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Semipalatinsk Nuclear Test Site: Morbidity and Mortality in Adjacent Area

Keywords: Ionizing Radiation; Semipalatinsk Nuclear Test Site; Lung Cancer; Cardiovascular Diseases

Abstract

This commentary is focused on morbidity and mortality in the population residing near the Semipalatinsk Nuclear Test Site. An explanation for higher detection rates and registered mortality of cancer and other deceases is the better coverage of exposed populace by medical examinations and autopsies as well as increased attention of the residents to their own health. Being informed about benefits provided by the government, some patients from non-contaminated territories registered themselves as exposed. The radiation background in the test site area is normal long-since. Studies of human populations exposed to low-dose radiation will hardly add reliable information on dose-effect relationships. Screening effect, selection and ideological bias will contribute to appearance of new reports on enhanced risks from anthropogenic elevation of the radiation background, which would not prove causality. Reliable results can be obtained in lifelong animal experiments. Numerous publications exaggerating medical consequences of elevated radiation background appeared after the Chernobyl accident. Manipulations with statistics have been not unusual, which should be taken into account by authors of reviews and meta-analyses. In the beginning, heated interest facilitated foreign aid and international scientific cooperation. Later on, other motives have come to the fore: anti-nuclear resentments hindered development of nuclear power in some countries, thus boosting fossil fuel prices.

Introduction

Since many years we have tried to show that certain scientific writers and environmental activists act in accordance with the interests of governments selling fossil fuels [1,2]. The overestimation of adverse effects of nuclear power production leads to its strangulation, supporting appeals to eliminate nuclear power plants (NPPs). The cost of dismantling each NPP may amount to billions of dollars [3]. The use of atomic energy is on the agenda today due to increasing needs of the growing humankind. Nuclear energy holds a promise of an abundant, clean, affordable and almost inexhaustible source of energy [4]. Fuelled by the Chernobyl accident in 1986, environmentalist movements mobilized political forces, which made nuclear energy untenable in some countries [5]. At the same time, the accident contributed to destabilization of the Soviet society with subsequent privatization of the state property by the Soviet rulers, so-called nomenklatura.

Among the causes of the Chernobyl disaster was non-compliance with instructions and safety rules. The number of control rods in the reactor was about a half of the minimum required for a safe functioning [6]. An emergency power system had been shut off, which is forbidden during on-line operation [7]. According to the literature, this was done to carry out an experiment [6,8], which might be a pretext to cover sabotage; certainly, not by the control-room personnel but by some upper management. Most international regimes channel liability to

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Jargin SV*

Department of Pathology, People's Friendship University of Russia, Russian Federation USSR

*Address for Correspondence

Jargin SV, Department of Pathology, People's Friendship University of Russia, Russian Federation USSR. E-mail Id: sjargin@mail.ru

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the person in control of an environmentally damaging activity. In the case of nuclear pollution, it is the operator of NPP. Persons in control of the harmful activity should bear the costs of inflicted damage [9]. These days, the single most important consideration against nuclear facilities is that they are potential war targets. Accordingly, military threats are arguments against NPPs. Escalation of military conflicts contributes to boosting fossil fuel prices. This might have been one of the motives to unleash the Ukraine war [10]. The Chernobyl disaster has been exploited for the same purpose. Considering vulnerability of large NPPs during armed conflicts, attention should be directed to smaller nuclear reactors, which have some economic advantages. Small reactors can be used also by the military [11].

