

Chernobyl, 10 Years After: Health Consequences

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INTRODUCTION

On April 26, 1986, reactor no. 4 at the Chernobyl (Ukraine) nuclear power plant exploded. Over the next 10 days, considerable quantities of radionuclides were discharged into the atmosphere (table 1). The passage of the radioactive cloud over Europe led to varying degrees of contamination according to region (figures 1 and 2); the most contaminated regions were in southern Belarus, northern Ukraine, and the Bryansk and Kaluga regions of Russia. The heavier particles (e.g., fuel elements) were deposited less than 100 km from the plant, but the more volatile fission products (such as cesium and iodine) were able to travel great distances (1).

The biologic effects of ionizing radiation are fairly well known, especially the carcinogenic potential. These effects are a function of the amount of energy absorbed by tissues per unit time (dose and dose rate). At high doses and high dose rates, above dose thresholds that vary for different organs and tissues, ionizing radiation can cause tissue destruction (table 2). Below these thresholds, or at low dose rates, the biologic damage is compatible with cell or tissue survival (causing, for example, DNA mutations or chromosomal alterations) and can be repaired. The effects of doses below 200 mSv at low dose rates are still little understood (8). The existence of a threshold dose below which there is no effect remains controversial.

Humanity, it must be remembered, is continuously exposed to natural radiation at a mean rate, worldwide, of 2.4 mSv/year, or approximately 170 mSv for a mean lifetime of 70 years (7).

The accident at Chernobyl resulted in the exposure of a huge number of people to doses and dose rates that varied substantially, creating a new situation for the epidemiology of ionizing radiation. Based on what has been learned so far, the occurrence of thyroid cancer and leukemia was, or is, plausible (10). The effects of stress may result from all types of accidents or catastrophes (11). Finally, various unexpected and ill-defined effects (digestive, respiratory, endocrine) have been mentioned and related to the accident.

This presentation reviews reports in the international scientific literature and discusses the plausibility of these reports in the light of current knowledge about both radiation and postdisaster effects.

DOSE UNITS

The Gray (Gy) refers to absorbed dose, i.e., the quantity of energy delivered by ionizing radiation per unit mass. One Gy equals 1 Joule/kg. When an individual is homogeneously and externally exposed, each part of the body receives the same dose; whole-body dose is then an appropriate concept. When exposure is heterogeneous, however, different organs or tissues receive different quantities of energy; in such events, the use of organ dose is more appropriate.

The equivalent dose takes into account the biologic potency of different types of radiation (x, gamma, beta, alpha, and neutrons) by applying weighting factors (respectively, 1, 1, 1, 20, and 10). The equivalent dose unit is the Sievert (Sv).

The effective dose, also expressed as Sv, results from a calculation that provides a single summary value to be used in different cases of irradiation. It sums and weights the equivalent doses received by tissues and/or organs according to their sensitivity to the effects of ionizing radiation. The weighting factors used in such cases are derived from previous epidemiologic studies of radio-induced cancers. Using the effective dose is more appropriate for radioprotection purposes.

For clarity's sake, external or predominantly external doses are expressed in Gy throughout this presentation. Sometimes the reports we reviewed expressed doses in Sv—in such instances, we made the appro-

Received for publication January 16, 1996, and accepted for publication June 12, 1997.

Abbreviations: CI, confidence interval; ECLIS, European Childhood Leukaemia-Lymphoma Incidence Study; EUROCAT, European Registration of Congenital Anomalies; OR, odds ratio; SIR, standardized incidence ratio.

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TABLE 1. Main radionuclide release into the environment from the Chernobyl accident*

Radionuclide	Physical half-life	Estimates of released activity	
		MCI	PBq
Cesium-134	2 years	0.5–1.3	18.5–48
Cesium-137	30 years	0.8–2.4	29.6–88.8
Iodine-131	8 days	17–45	629–1,665
Iodine-132/tellurium-132	3 days	11–49	407–1,813
Iodine-133	20 hours	67.5	2,497.5
Strontium-89	50 days	0.6–2.2	22.6–81.4
Strontium-90	28 years	0.03–0.2	1.1–7.4

* Based on Khan (2), the International Chernobyl Project (3), and Sich (4).

priate conversions. These conversions do not in any way change the order of magnitude of the doses in question.

