Lessons Learned from the Study of Immigrants to Israel from Areas of Russia, Belarus, and Ukraine Contaminated by the Chernobyl Accident

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During the past 6 years, immigration to Israel of 700,000 persons from the former Soviet Union (FSU) included about 140,000 from radiocontaminated regions of Belarus, Ukraine, and Russia near Chernobyl. In Beer Sheva, a major center for immigrant absorption in Israel, a primary objective was to evaluate their health status and to refer them for care. 137Cs levels in 1228 men, women, and children were measured with a portable whole-body counter. Whole-body counts showed clear correlation with the degree of 137Cs ground contamination in previous regions of residence. The population could thus be subdivided according to degree of exposure, based on previous regions of residence. The thyroid status of 300 local immigrant children was evaluated because of the increased risk of childhood thyroid cancer in the regions from which they came. This group was subdivided into comparative groups of children who came from less and more contaminated areas according to the International Atomic Energy Agency soil 137Cs contamination maps. Enlarged thyroids were found in about 40% of both groups. One 12-year-old girl from Gomel had a malignant papillary carcinoma. Thyroid-stimulating hormone levels, though within normal limits, were significantly greater (p<0.02) for girls from high exposure regions. Liquidators showed significant increases in serum clastogenic factor and in the number of circulating glycoporphin A-mutated red cells. In studies of over 700 people from both radiocontaminated and unaffected regions of the FSU, evidence for posttraumatic stress disorder was found more frequently in persons coming from the more contaminated areas. — Environ Health Perspect 105(Suppl 6):1523–1527 (1997)

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Introduction

It is estimated that explosion and fire at the Chernobyl nuclear reactor in the former Soviet Union (FSU) on 26 April, 1986, emitted more than 10^18 Bq of radioactive materials into the atmosphere. Radioisotopes posing considerable risks to health emitted during the first week of exposure included 131I, 132I, 133I, and 135I (half-lives of 8, 0.096, 0.875, and 0.280 days, respectively). During later phases of emission 134Cs and 137Cs (2.1- and 30-year halves), the long-lived beta-emitting bone seekers 89Sr and 90Sr (52-day and 30-year halves) and the alpha-emitting 239Pu, 239Pu, 240Pu (88-, 24,110-, and 6564-year halves) were more important (1, 2).

Events during the first 10 days after the accident were poorly documented, partly because of the habitual secrecy then given to technological failures in the FSU. Official reports of acute mortality soon after the accident were that 29 persons died and 203 had acute radiation sickness. The emergency response was considered a military operation and many soldiers from all areas of the FSU were assigned to work in heavily contaminated areas with little knowledge of or protection from radiation exposure. Later, these tasks were assigned to civilians and were better regulated. Because they were said to be liquidating the consequences of the accident, these salvage workers came to be known as liquidators. The total number of these liquidators in the FSU has been estimated to be as high as 800,000. The specially allowed radiation exposure limit for these persons was 25 cSv. However, later interviews with liquidators now living in Israel indicate that this dose limitation was not always adhered to, even though it may have been recorded as such in health records carried by the affected individuals.

Indicators of past acute radiation sickness, such as history of spontaneous abortion, radiogenic burns, loss of hair, nausea, nosebleeds, or bleeding from other orifices, anemia, and leukopenia, were assumed to assist in determining the severity of the health impacts. However, the reliability of postepisode data obtained by interview is subject to recall bias. Even more uncertain are the long-term effects of low-level radiation exposure, some of which were repeated or extended over periods of months.

In the FSU, there are now several countries affected by radioactive contamination from the reactor accident. The major ones include Ukraine, on whose northern border Chernobyl is located; Belarus, whose major city Gomel was heavily contaminated; and Russia, which provided many of the liquidators. Each country has priorities as it struggles with major economic burdens, but the health impact of the Chernobyl disaster looms as a major concern for all.
In Belarus and Ukraine an increasing incidence of childhood thyroid cancer has been found yearly since 1990 (3–5). Most investigators have gone on record as supporting the likelihood that the increase of cancer of thyroid is real (6–8) rather than being a consequence of improved surveillance.

