>95</sup>Nb.<sup>1,2</sup>

The doses of ionizing radiation received by the residents of the riverside villages were determined by external exposure resulting from the gamma-background along the river bank due to the deposition of radionuclides in bottom sediments, contamination of water surface, and floodplains, as well as by internal irradiation due to intake of contaminated river water and foodstuffs. The analyses in this paper were based on the Techa River Dosimetry System (TRDS-2000) dose estimates.<sup>5,6</sup>

External exposure and body intake mainly of <sup>137</sup>Cs uniformly distributed in soft tissues resulted in the accumulation of radiation doses in the gonadal glands of parents of TROC members. The total pre-conception doses accumulated in parental gonads due to external exposure and incorporation of cesium reached the maximum of 0.94 Gy (mean value=0.07 Gy). The accumulation of doses in the parents' gonadal cells due to external exposure and <sup>137</sup>Cs uniformly distributed in soft tissues actually ceased in 1959-1960, and its process was most intensive from 1950 through 1954.

Besides, external exposure to ionizing radiation and incorporation of cesium in the body of pregnant women led to the formation of intrauterine fetal doses.

Intake of bone-seeking strontium isotopes <sup>90</sup>Sr and <sup>89</sup>Sr through water and food brought about the formation of doses from internal exposure of bone surfaces and red bone marrow (RBM). Of special significance was the intake of the radionuclides in female residents since the strontium body contents in women at the reproductive age resulted, in case of pregnancy, in the formation of internal exposure doses to fetus.<sup>7,9</sup> The formation of fetal RBM doses was determined by penetration of strontium deposited in the mother's skeleton into her blood flow, the ensuing transfer via the placenta to the fetus and capture of the radionuclide by the fetal bone tissues. The second factor associated with the formation of internal dose to fetal RBM was mother's strontium body intake through water and food during pregnancy. In addition, strontium absorbed in the gastro-intestinal tract was transferred through the placenta to the fetus after it entered the

**Table 1.** Demographic characteristics of the Techa River Offspring Study Cohort

Parameter	Number of subjects	Percentage
Total	7,897	100
Gender		
Male	4,009	50.8
Female	3,888	49.2
Ethnicity		
Slavs	3,501	44.3
Tartars and Bashkirs	4,396	55.7
Year of birth		
1950-1956	3,140	39.8
1956-1959	1,276	16.1
1960-1969	2,721	34.5
1970-1979	688	8.7
1980-1992	72	0.9

blood flow. The total (external + internal) dose to fetus accumulated over 9 months of the gestational period reached the maximum of 197.5 mGy (mean value=5.07 mGy). The most significant fetal doses accumulated over the period of intrauterine development were received by children born during the first five years after the onset of exposure. The mean dose received over 9 months of gestation by children born after 1960 did not exceed 0.5 mGy.

The exposure to external and internal radiation in the cohort members continued after birth, and led to the accumulation in their bodies of postnatal exposure doses. The maximum dose accumulated after birth in their RBM was 0.66 Gy (mean value=0.02 Gy).

### Statistical methods

The infant mortality rates were assessed using the sanitary statistics methodology.<sup>10,11</sup> The calculation of the number of person-years at risk, analysis of dose-effect relationship and assessment of radiation risk for the offspring cohort were made using the package of the EPICURE statistical programs.<sup>12</sup>

The information available for each cohort member included gender, ethnicity, date of birth, date of last known vital status, the cause of death for deceased cohort members and individualized estimates of cumulative dose (internal plus external) to parental gonads at conception of the child, dose to fetus and annual doses of postnatal exposure of bone marrow. The follow-up started from the maximum of the date of birth and January 1, 1950, through the minimum of the date of death, last date of known vital status, date of migration from the catchment area and December 31, 1995. Infant mortality rates were analyzed using simple parametric excess relative risk (ERR) models. The basic ERR model for age-specific death rates can be written as:

$$\lambda(d, z) = \lambda_0(z_0)(1+\rho(d)\epsilon(z_1)),$$

where  $d$  is dose (in Gy);  $z_0$  represents other factors (such as gender, ethnicity, or time period) that can modify the baseline rates ( $\lambda_0$ ); and  $z_1$  represents factors (such as gender, ethnicity, birth cohort effect) that might modify the ERR.