EXPOSED POPULATIONS AND THEIR DOSES

The personnel at the Chernobyl plant and the rescue teams present on-site during the first hours after the accident received external beta and gamma radiation from reactor parts, from the plume, and from the radioactive debris and particles deposited on the ground. Their extremely high doses ranged, roughly, from 1 to 15 Gy (12, 13). Exposure by inhalation or ingestion was relatively very low (1).

The "liquidators," i.e., cleanup workers (numbering about 600,000), are the personnel who participated in the decontamination and cleaning on-site, in the 30 km zone around the site, and in other highly contaminated areas (14). Very few of these liquidators were equipped with dosimeters (15). They were irradiated for a mean period of 2 months, primarily externally; 10 percent of these liquidators received doses estimated to exceed 250 mGy, and 30 to 50 percent of them received doses ranging between 100 and 250 mGy (3, 16). Another estimate concluded that 25,000 liquidators received up to 700 mGy of external radiation between the accident and the beginning of 1987, and that a half million more who began this work later sustained a mean dose of 100 mGy (17).

The third group is composed of the 115,000 persons evacuated from the 30 km zone around the plant (14). They were irradiated externally and, to a lesser extent, by inhalation. Their average external dose has been estimated at 140 mGy (calculated from (7)). Other authors, however, have estimated the average external dose received by the 30,000 evacuees of Pripyat, Ukraine, and other towns in the 30 km perimeter at 15 mGy (range 0.1–383 mGy) (18).

The fourth group comprises the inhabitants of the contaminated zones who were continuously subjected to external and internal irradiation. Among them are

the 270,000 inhabitants of the so-called "strictly controlled zones," that is, the zones contaminated by a cesium-137 level of at least 0.6 MBq/m² (15 Ci/km²). Protective measures were and still are applied to these areas; in particular, restrictions on the consumption of agricultural products (19).

The less contaminated zones (1–15 Ci/km²) house a fifth group of 3,700,000 people who have been subjected to less strict protection. The 70-year effective doses received by this group are shown in table 3.

The general population of the three republics (Belarus, the Ukraine, and Russia) surrounding Chernobyl (roughly 280 million people in 1991) live in areas where the cesium-137 contamination level was lower than 0.04 MBq/m² (1 Ci/km²). The average effective dose that they received during the first year is estimated to be 0.26 mSv and, lifetime, 0.82 mSv (14).

In western Europe, the cesium-137 contamination levels ranged between approximately 1 kBq/m² (25 mCi/km²) and 0.04 MBq/m² (1 Ci/km²). Contamination in southern Germany, Austria, and northern Italy has been measured in this upper range (14, 21). Estimates of cumulative effective doses over 50 years range from less than 0.03 to 2 mSv (table 4).

These dose estimates actually indicate only orders of magnitude. They were calculated using data about ground contamination levels, plausible mean transfer factors, and hypotheses of food consumption patterns. They are thus applicable to groups and do not take into account individual characteristics that may be important from an epidemiologic point of view (e.g., age at exposure).

Work continues on the reconstitution or measurement of the individual doses received by inhabitants of the three contiguous republics. Large individual variations will probably be found, as they already have been for the thyroid doses received by Kiev (Ukraine) residents (22).

EFFECTS INDUCED (OR LIKELY TO BE INDUCED) BY IONIZING RADIATION

Short-term effects

Acute mortality. Five hundred people were hospitalized, 237 for acute radiation sickness. This syndrome caused 28 deaths. Three other deaths were caused by traumas or burns (23).

Congenital malformations after in utero exposure. In animals, in utero exposure to ionizing radiation has been shown to cause congenital malformations with dose thresholds on the order of 0.1 Gy (24). In humans, developmental anomalies (microcephaly and mental retardation) related to such exposure have been detected only in children of Hiroshima and Nagasaki