It is striking that no increase of leukemia has yet been reported from the affected areas, because this might have been expected based on prior experience from Hiroshima–Nagasaki as well as from the epidemiology of medical exposures. However, a later increase cannot be ruled out in the absence of a reliable radiation dose estimation for the population that lived in the Chernobyl radiocountamination areas. Dose reconstruction and its correlation with biological indicators of exposure is therefore of utmost importance.

Studies of Immigrants to Israel

Large-scale immigration to Israel during 1990 to 1996 involved about 700,000 people from the former FSU. An estimated 140,000 were from areas of Ukraine, Belarus, and southern Russia that were contaminated with radioisotopes as a result of the Chernobyl accident.

In 1990, medical staff at the Soroka Medical Center and the Faculty of Health Sciences of the Ben-Gurion University of the Negev in Beer Sheva responded to the many inquiries and deep concerns of the immigrants about their exposure to radiation from the Chernobyl disaster. A clinic was established on a volunteer basis to evaluate health problems of the immigrants. The volunteers sought to determine the degree of exposure that had occurred and to direct the immigrants to appropriate medical help. In addition standardized information about their health and exposure histories was obtained. The clinic began operation in February 1991 and has continued to the present time.

This particular group of immigrants to Israel has several advantages for the study of health effects and the identification of biological indicators of radiation exposure. First, the study subjects are all present within a small geographic area and can be reached through organized “Chernobyl” associations. They have almost identical living arrangements and receive the same quality of health care. Second, the people involved, the liquidator group in particular, experience face-to-face interviews, medical examinations, and histories taken under similar conditions and administered by the same trained staff. Passive and active follow-up is relatively easy because travel distances are short and inexpensive and epidemiologic registries are available. In addition, collection and analysis of biological samples from persons from the three main radiocountaminated countries of the FSU are relatively simple and can take place under the same controlled conditions.

Body Burden Assessment of Radiocesium

Realizing that part of the radiation exposure of FSU immigrants to Israel was attributable to radiocesium ($^{134}$Cs and $^{137}$Cs) in the environment, it was decided to measure the radiocesium body burdens by whole-body counting (9). Immigrants who elected to receive evaluation and counseling and who had given informed consent were the original subjects of the studies. The Canadian Department of Health and Welfare loaned a portable whole-body counter to the group. In collaboration with the Canadian Bureau of Radiation Protection, body burdens of radiocesium (mainly $^{137}$Cs) were assessed in 1228 volunteer men, women, and children who had emigrated from various areas of Ukraine, Belarus, and Russia. These measurements were accompanied by medical assessments based on clinical histories and examinations. Radiocesium levels were strongly dependent on the time of residence in Israel, with the highest levels found in the most recent immigrants. The maximum level, extrapolated back to the time of leaving the FSU, was estimated to be approximately 6 Bq/kg (0.75 kBq). Of the most recent emigrants from the Kiev region (< 101 days in Israel), only 15% had back-extrapolated body burdens more than 50 Bq, whereas 53% of those coming from Gomel and other towns in the contaminated zones (>3.7 × 10$^{10}$ Bq/km$^2$ of radiocesium) had detectable levels more than 50 Bq. Women and children had considerably lower values of radiocesium, probably because of lower muscle mass and faster excretion rate than males. People from Gomel had significantly higher measurable body burdens compared to those from Kiev. This was in agreement with the higher degree of ground radiocesium contamination reported for the former region (10). All radiocesium body burdens at the time of measurement were too low for any concerns about health (9). However, the whole-body radiocesium measurements of this population demonstrated that it could be divided into comparison groups coming from areas of relatively high or low levels of ground contamination.

Results

As a result of these studies, much general health information about the immigrants became available on the basis of questionnaires filled out at the time of the whole-body counting. Though these data were based on fallible memories and taken from a sample of volunteers, liquidators reported an excess of symptoms (compared to nonliquidators), suggestive of acute radiation responses.

