Radiat Environ Biophys (2002) 41:69–73
DOI 10.1007/s00411-002-0149-4

ORIGINAL CONTRIBUTION

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Fallout from nuclear tests: health effects in the Altai region

Received: 27 April 2001 / Accepted: 30 December 2001 / Published online: 9 March 2002

Background and aims of the studies

Fallout from nuclear testing at the Semipalatinsk test site led to considerable exposure to the public in certain areas of the Altai region [1, 2, 3]. But it was only in 1991 that this has been acknowledged by the government. Subsequently, a large scale research programme has been set up by the Russian Government: the Federal Research Programme Semipalatinsk/Altai beginning in 1993. It includes a number of studies to evaluate both radiation exposure and possible health consequences. One of the basic efforts was the establishment of a register of persons living in rural parts of the affected areas. This register is dedicated to building the basis for various studies. For comparison reasons it includes also individuals living in unexposed areas and persons who migrated to the affected areas after the end of atmospheric bomb testing in 1963. The register has been described in detail elsewhere [4, 5]. In this paper a short description will be given.

Within the framework of the Federal Research Programme Semipalatinsk/Altai, large research efforts comprising epidemiology, dosimetry, and biomedical studies have been started. Some of the results have been published in Russian reports or papers, e.g. the Bulletin of the Programme Semipalatinsk test site/Altai [1, 6, 7, 8]. An overview on some major Russian studies is given below followed by collaborative studies that have been started since. Current dose estimates for the Altai region are reported by Shoikhet et al. in this issue [3].

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Current results

Studies within the Russian Programme

A brief report of data sources of the Institute of Regional Medico-Ecological Problems (IRMEP) and studies funded by the Russian Federation since 1992 is given as well as first results of a retrospective mortality study, including cancer and non-cancer causes. This overview is mainly based on publications in the monographs and in the Bulletin of the Research Programme Semipalatinsk test site/Altai [7], but includes some additional information. Furthermore, information will be given on the prevalence of chronic non-cancer diseases and on the result from an immunological study.

Mortality patterns and establishment of the registry

At the beginning of the Scientific Programme Semipalatinsk test site/Altai in 1992, basic data on the health situation in the Altai region were extracted from the Official Statistics Committee of the Soviet Union (Goskomstat). Mortality rates for several causes of death were elevated in the Altai region, independent of whether compared to the entire Russian Federation, to Western Siberia (to which the Altai region belongs), or to Western Siberia without the Altai region (see Table 1).

In addition to the Goskomstat information and first results of dose reconstruction, demographic and health data were collected in the exposed areas and in a control area in the Altai region in order to develop a cohort of exposed persons and a comparison group for epidemiological studies. Focusing primarily on the assessment of the radiation impact, only rural populations not exposed to environmental risk factors such as industrial air pollution were chosen for these cohorts [4].

Table 1 Mortality caused by malignant tumours, infectious and parasitogenic diseases, diseases of respiratory organs (per 100,000 individuals) [8]

	Mortality from malignant tumours		Mortality from infectious and parasitogenic diseases		Mortality from diseases of the respiratory organs	
	1990	1991	1990	1991	1990	1991
Russian Federation	191.8	197.5	12.1	12.0	59.3	55.7
Western Siberia	165.2	176.5	14.7	14.0	52.9	49.2
Altai Region	195.8	209.3	18.8	19.1	75.8	65.9
Obl. Kemerovo	184.5	196.1	15.7	15.1	58.9	56.2
Obl. Novosibirsk	187.3	199.9	15.0	15.1	54.4	54.3
Obl. Omsk	184.7	196.0	13.0	13.5	43.3	35.7
Obl. Tomsk	163.2	168.0	14.7	16.1	50.6	47.9
Obl. Tyumen	89.0	99.0	10.8	10.2	30.0	31.6

Major difficulties resulted from the fact that the registry had to be established more than 40 years after the exposure. The Altai region is an area with considerable migration: in the early 1940s, during World War II, Russian Germans, Ukrainians, Chechens, and others were exiled to Kazakhstan, to the Altai region, and to other parts of central Asia. Beginning with Chrushchev's agricultural reforms in the 1950s involving irrigation and cultivation of steppe regions, Russian settlers came to these regions. From 1960 to 1980, with the industrial development in the Altai region, small villages were given up, and industrial centres like Barnaul, Byisk, Rubtsovsk, Novoaltaisk or Slavgorod gained inhabitants. After the dissolution of the Soviet Union in 1991, most of the Russian Germans living in the Altai region since 1941 left for Germany. Part of the Russian population in northern Kazakhstan migrated to adjacent territories of the Russian Federation, e.g. to the Altai region.