Focused review

The overestimation of ecological and medical consequences of Chernobyl accident and radioactive contaminations in the Urals were discussed previously [1,2]. A similar tendency has been noticed in regard to nuclear tests in the former Soviet Union (SU) [12]. The Semipalatinsk Test Site (STS) in today's Kazakhstan was the place where 456 nuclear explosions were carried out between 1949 and 1989, including 111 atmospheric tests in the period 1949-1962 [13]. STS was shut down in early 1990s. The villages most affected by the atmospheric tests were located northeast of STS. The wellknown cytogenetics expert Yuri Dubrova stated that "according to the results of numerous studies the doses for the families living in the Semipalatinsk District of Kazakhstan have been estimated as 0.5 Sv and higher" [14] with reference to the review [15]. However, in the abstract of the latter review it is written: "The village of Dolon, in particular, has been identified for many years as the most highly exposed location in the vicinity of the test site. Previous publications cited external doses of more than 2 Gy to residents of Dolon while an expert group assembled by the WHO in 1997 estimated that external doses were likely to have been less than 0.5 Gy" [15]. Earlier publications estimated maximum external doses for adult residents of Dolon at 1.3 Sv [16] or 0.63 Gy (with a remark that integral exposures at Dolon may have been less than estimated) [17]. Other experts reported lower doses [18]. Apparently, the single historical

Commentary

measurement was performed at the axis of the radioactive trace about 1.5-1.6 km northwest of Dolon, while the width of the cloud was narrow [19,20]. The dose estimate based on this measurement is believed to be a maximum rather than average for Dolon residents [19], while in other villages the doses were much lower. The average individual dose estimates for townships near STS, received in the period 1949-1953, have been estimated as follows: Dolon 1600 mGy, Abai 370, Kainar - 240, Sarzhal - 200, some other villages - 5-20 and Semipalatinsk city \leq 5.6 mGy. In the period 1971-1990 annual individual doses in the area were $\leq 5 \text{ mGy}$ [21]. In 2008 the annual individual dose in the STS compound was 0.073-0.749 mSv and outside STS - 0.036-0.37 mSv [22], which is a negligible addition to the natural radiation background (NRB). The worldwide annual exposures to NRB are generally expected to be in the range 1-10 mSv but can be higher [23,24]. There are populated areas in the world where dose rates from the NRB are 10-100-fold higher than the global average (2.4 mSv/year) with no health risks reliably proven [25].

Dubrova et al. stated that individuals, from whom the specimens for genetic analysis were collected "around the Semipalatinsk nuclear test site... characterized by the highest effective doses of exposure to ionizing radiation (>1 Sv)" [26], which is at variance with the dose comparisons above. Furthermore, Dubrova argued that Jargin [27] "makes a very serious accusation stating that 'statistics with unknown levels of significance' was used in our publications [14,28]. I would like to stress that the main result of these two studies, showing significantly elevated mutation rate in the germline of irradiated parents, was verified by means of the most conservative statistical test - Fisher's exact test" [14]. However, in the letter [27] it was written that negative correlation between the mutation rate and a paternal year of birth among inhabitants of Semipalatinsk area is claimed without providing the value of the correlation coefficient and its level of significance [26,29]. Considering configuration of diagrams in [29], this correlation may be insignificant [27]. Nevertheless, a discussion is led on its basis, e.g.: "Most importantly, this correlation provides the first experimental evidence for change in human germline-mutation rate with declining exposure to ionizing radiation and therefore shows that the Moscow treaty banning nuclear weapon tests in the atmosphere (August 1963) has been effective in reducing genetic risk to the affected population" [14]. The above-cited argumentation from [27] remained unanswered. Moreover, the Fisher's exact test, mentioned in the reply by Dubrova [14], is not used for the evaluation of the level of significance of correlation coefficients.

The tendency to overestimate medical consequences of enhanced background radiation in the Semipalatinsk area can be exemplified by the international study [30]. The following was stated in the abstract: "17 patients (group 1) lived close to the testing area from the childhood to 1993 and were exposed to the radiation at the year dose 0.1 ber." A radiation dose unit "ber" (Biological Equivalent of Rad), used in Russia, is designated internationally as rem. The annual individual dose of 0.1 rem (1 mSv) is below the global average for annual doses from NRB, which is 2.4 mSv. The term "radiogenic carcinoma" was used for cancers of unknown etiology. Unfounded suppositions about their rapid growth and "poor prognosis" were made [30]. The study was based on two sets of tissue specimens from patients with lung carcinoma: the "exposed" group - 17 cases from the area of