Blood Pressure

Analysis of the physical examination results of 328 subjects from less-exposed areas and 438 from more-exposed areas, followed by a second series of 121 subjects from more-exposed and 253 from less-exposed areas, and 334 subjects from unexposed areas, all led to the finding that older groups of immigrants from high radiopolluted areas had blood pressure levels significantly higher ($p < 0.01$) than those coming from less-exposed regions. This was even more marked for the liquidator group (11–14). The reasons for these blood pressure findings are not clear, but evidence for an association with posttraumatic stress disorder was found using a structured questionnaire based on Horowitz’s Impact of Events Scale (IES) (15).

Thyroid

We sought children for evaluation of thyroid status when it was realized that this was a particularly high-risk group that had been exposed to the short-lived radioiodines $^{131}$I, $^{132}$I, $^{133}$I, and $^{135}$I. Together with Dr. Jason Wynnberg of the University of Toronto, we initiated an investigation of children from the affected regions because of (a) the presumed higher sensitivity of children to ionizing radiation; (b) their high consumption of dairy products; (c) the increased prevalence of goiter among residents of these iodine-deficient regions (16–18); (d) the unknown contribution to dose of the short-lived radioisotopes of iodine; and (e) the reported increase of thyroid cancer in children living in Belarus, Ukraine, and southern Russia (3–5).

In a preliminary study of 300 young adults and children brought to the clinic voluntarily by parents, our initial intention was to assess the incidence of space-occupying lesions and autoimmune changes of the thyroid. All children or young adults who came
voluntarily were received for examination. Participants were 0 to 16 years of age at the time of the Chernobyl accident. A natural comparative experiment was suggested by the identification of subjects coming from the more-contaminated and less-contaminated areas ($^{137}$Cs < or > than 37 kBq/m$^2$), as defined by the International Atomic Energy Agency (IAEA) $^{137}$Cs soil contamination maps (10). General physical examination of subjects from the more- or less-contaminated areas included thyroid palpation by the same two experienced physicians (blind as to the origin of the participants), and laboratory tests included measurements of thyroid-stimulating hormone (TSH), thyroxine, thyroglobulin, antithyroglobulin (ATG), and antimicrosomal antibodies (AMA). The laboratory tests were all carried out blindly. The prevalence of palpably enlarged thyroids was about 40%, which varied somewhat with the examiner but without relationship to ground-level contamination. Ultrasound measurements confirmed these findings (although it became clear that results from ultrasound and manual palpation do not always agree because they do not necessarily measure the same thing). These findings probably reflect the goiterogenic regions from which the group came. Of the total group, one 3-year-old girl from Gomel (high-contamination area) was found to have a malignant papillary carcinoma. An additional 23 children had palpable thyroid irregularities, but these could not be described as nodules. No regional differences concerning thyroid morphology were found. Serum antibody levels showed three sera with AMA elevated for 73 children from Gomel; there were no abnormalities in the Kiev group. Antibody studies were carried out for 252 participants. Of the 128 children from the highly contaminated areas, 4 were found to have elevated AMA, compared to 1 of 124 from the less-contaminated area.

In summary, no evidence for significant changes in autoimmune status was detected in the group so far examined. However, TSH serum levels were significantly greater ($p<0.02$) for girls from high-exposure regions, although these values were within normal limits. Our working hypothesis is that the observed increases in TSH represent physiologic and homeostatic response to past radiation damage to the thyroid of some of the children examined (19,20).

Salvage Workers
A small number of salvage workers (liquidators), possibly about 500, are present in Israel although this may be an underestimate. Some of these individuals had elevated exposures during early work on the reactor before the radiation upper dose limit was provisionally restricted to 25 cSv. For individuals who subsequently worked in the strict control zone, it now appears unlikely that this limit was adhered to by all. Goldsmith et al. (12) have been evaluating health correlates of exposure histories and immediate reactions in order to provide a working index of dose correlates. Biological indicators of past radiation exposure are also being studied in our laboratory including serum clastogenic factor and glycoprophin A (GPA) in red cells. The levels of both parameters were significantly elevated in the liquidators tested.