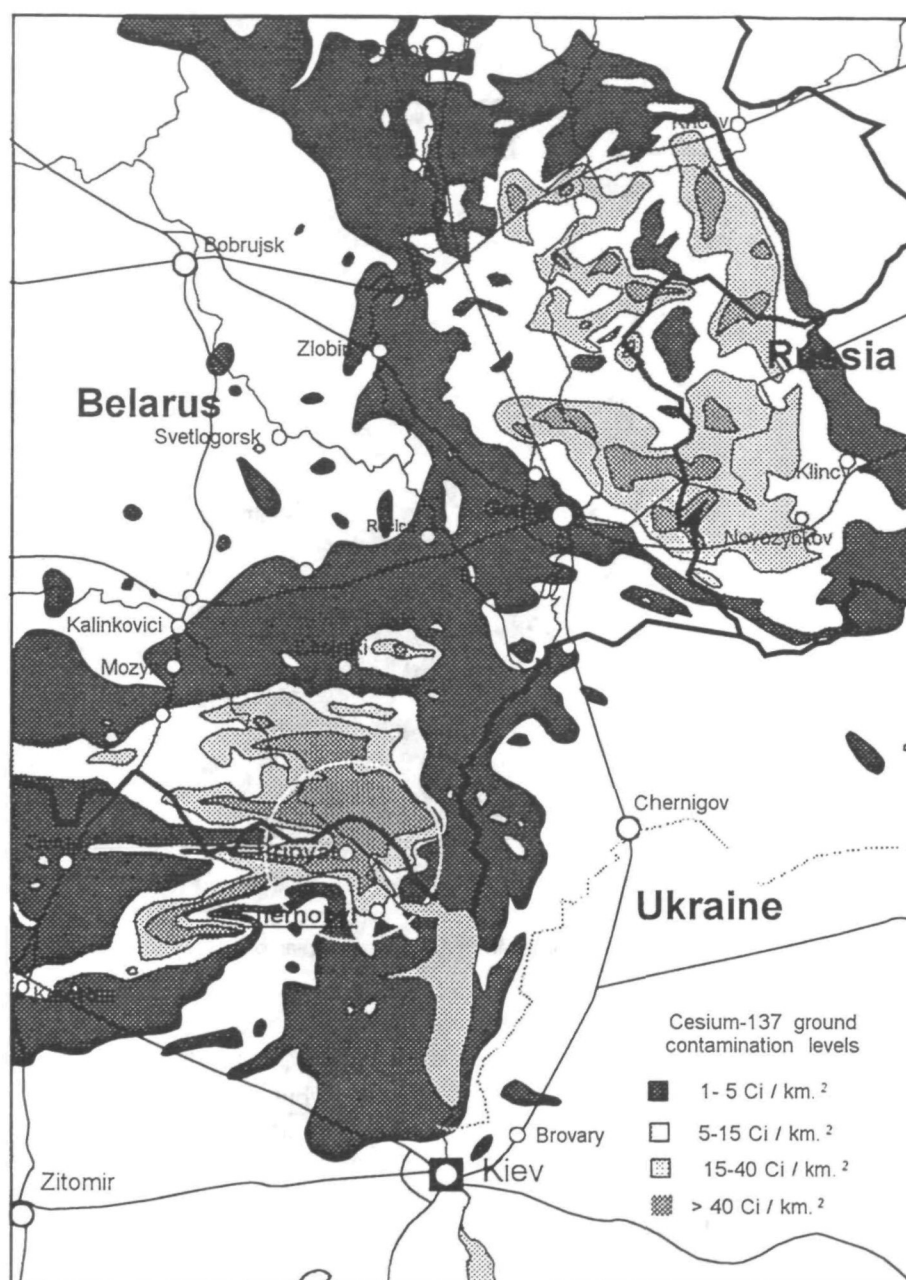


FIGURE 1. Cesium-137 ground contamination in the Ukraine, Belarus, and Russia after the accident at Chernobyl (Ukraine).

survivors. The data suggest there is a threshold dose for mental retardation (0.12 to 0.2 Gy) but not for microcephaly (25, 26).

Lazjuk et al. (27, 28) conducted a three-part study on this subject. In the first portion, more than 21,000 embryos and fetuses aged 5 to 12 weeks (the products of legal medical abortions throughout all of Belarus from 1980 through 1991) were examined by stereomicroscope. More than half the abortions took place after the accident. Only 56 percent of the embryos and fetuses from the control region (Minsk, Belarus) and

28 percent of those from contaminated zones could be examined thoroughly. The authors did not state whether the pathologists were blinded to the zone and time period from which the samples came. The prevalence of congenital malformations (all types) was higher for contaminated zones ($>0.6 \text{ MBq/m}^2$) from 1986 to 1991 than for Minsk between 1980 and 1991 (8 percent and 4.9 percent, respectively). The periods were not matched and selection bias cannot be ruled out. Thus, no conclusions can be reached.