Semipalatinsk, and the control (40 specimens). Cumulative doses were unknown. The following data are remarkable (from Russian): "The specific cytogenetical feature of the lung carcinoma in patients from the area of Semipalatinsk was the neuroendocrine differentiation of cancer cells in all tumors independently of their histological structure. We have established it by means of immunohistochemical and ultrastructural investigations." At the same time, "no neuroendocrine differentiation was shown in the control group." It means that the marker was found by two methods in 100 % (17/17) of the cases and in 0 % (0/40) of controls. The extremely high level of significance (P<0.0001) agrees with the supposition that the "lung cancer in persons exposed for a long time to radionuclide radiation pollution" [30] is a distinct entity, different from spontaneous lung carcinoma. Significant differences between the two groups were found also for other markers, which additionally enhanced statistical significance of the difference. It was concluded that "lung carcinoma in patients, who resided in the area of Semipalatinsk and underwent elevated radioactivity, can be classified as neuroendocrine carcinoma" [30]. In the general population, tumors from neuroendocrine cells (small cell carcinoma and carcinoids) represented at that time 20-30 % of lung malignancies [31]. The age and sex data in the "exposed" group were typical for spontaneous cancer possibly caused by cigarette smoking or industrial air pollution: 15 from 17 patients were 51-70 years old. Patients with radiation-induced cancer could be younger. In particular, spontaneous lung cancer is characterized by male predominance due to cigarette smoking and professional carcinogens. Radiation would exert a similar effect on both genders. In the "exposed" group there were 16 males and one female [32]... The designation "radiogenic carcinoma" and discussion of its supposedly rapid growth and poor prognosis [30] contributed to exaggeration of medical consequences of low-dose exposures. Papers of this kind, similarly to those about Chernobyl and radioactive contaminations in the Urals [1,2], often have limitations: interpretation of spontaneous diseases as radiationinduced, indication of dose levels without comparison with the NRB, conclusions about incidence increase without correct comparisons with a control. Other studies on STS and Chernobyl by the same authors [33-36] are characterized by similar limitations. For example, a discussion of molecular markers of "radiogenic cancer" is led on the basis of 15 random autopsy and surgical cases of lung cancer from the areas quite distant from Chernobyl: eight cases were from the Tula province in Russia [33].

Studies discussed above illustrate the approach persisting until today. Biased researchers have just gathered experience and learned to formulate their reports ambiguously to evade criticism. Despite the low average doses, long-since within limits of NRB, residents of the Semipalatinsk area are designated as "exposed to radiation" [37-39]. Admittedly, some nuclear tests, conducted from 1949 to 1956, resulted in non-negligible external doses [40]. However, the last atmospheric test at STS was performed in 1962, and underground test in 1989 [41]. After the 1963 Partial Test Ban Treaty, the nuclear testing was restricted to underground so that, with a few exceptions, little or no off-site environmental contamination was caused. The exceptions included cratering events in the period 1965-1968 [41]. To calculate the external cumulative dose, it is generally sufficient to take into account residence history during the first year following a nuclear test [40].

The medical and ecological research about STS is associated with limitations and confounding factors. Studies are not well connected with each other. Biological specimens were not always properly stored and labeled, individual migration and residence histories often unknown [13]. In regard to cancer, the morbidity and mortality in exposed people were reported to exceed those in control groups [42]. This problem has been discussed with regard to radioactive contaminations in Chernobyl and the Urals [1,2]. An explanation for higher detection rates and mortality from cancer and other diseases in the exposed populations is the better coverage by medical examinations (including post mortems) and increased attention of exposed individuals to their own health: the selection and self-selection bias. Undiagnosed cancers are often found at autopsies. Besides, people knew about the Kazakhstani law "Social protection of citizens who suffered as a result of nuclear tests conducted at the STS" [39]; not surprisingly, some patients from non-contaminated areas have been falsely registered as exposed. It is feasible under conditions of corruption. The circumstantial evidence thereof is a marked increase in the incidence of diseases, unrelated to radiation on the face of it, in contaminated compared to "clean" territories. For example, the incidence of tuberculosis in children in the Semipalatinsk province was 1.5 times higher than in the whole Kazakhstan with a threefold higher frequency of severe and complicated cases [43]. Remarkably, the incidence of neoplasia in children of exposed parents was found to be nearly fourfold higher than among controls: 92.6 vs. 24.7 per 1000 children [44]. At least in part, this was caused by diseased children brought from non-contaminated areas and registered as radiation-exposed. Moreover, oncologic patients tend to recollect the circumstances related to radiation better than healthy controls (recall bias) [45], thus getting higher dose estimates, contributing to doseeffect correlations.