Therefore, the follow-up of the registry that is based on records from the vital statistics offices (ZAGS) is not complete. Initial data were collected from all available sources, such as kolkhoz books listing every household, school records as a source of information on exposed children, and interviews with present day inhabitants.

As a result, a list of people exposed to effective doses ranging from 20–1,500 mSv in 1949 was compiled. Earlier official dose estimates relevant for the compensation policy ranged from 50 to 2,700 mSv. Causes of death are listed according to death certificates of the Altai Region Vital Statistics Office and Table 2 summarises the available information.

Table 2 Registry of exposed individuals (after 1949 test) and their descendants

	Total number of exposed	Vital status known	Deceased	Alive
Exposed	40,225	11,638	5,484	6,154
Controls	37,037	37,037	8,495	28,542
Descendants of exposed				
First generation			4,276	
Second generation			3,798	
Total			8,074	

Table 3 Dose groups for the cause-of-death study

Dose group	Individual doses (mSv)	Mean doses (mSv)
1	10–179	80.3
2	180–349	244
3	350–999	468
4	>1,000	1,523
All dose groups		395

First analysis of the registry

In a first evaluation, causes of death were studied using mortality data of the Registry as of 1994 and reported by Algazin et al. [7] and Shoikhet et al. [2]. Up to the late 1990s, the level of follow-up for women was very low, therefore at that time, the first study was restricted to men. Emigrants from the Altai region after the exposure could not be included into the study, since there was no follow-up available. Information on causes of death was based on death certificates from 1949 to 1993. The study group included 4,595 men from 36 exposed settlements in 5 rayons, who died before 1993, i.e. 30.5% of all men in the exposed cohort who were assigned to 4 dose groups (Table 3). A portion of 1,433 men from control rayons and 2,489 immigrants were included as a control group for the study. Relative risks for general mortality and specific causes of death (according to ICD 9 main groups) were calculated using a person-years approach and are reported by dose groups and age at exposure. In addition, the temporal development of annual mortality rates was analysed. Over all age groups, no significant difference in mortality of all causes of death was found between exposed and control groups. In the group aged >20 years old at exposure, general mortality differed in the first 24 years after exposure. For individuals aged 20–49 years old at exposure, the relative risk of mortality was 1.16 (1.05–1.27, 95% CI), for those aged ≥50 years old at exposure the relative risk was 1.34 (1.23–1.45, 95% CI).

For all dose and age groups no significant differences were found for mortality due to non-cancer causes of

Table 4 Relative risk (95% CI) for cancer mortality (excluding leukaemias) by dose group and age at exposure with a time lag of 10 years

Age at exposure (years)	Relative risks (95% CI)			
	Dose group 1 (10–179 mSv)	Dose group 2 (180–349 mSv)	Dose group 3 (350–999 mSv)	Dose group 4 (≥1,000 mSv)
0–19	0.95 (0.55–1.52)	0.57 (0.32–0.92)	1.13 (0.74–1.65)	1.03 (0.33–2.40)
20–49	0.93 (0.69–1.23)	0.95 (0.75–1.19)	1.24 (1.03–1.49)	1.50 (1.04–2.08)
>50	1.17 (0.66–1.89)	1.42 (1.01–1.93)	1.00 (0.67–1.44)	1.65 (0.90–2.77)

Table 5 Dose groups, number of subjects, and dose ranges by birth year as used for the analysis of the prevalence of non-cancer diseases

Dose group No. of settlements, mean effective dose	Number of subjects			Dose ranges in mSv by birth year		
	Total	Male	Female	1930–1934	1935–1948	after 1948
1. 12 settlements, mean ED: 86 mSv	1,328	540	788	<120	<150	<620
2. 14 settlements, mean ED: 238 mSv	1,924	789	1135	120–180	150–230	620–980
3. 7 settlements, mean ED: 629 mSv	1,811	725	1,086	250–1,180	300–1,380	1,100–4,700

death (except for age ≥50 years old at exposure, but without a dose-effect relationship).