Parameters were estimated using maximum likelihood method for Poisson regression model. Likelihood ratio statistics were used for significance tests and confidence intervals (CI).

Taking into account a statistically significant dependence of the infant mortality rates on the period of follow-up, as well as the dependence of the cumulative doses to parental gonads and those received by the fetus during the period of gestation on the child's birth year, it was considered appropriate to eliminate the confounding effect of the temporal factor. Thus, the evaluation of the contribution of radiation factors was conducted on the basis of the data stratified by calendar-year periods of the follow-up.

## Results

### Baseline infant mortality rates

The person-years for TROC members over the period of residence

in the catchment area from January 1, 1950 through December 31, 1995 amounted to 183,340. Over the 46 years of follow-up, 916 death cases from all causes were identified in the TROC. Death cases aged under 1 year were 456 (49.8%), and the cause of death was known for 441 (96.7%) of them. The major causes of death in infants aged under 1 year were as follows: diseases of the respiratory organs 38% (167/441); infectious diseases 27% (119/441); and conditions originating in the perinatal period 12.5% (55/441). Congenital developmental defects (CDD) were indicated as causes of death in 22 cases (5%), in which congenital heart defects accounted for 19 (77%); in 2 cases the morphology of the developmental defects was not specified. The causes of death in the remaining 3 cases were CDD of small intestine, Down's syndrome and spina bifida.

Fifty-five per cent of death cases among children under 1 year were male (242/441). A higher frequency of mortality was noted in Tartars and Bashkirs among infants who died during the first year of life (258/441 or 59%). The dynamics of the infant mortality rates over the 40-year period of follow-up is presented in Figure 1. The infant mortality rates in unexposed rural population of the USSR (control) are also presented for comparison.<sup>23</sup>

The highest infant death rates were noted in the post-war years for both the offspring under study and the control. In 1950-1955 the infant mortality rate was 99.44 per 1,000. A decrease in infant death rates was noted with time of follow-up. Attention is drawn to the fact that death rates for infants aged under 1 year was significantly higher in the offspring cohort compared to the control.

It should be kept in mind that the characteristics, such as neonatal and infant mortality, are influenced by the following non-radiation factors: mother's diseases during pregnancy, complications of pregnancy and labor, and age at delivery. The latter factor (gestational age) directly influences the neonatal mortality rate. Thus, in children born at gestational week 28, death rate of 70.2% was observed over the first 4 days of life, which decreased to almost half (38.5%) in those born at gestational week 30. The neonatal death rates in children born at gestational week of 38-40 were 0.35-0.17%.<sup>11,14</sup>

In our study infants were regarded as premature if they were born between gestational weeks 28 and 38. Since for a part of neonates included in the TROC, information on gestational age at birth was

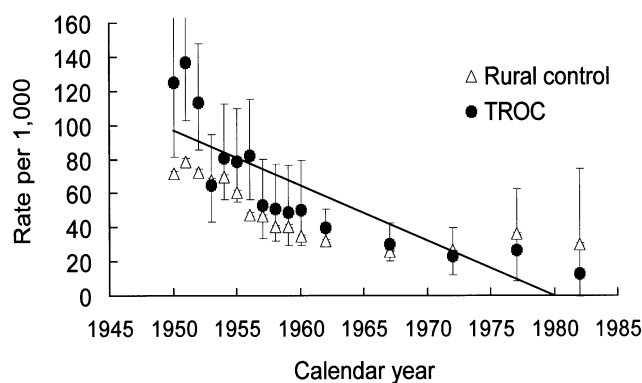


Figure 1. Dynamics of infant mortality rates in the Techa river offspring cohort (TROC).

lacking, and only information on their physical development was available; children with low birth weight (2,880 g or less) were considered to be premature or immature (infant with low birth weight compared to gestational age). Inclusion of low birth weight infants in the group of premature infants was based on the recommendations published by the WHO experts on prematurity (1961) who pointed out that in all countries higher morbidity and mortality rates were noted for low-birth weight infants. The premature infants with specific weight account for 5-8%.<sup>11,14</sup>

Data on gestational age (gestational week at the time of birth) and/or the newborn's body weight in TROC were obtained by a random sample of 1,104 subjects (14%) from the cohort. The proportion of subjects born at gestational week 38 or earlier with low birth weights (2,800 g or less) was 5.6% (62/1,104). It can be assumed, therefore, that the proportion of premature infants in the study cohort does not, on the whole, differ from that in unexposed populations (5-8%).