The second part of the articles by Lazjuk et al. (27,

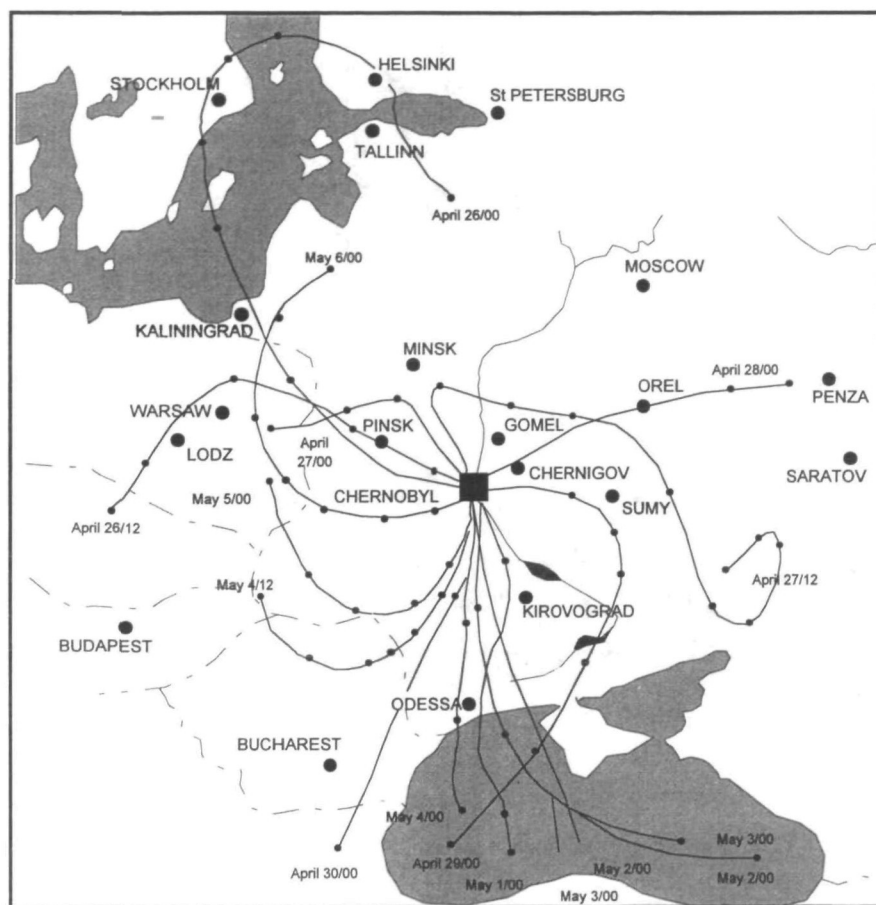


FIGURE 2. Trajectory over Europe of radionuclides discharges from the damaged reactor at Chernobyl (Ukraine); emissions at 0 and 12 hours, and distance in 12 hours (based on references (5) and (6)).

28) examined the prevalence over time of various malformations among live births, using data collected by the congenital malformation monitoring system that began functioning in Belarus in 1979. The authors considered the following malformations: anencephaly, spina bifida, cleft palate and cleft lip, polydactyly, phocomelia, esophageal atresia, anal atresia, Down syndrome, and multiple malformations. The prevalence of congenital malformations (all types) increased significantly after the accident, in both contaminated and noncontaminated zones, suggesting the influence of a detection bias.

Finally, a geographic correlation analysis, carried out at a district level and only in contaminated zones, observed no correlation between the indicators of mean exposure per inhabitant and the observed prevalence of congenital malformations.

Kulakov et al. (29) conducted a cross-sectional study of 688 pregnant women and their offspring and also retrospectively analyzed the hospital records of 7,000 pregnancies (1982–1990). Subjects lived in two districts, one in the region of Gomel (Belarus), the

other in Kiev. They had similar socioeconomic characteristics but different levels of contamination. The prevalence of congenital malformations (congenital heart disease, esophageal atresia, anencephaly, hydrocephaly, multiple malformations) increased twice as much in the more contaminated zone. The article contains few details about the methods underlying these observations (e.g., neither maternal age distribution nor the methods for selecting subjects or ascertaining congenital malformations are described). There are obvious errors in contamination units (kCi instead of Ci?), and it is difficult to know exactly how contaminated these zones were.