Several publications discussed the enhanced morbidity and mortality from cardio- and cerebro-vascular diseases in people residing near STS [46]. Admittedly, no direct conclusions on causeeffect relationships are made in recent papers [37-39]. When account was taken of the difference in baseline rates between the exposed and unexposed groups, no statistically significant dose-response relationship was observed either for cardiovascular diseases (CVD) or for stroke [46,47]. This is in agreement with the fact that no doseresponse relationship for circulatory diseases among the atomic bomb survivors in Japan (life span study – LSS) was observed at doses \leq 0.5 Gy [46,48,49]. The selection, self-selection and recall bias were probably active also in LSS, contributing to higher risk estimates.

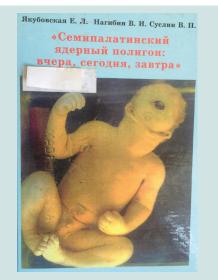
Furthermore, there are confounding factors preventing reasonable interpretation of medical statistics from some countries of the former SU. Like in Russia, CVD mortality in Kazakhstan is higher compared to West Europe [50]. The causes thereof are known by anatomic pathologists. Since the Soviet time, the autopsy remained obligatory for patients dying in hospitals but the quality deteriorated. Post mortem examinations were often made perfunctorily. The quality decrease in anatomic pathology during the 1990s coincided with the increase in the registered CVD mortality. If a cause of death is not entirely clear, it has been usual to write on a death certificate: "Ischemic heart disease with cardiac insufficiency" or a similar formulation. It is known that ill-defined cardiovascular codes from the International Statistical Classification of Diseases (ICD) are used in cases with insufficient clinical information. The frequent cause of cardiovascular death in some countries of the former SU has been "coronary atherosclerosis". The nonstandard disease classifications used in Russia complicated the evaluation of medical statistics [51]. It has been noted in the recent review that a "diagnosis (by a physician knowing the patient's history) could vary with dose" [52]. The tendency that radiation-exposed people are on average more thoroughly examined was noticed [1,2]. Finally, manipulation with statistics following official or unofficial directives has been widespread in Russia [53]. This human factor has remained largely unchanged.

A tendency to over-diagnose CVD is generally known also for people dying at home and not undergoing post mortem examination. It can be confirmed by the following: "Increases and decreases in mortality related to CVD... but not to myocardial infarction, the proportion of which in Russian CVD mortality is extremely low" [54]. The diagnosis of myocardial infarction is usually based on clinical or morphological criteria, while the diagnoses of ischemic heart disease and coronary atherosclerosis are often used post mortem without strong evidence. Furthermore, contrary to myocardial infarction, gross features of ischemic brain infarction were sometimes mimicked destroying brain tissue using autopsy knife by a pathologist or postgraduate student not inclined or unable (for a lack of toxicological tests) to search for the true cause of death even at university mortuaries let alone peripheral institutions. The post-mortem diagnosis of stroke has been overused for poisonings, especially with alcoholic beverages and surrogates [55]. Along with inadequate treatment of arterial hypertension, this was probably the cause of higher reported stroke mortality in Russia compared to other developed countries [56,57].