The studies of the distribution of premature and full-term neonates in the TROC by gender, ethnicity, year of birth and intrauterine exposure dose revealed the following: the proportion of female neonates with specific weight was slightly higher in premature infants than in full-term neonates (55% and 49%, respectively); the proportion of Slavs was about 2-fold higher in premature infants than in full-term infants (60% and 29%, respectively). One of the possible explanations for such difference may be frequent abortion (medical and criminal) among Slavic mothers compared to Tartars and Bashkirs whose religion (Islam) prohibits abortion.

The proportion of infants born during the period of maximum release of radioactive wastes (1950-1952) in premature neonates accounted for 13%. In 74% of premature offspring, the dose received over the 9 months of gestation did not exceed 1 mGy.

Thus, it can be assumed, based on the available data on gestational age at birth and the parameters of physical development in 1,104 neonates randomly sampled from TROC, that the proportion of premature neonates in the offspring accounts for 6%, which does not, on the whole, exceed the similar values cited in the literature. Thus, there are no grounds to suggest that the effect of the prematurity factor on the neonatal and infant death rates was more significant in TROC than in unexposed population.

The second factor, which can determine the rates of neonatal and infant mortality, is the mother's health status before and during pregnancy, as well as labor complications. Unfortunately, the information on maternal health status in the period prior to the birth of children of TROC was insufficient for evaluating the influence exerted by this factor on the neonatal and infant mortality rates.

The analyses of other risk factors of non-radiation nature which are capable of influencing the infant mortality rates showed that the risk of infant mortality was lower by 16% in female neonates than in male neonates; the difference, however, was not statistically significant though marginally significant ( $p=0.067$ ). The risk of infant mortality was significantly lower in Slavic neonates than in Tartar and Bashkir neonates; the infant mortality risk in Slavs relative to Tartar and Bashkir was estimated to be 0.75 (95% CI: 0.61-0.92;  $p=0.006$ ). An increase in infant mortality with maternal age at delivery

was less than 1% and was not significant ( $p>0.05$ ). If the mother had already given birth to 5 or more children by the time of pregnancy of interest, the risk of death in neonate during the first year of life increased by 17% compared to those born from mother with less children; the increase, however, was not statistically significant ( $p>0.05$ ).

A marked, statistically significant, decrease ( $p<0.001$ ) in infant mortality risk was noted from 1950 to 1975. It can be suggested that this positive dynamics is the result of the improved quality and accessibility of medical services rendered to residents of rural areas.

#### *Radiation risk analysis*

Radiation risk analyses were based on simple parametric linear excess relative risk model with adjustment of baseline rate for gender, ethnicity, year of birth. The results of the analysis of the influence exerted by the parents' total gonadal dose at conception on the infant mortality rate provide no sufficient grounds to conclude that there is an increase in the infant mortality rate under 1 year of age with the parents' total gonadal doses (results not shown). An explanation for the fact consists in the possibility that the effects of exposure to parental gonads might have become manifest as increased spontaneous abortions and miscarriages in mothers at different stages of pregnancy, which is beyond the scope of the present study.

The analysis of the radiation-related risk of infant mortality was also conducted for TROC taking account of doses accumulated in the RBM both during the gestation period and the first year of life. This approach was adopted because of a specific nature of the effect produced by radiation exposure to the RBM stem cells of the offspring. An important characteristic was, primarily, a chronic (continuous) nature of the combined (external and internal) exposure which started during the period of intrauterine development and continued after the birth. Thus, the process of dose accumulation in the cells of the RBM, which started at the time formation of child's hemopoietic organs, did not stop after birth, but continued through the postnatal period.