Overall, since cumulative in utero doses over the entire pregnancy did not exceed 100 mSv for any of the exposed women (27), it is unlikely that even a properly designed epidemiologic study could show any excess risk for congenital malformations attributable to ionizing radiation alone. No study of the populations affected by Chernobyl that we know of measures their folate levels, although these are known to influence the occurrence of neural tube defects (30).

TABLE 2. Effects of ionizing radiation observed at various dose levels (high dose rates)*

Dose level (organ)†	Observed effect
3–5 Gy	Dose at which half the individuals would be expected to die within 60 days
5 Gy (eyes)	Cataract with impaired vision
>0.5 Gy	Depression of hematopoiesis
0.2 Gy	Significant increase of leukemias and solid tumors (incidence and mortality)‡
0.1 Gy (thyroid)	Significant increase of thyroid cancers§

* Based on Sources, Effects, and Risks of Ionising Radiation (7,8) and the International Commission on Radiological Protection (9).

† If not specified, whole body.

‡ In Hiroshima and Nagasaki survivors.

§ After external irradiation of children for medical purposes.

The lifestyle of the populations directly touched by the accident changed, however, and their subjection to food restrictions may have modified their vitamin intake.

Mental retardation. Kozlova et al. (31) studied 2,189 children from contaminated zones (15 to over 40 Ci/km²) in the three countries; they had been irradiated in utero at different periods of gestation. The reference group comprised 2,021 children from zones with less than 1 Ci/km² of contamination who were matched for age, socioeconomic level, and parents' educational level. They observed reduced intellectual performance (on psychometric tests) in the exposed group. These results are descriptive and do not take into account the parents' psychologic condition, even though this same study also finds a higher prevalence of psychologic disorders among exposed parents.

Case clusters in Europe and Asia Minor

Down syndrome. Clusters of Down syndrome cases have been reported in several different European countries after the accident at Chernobyl: in West Berlin, 12 cases were observed 9 months after the accident, while only 2–3 were expected (32). An abnormally high prevalence was also noted in the region

TABLE 3. Estimated effective doses (mSv) over 70 years for the population in the contaminated zones

Type of exposure	Strictly controlled zones (3)		Other contaminated zones (20)
	International Atomic Energy Agency	"Official"*	
External irradiation	60–130	80–160	40
Internal irradiation	20–30	60–240	30–180
Total irradiation	80–160	150–400	70–220

* First estimates of experts from the former USSR.

TABLE 4. Estimates of the cumulative effective doses over 50 years after the Chernobyl accident in various western European countries*

Countries	Effective dose equivalent (mSv)
Austria and Finland	1–2
Greece, Norway, and Sweden	0.5–1
Germany, Italy, and Switzerland	0.25–0.5
Ireland	0.12–0.25
Belgium, Denmark, France, Luxembourg, the Netherlands, and Turkey	0.06–0.12
United Kingdom	0.03–0.06
Portugal and Spain	<0.03

* Based on Bengtsson (21).

of Lothian, Scotland (33). EUROCAT (European Registration of Congenital Anomalies), a network of regional registers monitoring congenital malformations, was called upon to assess the significance of these clusters. In 1991, EUROCAT included 24 registers in 14 European countries, covering approximately 350,000 births a year (about 10 percent of the births in these countries). Its comparison of the incidence of Down syndrome before and after the accident at Chernobyl revealed no significant differences between the two periods (34).

The apparent clusters that have been reported may result from different biases (e.g., improved screening and awareness, selection) (35). It is also highly probable that the medical teams studying the consequences of Chernobyl would observe some isolated clusters, and that they would be published more frequently than negative results (34).

Neural tube defects. The prevalence of neural tube defects apparently increased in some regions of Turkey in the months after the accident (36–39), although it did not rise in other areas in the country (40, 41). The first-year average effective dose for the Turkish population is estimated to be 190 μ Sv (14). Compared with the estimated yearly dose of about 2 mSv from natural background radiation, this incremental dose appears trivial, and the purported effect implausible. The chronologic differences in their occurrence in different parts of Turkey suggest that these observations result from screening or selection biases.