Due to the expected early onset of radiation-induced leukemias and lack of diagnostic techniques in the 1950s, no valid information on leukaemia is available from the registry. Thus, only solid tumours were considered and the analyses were conducted under allowance of a time-lag of 10 years as latency period. The relative risk for dose group 1 (10–179 mSv) was 0.96 (0.76–1.20, 95% CI) and for dose group 2 (180–349 mSv) 1.04 (0.87–1.23, 95% CI). For the dose groups 3 (350–999 mSv) and 4 (≥1,000 mSv), the relative risks were 1.16 (0.99–1.36, 95% CI) and 1.38 (1.04–1.79, 95%CI), respectively. The highest relative risks were found for the period 10–29 years after exposure. Table 4 lists relative risks for four dose categories by age at exposure.

Among all solid cancers, malignant neoplasm of digestive organs was the most frequent contributing 46.7% of the total. An increased mortality rate was found in the dose group 4. The relative risks were 2.37 (1.36–4.10) and 2.77 (1.14–6.75), 10–19 and 20–29 years after exposure, respectively.

The second-most frequent subgroup of solid cancers was those of the respiratory organs (33.1%).

Health status of the offspring

Based on the registry, 231 children could be identified as having parents who were exposed from the 1949 test. A comparison group includes 3,117 children of unexposed parents. First results indicate increased rates for various diseases in the group of children with exposed parents compared to the unexposed, whereas no differences were found in psychological, neurological, sense organ or urogenital tract diseases. These results need further thorough investigation.

Prevalence of chronic non-cancer diseases

The exposed group for the prevalence study of chronic non-cancer diseases of various organs and systems includes 5,063 individuals (2,054 men and 3,009 women). These are people from the same settlements as those chosen for the registry who were permanently resident since the time of the 1949 test until the time of investigation. Three dose-groups were assigned according to settlements of residence and in accordance with effective dose ranges. These dose groups were subdivided into three age subgroups for subjects born in the years 1930–1934, 1935–1948 and after 1948 (Table 5). The unexposed group includes 9,421 individuals (4,005 men and 5,416 women). Medical examinations were carried out by teams of specially trained physicians. The prevalence ratio (PR) was used to quantify differences in mortality and disease levels between the study groups.

This investigation detected that the prevalence of chronic non-cancer diseases was higher in the exposed group than in the unexposed group, independent of gender and age at exposure. The maximum PR has been observed in the dose group 3 with age at exposure under 15 years. The PR for an array of chronic diseases of the endocrine, circulatory, genitourinary and nervous systems, respiratory, digestive and sense organs was estimated to be 1.52 (1.49–1.55) for males of all age groups. For those under 15 years of age at time of exposure, the PR was 1.60 (1.54–1.67). The corresponding values for females were found to be 1.59 (1.56–1.62) and 1.62 (1.57–1.67), respectively.

As stated, an increased prevalence of chronic non-cancer diseases was found among the population of group 3 regardless of gender and age at exposure, while this has also been found in lower dose groups for those persons younger at time of exposure.

Immunological situation

An immunological study among the residents of the Altai region settlements exposed to the radioactive fallout from the August 29, 1949 test at the Semipalatinsk test site showed significant increases of main immunological syndromes, including infectious (syndrome of secondary immune deficit), allergic, immune, hematological and oncological syndromes among exposed individuals as well as their offspring compared to the frequency of these syndromes in the population of Siberia.

An increase of the frequency of immunopathological syndromes in individuals exposed to radiation happens against the background of significant alterations in subpopulation structure of immunocompetent cells of the peripheral blood which are accompanied by changes in the functional abilities of mononuclear cells, in particular by an increase of proliferative activity and production of TNFα.

A positive dose dependence was detected in the increase of the percentage of individuals having positive expression of the gene IL-1β in mononuclear cells of peripheral blood from the collective ED of radiation exposure. Analogous alterations were detected for two other genes of antiphlogistic cytokines IL-6 and TNF-α. Alterations in the expression of cytokine genes in mononuclear cells from peripheral blood were observed not only in the first generation (the exposed) but also in their offspring in the second and third generations. These alterations were more explicit in the first and third generations than in the second. An increase in gene expression of IL-6 and TNFα in mononuclear cells of peripheral blood in individuals exposed to radiation is associated with derangements in the expression of gene IL-1β, that principally differ from the character of alterations in the expression of genes in mononuclear cells of peripheral blood from individuals that suffered from chemical exposure. In these individuals alterations of the expression of gene TNFα were observed. The alterations in the cytokine genes expression were accompanied by an increase in content of antiphlogistic cytokines IL-1β and TNFα, IL-4 and IFN-γ in the blood serum of individuals exposed to radiation as well as in their offspring of the second and third generations. In women the concentration of cytokines in the blood serum was higher than in men.