The analysis of the dose-effect dependence in infant mortality rate as a function of RBM doses formed during the prenatal period and during the first year of life indicated a statistically significant linear trend ( $p=0.017$ ). The inclusion of dose as a continuous variable in the relative risk model yielded the relative risk of 1.027 (95% CI: 1.005-1.051) per 1 cGy. The results of relative risk model with categorized dose are shown in Table 2. A statistically significant increase in the relative risk of infant mortality was observed at RBM dose of 5 mGy or higher. At RBM dose of 100.0 mGy or higher, the risk of infant mortality increased by 3.4-fold compared to those with RBM dose less than 1 mGy ( $p=0.0003$ ).

The standardized mortality ratio (SMR) was calculated for TROC members aged under 1 year using the annual infant death rates for the rural population of the USSR from 1950 through 1987.<sup>13</sup> Infant death rates in TROC were shown to be significantly higher from 1950 through 1952, i.e. the period of maximum releases into the Techa River; the SMR was 1.73 (95% CI: 1.07-2.40) in 1950, 1.73

**Table 2.** Relative risk of infant mortality by red bone marrow (RBM) dose accumulated during the period of intrauterine development and the first year of life

RBM dose (mGy)	Relative risk	95% CI <sup>a</sup>	<i>p</i> -value
<1.0	1	NA <sup>b</sup>	NA
1.0- 4.9	1.20	0.88-1.63	0.259
5.0-24.9	1.76	1.17-2.65	0.007
25.0-49.9	2.23	1.29-3.87	0.004
50.0-99.9	2.58	1.39-4.77	0.003
≥ 100.0	3.40	1.75-6.61	0.0003

<sup>a</sup>Confidence interval.<sup>b</sup>Not available

(95% CI: 1.26-2.19) in 1951, and 1.55 (95% CI: 1.14-1.96) in 1952. From 1954 through 1963, SMR varied from 1.16 to 1.74, but the 95% confidence intervals all included 1.

## Discussion

It has been asserted by the UN Scientific Committee on Atomic Radiation Effects (UNSCEAR) that fetus is characterized by higher radiosensitivity which is likely to be more manifest than that shown by the organism of child. Among the effects of ionizing radiation on the embryo and fetus that have been described to date, there are fatal effects observed in the early weeks of gestation, developmental defects, mental retardation, induction of malignant neoplasms, including leukemia.<sup>15,16</sup> The characteristics, such as coefficients of neonatal mortality (in infants aged up to 1 month) and infant mortality (in infants aged up to 1 year), of which the rates may be influenced by the effects of unfavorable environmental factors on the fetus during the prenatal period, but the data on the effects of the radiation factor are fairly limited. The basic population in which relatively reliable estimates of radiation-related mortality risk have been obtained is the cohort of in-utero exposed A-bomb survivors of about 3,000 persons.<sup>17</sup> The preliminary results of our study are consistent with those for exposed A-bomb survivors, which showed a significant increase in the death rate over the first year of life, especially in infants aged under 1 month, and a linear dependence of the perinatal mortality on the dose of prenatal exposure.<sup>18-20</sup> Of 237 A-bomb survivors who died of all-causes, 43% died under the age of 1 year. The infant mortality rate was higher by 3-fold in those with intrauterine dose of 1 Gy or higher than in the unexposed population. Researchers reporting these results tended to attribute the increased mortality rate in infants to the mechanical damage caused by blast.<sup>17-20</sup> However, an increase in mortality rate was also observed in those antenatally exposed without mechanical injury.<sup>18-19</sup>

Infant mortality structure and its baseline rate in TROC represent the same patterns attributed to unexposed population. A significantly lower infant mortality in Slavic neonates compared to Tartar and Bashkir neonates (Relative risk=0.75; 95% CI: 0.61-0.92; *p*=0.006)

can be explained by the relationship between the population reproduction rate (birth rate, fertility) and the rate of early childhood mortality. It is known that population with high birth rate is characterized by high rate of early childhood mortality.<sup>21</sup> Thus, higher birth rate noted in Tartar and Bashkir population compared to Slavic population may account for the above-mentioned difference in infant mortality between the two ethnic groups.

The assessment of radiation risk of infant mortality presented in this paper should not be regarded as ultimate since it is envisaged to re-calculate the risk using verified intrauterine dose estimates,<sup>9</sup> with the inclusion of fetal doses accumulated over the first 2 trimesters of pregnancy in the calculation of internal exposure doses received by the fetus during the prenatal period.

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