Another EUROCAT study considered developmental anomalies of the central nervous system and the eyes. It analyzed the registers and found that the prevalence rate among the cohort exposed in utero during the first 5 months after Chernobyl did not differ from the expected rate based on the period 1980–1985, nor was any relation to exposure detected. Nonetheless, during the individual register analyses, a significant increase in neural tube defects was observed for Odense, Denmark (four cases observed versus 0.9 expected) (34).

Data from congenital malformation registers in Finland, Norway, and Sweden did not reveal an increase in the prevalence of malformations in the regions most exposed to the Chernobyl radioactive fallout (42–44).

Because in utero doses in the western European countries were evaluated at a maximum of 1.5 mSv (35), the detection of an excess of congenital malformations secondary to the accident at Chernobyl is highly improbable, even in the absence of a threshold dose. Obviously, it becomes progressively more improbable at current exposure levels. The issue of congenital malformations is discussed in detail by Little (45).

Spontaneous abortions and miscarriages. No significant excess of untoward pregnancy outcomes has been observed in the descendants of Hiroshima and Nagasaki survivors (mean gonadal dose 0.3–0.6 Gy) (46). A synthesis of the data supplied by the governments of the three contiguous republics on this subject (3) provides no details about the methods used and does not allow a conclusion to be drawn on this point. In Norway, Irgens et al. (47) reported a statistically significant 1 percent increase in spontaneous abortion rates in the 12 months after, compared with the 12 months before, the accident; it was most marked during the second and third trimesters after the explosion. They provide little detail about their methods. A study in Styria (Austria) (48), where greater environmental contamination occurred and whose population received higher doses (14), found no such increase.

Genetic damage. Ionizing radiation can damage genetic material of both somatic and germline cells (24, 49). Cytogenetic studies in blood cells (finding and counting such chromosomal aberrations as dicentrics, acentric fragments, and chromatid rings and aberrations) have been performed on small groups in the neighboring republics, yielding conflicting results (3, 50–54). All of these studies are marred by methodological weaknesses (e.g., too few subjects, geographically-based comparisons, absence of control groups and of dose estimates). These problems make it difficult to draw any conclusions.

Geographic studies in western Europe have also produced contradictory results (55–57). No clear link appears to associate the excess of chromosomal anomalies with the doses received by inhabitants, estimated geographically on the basis of fallout measurements.

The possibility that germline mutations may be passed on to offspring is suggested by observations among 64 children of atomic bomb survivors (58).

Following the accident at Chernobyl, a relation between the mutation rate of minisatellites of human lymphocyte chromosomes and exposure to radioactive contamination was observed in an ecologic study (59).

The reference population, from the United Kingdom, probably differed from the Belarussian population for genetic and environmental risk factors for mutations. The two groups do not appear to have been matched for age, although the risk of mutation probably increases with age, as it does for stable chromosomal aberrations (60). The unavailability of adequately detailed information about the study subjects means that this hypothesis cannot be ruled out.

Immunologic effects. Lymphocyte disorders lasting many years have been noted among patients irradiated by high doses (typically above 1 Gy) in some studies (14, 61), but these results have not been reproduced in other studies (62). In a group of workers occupationally exposed to very low doses (around 10 mSv) in Austria (63), some changes in the lymphocytic subsets were the opposite of previous results. This study suffers from several methodological weaknesses (cross-sectional study, too few subjects, no control for such confounding factors as immunity status or age before exposure, no statistical analysis).

A cross-sectional study after Chernobyl discerned no difference in the immunologic status of residents of contaminated zones and those living in control zones (3, 15). It involved 1,356 subjects from five age brackets (children born in 1988, 1985, and 1980 and adults born in 1950 and 1930) nonrandomly selected in contaminated (>5 Ci/km²) and uncontaminated villages. In 1991, the comparison of 71 healthy subjects with 30 liquidators close in age whose external exposure had varied between 0.1 and 0.5 Gy showed reduced CD8+ lymphocytes in the exposed subjects, results fairly consistent with those previously reported (64). The article furnishes few details about its sampling technique, however, and the sex ratio differed between the two groups. These drawbacks raise questions about the reliability of the results. A clinical study of children 10 to 15 years of age (34 from a zone contaminated by 16 Ci/km², and 30 from a zone with less than 1 Ci/km²) showed no significant correlation between cesium-137 physical activity and natural killer-cell activity (65). Immunologic studies of Hiroshima and Nagasaki survivors have shown no change in natural killer-cell activity (61).