Clastogenic Factor
Persons exposed to ionizing radiation carry substances in their plasma that induce chromosome damage when transferred to cell cultures from unexposed donors. Such clastogenic factors (21) were first described by Hollowell and Littlefield (22) and by Goh and Sumner (23) in the plasma of patients exposed accidentally or therapeutically to ionizing radiation.

Clastogenic factor (CF) was measured in sera from liquidators and children from highly radiocontaminated areas. Frozen plasma from liquidators, children, and adults from contaminated and noncontaminated areas of the FSU as well as control samples from persons in Israel who were not emigrants from the FSU were sent to the Paris laboratory of Dr. J. Emerit where they were studied blindly. The results showed that there were elevated levels of CF in most of the liquidator samples and, in addition, the Chernobyl children showed increased CF levels, compared to control samples (24,25). Of 47 liquidators now living in Israel and Armenia, plasma ultrafiltrates from 33 caused in vitro chromosome and chromatid aberrations in activated unirradiated lymphocytes in excess of 10/100 cells. In contrast, of 41 healthy blood donors only 2 plasma ultrafiltrates were associated with more than 10 aberrations/100 cells (18). Clastogenic scores for 170 children who came to Israel from Kiev and Gomel also showed significant excess ($p<0.001$) with 40 above the upper normal limit, compared to only 3 of the 70 normal unexposed children, 24 from the FSU, and 46 from Israel (25).

Glycophorin A
This sensitive technique, originally described by Langlois et al. (26,27), measures the frequency of red cells carrying a mutation at the GPA locus in red cells, presumably due to mutation of erythroid precursor cells. Fluorescent monoclonal antibodies specific for group M or N alleles were used to identify the cells that express only one allele.

The GPA assay has been used to show elevated levels of red cell variants due to somatic mutation in human groups exposed to radiation such as those from Hiroshima and Nagasaki (28–30) and victims of the Goiania radiation exposure accident (31). Increases in the frequency of variants have been found after exposure to mutagenic drugs as well as in cancer-susceptible patients with ataxia telangiectasia (32,33) and Bloom’s syndrome (34). The GPA somatic mutation assay therefore has been suggested to be useful for assessing cancer risk (30,35).

Jensen et al. (36) evaluated clean-up workers from Russia and Ukraine and found significant increases in N(blood group)/null alleles (N/O) red cells in 115 individuals that were associated with the estimated radiation exposure. The increased frequency of N/O variants was stable in 10 donors over a 7-year period. Somatic mutation analysis using the GPA assay were also carried out by Bigbee et al. (37,38) on Estonian clean-up workers exposed to ionizing radiations as a result of the Chernobyl accident. However, in this group, the frequency of variant erythrocytes was low, suggesting that the dose to the workers did not exceed 10 cGy, probably too low a dose to result in detectable damage to erythroid stem cells.

We used the GPA assay to measure the frequency of somatic mutation in red cells of a sample of clean-up workers who immigrated to Israel. As described by Wishkerman et al. (39) elsewhere in this issue, the Israeli liquidator group showed significant elevation ($p<0.001$) in the frequency of red cell mutations at the GPA locus compared to an unexposed control group.

Psychosocial Studies
The Chernobyl immigrants underwent severe and chronic periods of psychological stress after the accident. They are still fearful and concerned about the potential hazards of radiation exposure, and added to this are many of the other stresses they have had to undergo as a result of relocation and immigration. Recognizing these problems, studies on how best to interact, diagnose, and treat these people were initiated in conjunction with Dr. Benjamin Maoz and...
Dr. Facteurovitch of the Department of Psychiatry of the Soroka Medical Center and Ben-Gurion University of the Negev (40). Interviews were conducted with 700 people, half of whom were controls from areas of the FSU distant from Chernobyl. A striking association (p< 0.001) was found between the percent of subjects with elevated IES scores (15) and the degree of radiocontamination of the region of origin (14). Our studies therefore provide evidence for posttraumatic stress disorder among the immigrants, the prevalence of which becomes higher the nearer the previous residence was to Chernobyl (7%) in nonexposed areas, 15% in regions of relatively low exposure, and 30% in persons coming from areas of relatively high exposure. Moreover, significant correlations were observed between blood pressure increase and cancer fear, and somatization of symptoms and symptoms of PTSD. This work is currently ongoing and and has recently been reported (13,40). Current work indicates a diminishing of these abnormalities with time since immigration.