The alterations in the expression and production of antiphlogistic cytokines are of primary importance in the pathogenetic impact of radiation exposure to the cytokine network. The alterations in the expression of antiphlogistic cytokines finally leads to changes on the level of production of cytokines, types Tx1 and 2. The alterations found in the sub-population structure of immunocompetent cells in peripheral blood, functional abilities of mononuclear cells, level and balance of serum cytokines are based on the increase in frequency of main immunopathological syndromes in the exposed residents of the settlements situated on the explosion trace and their offspring.

Additional studies

Cataracts

In collaboration with the Institute for Radiation Biology, Munich, Scheimpflug investigations have been performed in the Altai region in September 1997 to determine the degree of opacity of lenses of the eye: 180 inhabitants of the exposed villages Veseloyarsk, Laptev Log, and Topolnoe were examined in the Rubtsovsk town hospital by a scientist from Munich (Dr. Berg) and local ophthalmologists. Results are not yet available, but if the Altai data are compared to those of a Munich control group they exhibit a shift to higher opacities. However, no conclusion on the influence of exposure to ionizing radiation can be derived until results from a local control group are available [9].

Nested case-control study on stomach cancer

Based on the follow-up data in the registry, a nested case-control study has been set up [10]. Cause of death information was included for a follow-up period of 41 years, i.e. from 1959 to 1999, allowing for a latency period of 10 years following the first exposure in 1949. When cases and controls were selected for this investigation, mortality follow-up was completed only for about 40% of the persons identified as living in exposed areas of the Altai region in 1949. A sample of 285 recorded stomach cancer cases and 1,419 controls individually matched by gender and year of birth and having reached the age of the corresponding case were obtained. Dose estimates were obtained from a first exposure assessment conducted in the Russian Federation, mainly by the Institute of Biophysics in Moscow and by the Central Physical Technical Institute in Sergiev-Posad. Data analysis was performed using conditional logistic regression for individually matched data. In the obtained sample, preliminary estimates of absorbed organ doses to the stomach ranged up to 0.8 Gy with a mean dose of 0.1 Gy. First results comparing the exposed and non-exposed group show a significantly increased odds ratio of 2.03 (1.26; 3.28, 95% CI) for stomach cancer. After stratification by gender, a significant increase among men (2.86/1.37; 5.21, 95% CI), but not among women (1.39/0.69;2.80, 95% CI) was found. Stratification by age at exposure showed significantly elevated risks for the groups aged 0–19 years and 20–39years in 1949 with higher risks for those younger at time of exposure. The derived estimates have to be interpreted with caution since the available data did not allow further effect modification to be accounted for, e.g. by nutrition. However, results of this first evaluation indicate that within the study groups, stomach cancer mortality in the Altai region is associated with radiation exposure, with age at exposure as a significantly important modifying factor.

Problems, limitations, potential solutions

At this point in time, all the results have to be considered as preliminary due to various reasons: the follow-up of the registry's cohort is still incomplete as it was at the time of the first studies reported by Algazin et al. [7]. Thus, this analysis was based only on part of the registry's population, and the first study conducted by IRMEP studies was restricted to men. Meanwhile, a scheme has been developed for a follow-up of women, which was in the beginning hampered by names changed after marriage. The efforts to complete the follow-up for the registry's population are still on-going. Part of this was the establishment of a death register in the area [11]. Of special interest will be the offspring group, which has been described. Outlines for further research are given elsewhere in this issue [12]. The results from the immunological study should be evaluated in more detail and in the light of other international findings. Although results have to be considered as preliminary, current findings strongly indicate that the health situation among the exposed population is worse than that among the unexposed comparison population. Further research is needed to clarify the situation.

Acknowledgement Most of the studies where conducted under the Russian Programme Semipalatinsk test site/Altai, while further studies and analyses were supported by the European Union under Contracts FI4C-CT96-0013 and IC15-CT96-0312.

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