Medium and long-term effects

Lens changes. Posterior capsular lens changes were observed among Hiroshima and Nagasaki survivors with a threshold dose estimated at 200 mGy (3). The prevalence of lens changes was studied among Ukrainian children between the ages of 5 and 17 years, in part randomly selected. The control children were randomly selected, came from an uncontaminated zone, and were matched by age and sex. In all, 996

subjects representing 35–40 percent of the eligible children in the high exposure zone were included, with 791 controls. The exposed group showed a slight but significant excess ($p < 0.001$) of subclinical posterior subcapsular lens changes (66). Nonetheless, the external mean cumulative doses (estimated between 29 and 85 mGy, depending on the dose reconstruction method) received by the exposed group were below those generally considered the threshold for such effects (3). Information about the beta radiation doses related to exposure to contaminated dust is apparently not available. The authors concede that bias could explain their results (e.g., the investigators knew the children's exposure status) (66).

Cardiovascular disease. Studies among Hiroshima and Nagasaki survivors who were exposed to at least 2 Gy have reported a relation between external irradiation and various factors (arterial calcification, coagulation impairment, hypertension) that contribute to arteriosclerosis and, thus, to coronary disease. No evidence of myocardial infarction risk was seen below 1 Gy (67, 68). Nonetheless, Darby et al. did not observe an excess risk of cardiovascular disease among patients with ankylosing spondylitis treated with x-rays (69). A causal association remains to be demonstrated between cardiovascular risk and exposure to relatively prolonged low-dose radiation.

In a short statement, Russian doctors (3) have reported an increase in cardiovascular diseases among the exposed population. Despite the lack of methodological detail, these results may be connected to the findings in Hiroshima and Nagasaki survivors. The cardiovascular impact of stress should probably also be taken into account.

Benign thyroid disorders. Studies of atomic bomb survivors (70) and persons exposed to the fallout from nuclear testing (71, 72) suggest that ionizing radiation may affect the risk of benign thyroid nodules. Transitory functional thyroid disorders (levels of circulating T3 and T4 hormones, antithyroglobulin or antimicrosomal fraction antibodies) have been reported in the Ukraine (73) and in Russia (74). Among children examined in Russia, the prevalence of goiter varies substantially from one district to another (5–25 percent of children examined) (74). Unfortunately, the procedures for selecting the subjects are not detailed in these studies. The intensity of the screening may not be entirely independent of the degree of ground contamination. Moreover, the endemic character of iodine deficiency, a risk factor for goiter, has been confirmed in the regions affected by the accident at Chernobyl (75).

Other effects. Since the accident, doctors from the Community of Independent States have reported observing an abnormally frequent rate of a series of

disease symptoms (e.g., endocrine, digestive, neurologic, respiratory, etc.) among the exposed populations (3). It is thus appropriate to discuss these problems as possible effects of ionizing radiation, although epidemiologic verification is required.

Pregnancy disorders. The study by Kulakov et al., discussed above, concludes that miscellaneous pregnancy disorders not specifically related to the reproductive system (anemia, renal disorders, transient hypertension, abnormalities of fat metabolism) have increased from 23.1 to 33.9 percent in the most contaminated district they studied, and from 7.1 to 51.2 percent in the less contaminated zone (29). Since the annual migration rate is evaluated at less than 3 percent, the increase is probably not due to a change in the population structure. The two districts differed by a factor of three in their prevalence of these disorders before the accident, suggesting that the attention paid to these problems varied between the two zones and that more intensive screening since the accident may explain these increases. The authors also reported an increased incidence of toxemia and complications of labor in both districts. The very brief description of methods makes it impossible to draw a conclusion about the reality of these results, especially since, to the best of our knowledge, similar facts have never been reported in connection with exposure to ionizing radiation.