Dose levels associated with cancer or CVD in animal experiments and in humans after radiotherapy have been higher than averages in the cohorts from contaminated areas of the former SU; details and references are in [1,2]. Results of experiments are generally not supportive of detrimental effects of low doses, with possible exception of genetically modified cancer-prone animals. In humans after radiotherapy, myocardial fibrosis developed after exposures ≥30 Gy. An increased risk of coronary disease has been reported after radiotherapy with doses 7.6-18.4 Gy [58], which is still much higher than averages in the exposed cohorts discussed above. In certain experimental and epidemiological studies, low doses turned out to be protective against CVD and other adverse effects. There is considerable evidence in favor of hormesis, summarized in [1,2]. Unrealistic CVD risks at low-dose exposures call in question cancer risks reported by the same and other researchers. A major part of the literature about STS is characterized by large volume, abundant details and mathematical computations, but no clear insight into medical consequences of contamination. Papers on dosimetry or retrospective dose estimation contain discourses e.g. about diets of different ethnic communities, living in or relocated to the Semipalatinsk area; but provide no clear information on radiation doses, morbidity and mortality. Along with other ethnic groups, more than 440,000 Germans were deported to Kazakhstan during 1941-1945 [59] including the subsequently contaminated areas near STS [46,60].

Mechanisms of damage at low doses remain speculative and the evidence inconclusive [61,62]. Summarizing the above and previously published arguments [1,2], the harm caused by anthropogenic radiation would tend to zero with a dose rate decreasing down to NRB. The damage and repair are normally in a dynamic balance. Accordingly, there must be an optimal exposure level, as it is for many environmental agents: visible and ultraviolet light, various chemical elements and compounds. Evolutionary adaptation to a changing environmental factor would lag behind its current value and correspond to some average from the past. NRB has been decreasing during the time of life existence on Earth [63]. There are many substances and physical factors in the environment that are toxic at some dose level. The lower would be anthropogenic exposure, the less would be its significance compared to NRB and other factors.

Numerous publications exaggerating medical consequences of elevated radiation background appeared after the Chernobyl accident. The motives have been discussed previously [1,2]. In the beginning, heated interest to Chernobyl facilitated foreign aid and international scientific cooperation. Radiophobia hindered the development of nuclear power in many countries, thus boosting fossil fuel prices. Certain publications apparently served two purposes: fostering radiophobia (Figure 1) (Figure 2) by truisms about radiation-related health risks and, at the same time, obfuscating real consequences of long-term contaminations in the Urals and Semipalatinsk areas. It seems that some writers, exaggerating medical and ecological consequences of the anthropogenic increase in the radiation background, do not realize that they serve the interests of fossil fuel producers. Some of them may have good intentions; others are ideologically biased, serve certain companies or governments. Today there are no alternatives to nuclear power. The energy carriers will become increasingly expensive in the long run, contributing to excessive population growth in fossil fuel producing countries, and poverty elsewhere. The global development of nuclear energy must be managed by an international executive based in developed countries. [64].



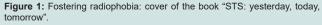




Figure 2: Diseased children presented in [64] without any proven causeeffect relationship with radiation.

Conclusion

Limitations of many publications about STS include lacking consideration of bias and confounding factors [65]. Some reviews analyzed together papers of different quality and reliability. The heterogeneity complicates causal interpretation of results [62,66]. As discussed here and elsewhere, political and economical interests sometimes overweighed scientific objectivity [1,2]. Dose-effect relationships should be clarified in experiments with known doses and dose rates. Animal studies can provide reliable information. Further work with different species would quantify their radiosensitivity and enable more precise extrapolations to humans. Studies of human populations exposed to low-dose ionizing radiation, though important, will hardly add much reliable information on dose-effect relationships. Screening effect, selection, self-selection and ideological bias will contribute to appearance of new reports on enhanced risks from a moderate anthropogenic increase in the radiation background, which would not prove causality. Manipulations with statistics have been not unusual in the former SU [53], which must be taken into account by authors of reviews and meta-analyses.

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