Discussion

Our body-burden measurements that are among a part of the immigrant population seeking evaluation and care have allowed us to document the importance of ground-level radiocontamination of areas of previous residence as a variable that permits separation of immigrants into groups with greater or lesser past radiation exposure that can be compared for different possible health effects. We compared such groups for thyroid function, the presence of blood cell mutations, and psychosocial changes.

The finding of a relative increase in TSH among girls from higher exposure regions (though most TSH levels were within normal limits) has several alternative explanations. One possibility is that there may be more iodine deficiency among immigrant who lived in regions closer to Chernobyl. However, in the higher exposure group examined, we did not find evidence for more incidence of goiter either by direct palpation or by quantitative measurements of thyroid size through ultrasound. Therefore, this explanation is rejected. Our working hypothesis is that the trend toward higher TSH values in girls who came from regions of higher exposure is due to subclinical radiation damage from radiodine exposure, with homeostatic increases in TSH resulting in the observed normal T3 and T4 levels.

Our approach to this working hypothesis is to determine the distribution of TSH values in children coming from exposed areas and to compare TSH values of those who were born before with those children who were born after the accident. If the working hypothesis is true, the former groups should have a trend toward higher TSH values compared to the latter group. The significance of these results is that they may indicate which population groups are at higher risk. Therefore, confirmation of these results by extending the study to involve larger numbers of children would be desirable.

These results provide evidence for past radiation exposure of salvage workers (liquidators) based on the measurement of clastogenic factor and of the GPA locus in erythrocyte cell mutants. When the cytogenetic and exposure index measurements have been completed, we shall better be able to determine how accurately these parameters reflect the degree of past radiation exposure. Whether these parameters have prognostic significance in terms of predicting health outcome is yet to be determined.

The results indicative of PTSD in some of the immigrant population are of particular interest. It is well understood by investigators working with people exposed in the Chernobyl accident that some people's complaints may be psychosomatic in origin. Indeed, for some this may be the most important health problem at this time. The rise in blood pressure observed among some older people from the affected areas may be a manifestation of this disorder. Therefore, some of our current work is concerned with approaches to the treatment of PTSD in immigrants from areas affected by the Chernobyl accident.

Conclusions

Lessons learned from these studies include the following points.

• It is unwise to assume that conclusions concerning the health consequences of Chernobyl can be drawn from past experience with Hiroshima-Nakagasaki or from medical radiation exposure. The relatively early onset of thyroid cancer among immigrant children was not predicted. Also, the apparent absence of the onset of leukemia was unexpected. Therefore, it is essential to carry out well-controlled epidemiologic studies to obtain original data.

• Data from control groups of unexposed persons are difficult to obtain because it is almost impossible to select groups with no radiation exposure from Chernobyl but that have the same ethnic and environmental backgrounds and disruption of life from political changes of the area. However, we have learned that it is possible to select comparison groups with similar backgrounds but who have experienced different degrees of radioisotope exposure based on previous residential exposure in areas with more or less ground-level contamination.

• Not all radiation effects that affect quality of life are malignant. Therefore, it would be unwise to select malignancy as the only parameter for the assessment of health effects. We propose three possible indicators in this report: the change in TSH levels in girls from areas of higher radiation exposure; the increase in blood pressure of older people; and evidence for PTSD, which is probably associated with the development of psychosomatic effects.

In view of the lack of knowledge about the long-term effects of this type of nuclear accident on the populations involved, a long period—perhaps 10 to 15 years—of observation is clearly needed for the comparison of populations known to have resided in areas of relatively high or low exposure or to have received increased doses of radiation the liquidator group. Information obtained from such a study would be useful to assess relatively low-level consequences of radiation as well as to determine the health effects on a population due to radiation exposure from a nuclear reactor accident.

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