Changes in neonatal health. The same study (29) also reports that neonatal morbidity increased in the period 1986–1990, compared with the levels of 1983–1985, by three times in the more contaminated district and by two times in the less contaminated district. For specific problems, however, such as hemorrhages in newborns (incidence multiplied by nine after the accident), the increase was not greater in the more contaminated district. Another study (3) concluded that perinatal mortality had declined since the accident, perhaps because of improvements in the quality of care. Other reports do not suggest any excess of pathologic symptoms, with the possible exception of postnatal respiratory distress, among newborns in the Ukraine strictly controlled zones in the first post-accident year. Nonetheless, these reports are declarations rather than epidemiologic studies presented in a scientific format (76).

In the southern regions of West Germany, that is, those most contaminated by the fallout from Chernobyl, a marked change towards excess infant mortality was observed from the previous rate, beginning in May 1986 (77). A causal relation with the accident remains to be shown. In Sweden, a significant increase in the number of infants with birth weights below 1,500 g (odds ratio (OR) = 1.37, 95 percent confi-

dence interval (CI) 1.03–1.73) and in perinatal mortality (OR = 1.50, 95 percent CI 1.12–2.0) was observed in June and July of 1986, after adjustment for maternal age and parity (44).

On the whole, the reports published so far do not show any clear trend related to population exposure.

Vegetative dystonia. A syndrome called “vegetative dystonia” is said to be very frequent among Ukrainian children. Its symptoms include fatigue, pallor, inattention, abdominal pain, headaches, and poor school performance. Clinical examination and complementary tests that are not practiced in Western countries, such as whole-body thermography, are said to allow the clinical form of vegetative dystonia to be diagnosed (78). The author points out the resemblance of this syndrome to “chronic fatigue syndrome,” which is also the subject of much debate and skepticism.

The appositeness of grouping these symptoms together in a separate syndrome remains problematic as long as serious clinical epidemiology studies have not been performed. It is no less true, however, that its effect on public health may be substantial, even if its extent is difficult to assess.

Cancer

Thyroid cancer. Thyroid cancer is rare among children younger than 15 years. The incidence in the West is 0.1 to 0.3 cases per 100,000 annually (79, 80), similar to that in Belarus between 1986 and 1988 (81). In the Ukraine, the incidence between 1981 and 1988 was lower (0.04–0.07 per 100,000). The incidence is approximately three times greater among girls than among boys (82). The great majority of differentiated thyroid cancers are of two morphologic types, papillary and follicular (83).

Thyroid cancer and ionizing radiation. Exposure to acute external radiation is a well-documented risk factor for this disease in children and adolescents (84). Populations in whom this risk has been observed include Hiroshima and Nagasaki survivors as well as adolescents and children who underwent irradiation of the head or neck for therapeutic purposes. A joint analysis of seven cohorts has shown that the human thyroid is a very radiosensitive organ. A significant excess risk (at or above 100 mGy) has been established for external thyroid doses (85). The risk of thyroid cancer is highest for those who were youngest at exposure. In most studies, the increased incidence becomes clear between 10 and 15 years after exposure. Several studies have pointed out more moderate increases between 3 and 7 years after exposure (84). On the other hand, no increased risk of cancer has been observed after internal thyroid irradiation by iodine-131 alone (treatment for hyperthyroidism and diagnos-

tic use) among adults (86), or among children and adolescents (84). Nonetheless the information about children younger than 15 years is limited. The carcinogenicity of iodine-131 has been shown in animals, particularly among rats and mice (87, 88). Some experimental studies suggest that malignant thyroid tumors can be induced four to 10 times less effectively with iodine-131 than with x-rays, although another study could not replicate this result (89). Studies of the inhabitants of the Marshall Islands, who were exposed to fallout from nuclear tests on the Pacific atoll of Bikini in 1954 have shown a significant excess risk of thyroid cancer in children and adolescents. They were exposed to high doses (mean, 12.4 Gy) of short-lived iodine isotopes (iodine-132, iodine-133, and iodine-135). Iodine-131 and external gamma radiation each represented 10 percent or less of the exposure (84).

Thyroid doses due to Chernobyl in the three republics. The iodine family represents a significant portion of the emissions from the Chernobyl reactor (see table 1). Stable iodine taken prophylactically saturates the thyroid gland, preventing radioactive iodine from concentrating there. After the accident at Chernobyl, stable iodine appears to have been administered in a very limited fashion (90). The half-lives of radionuclides from the iodine family (see table 1) are such that 99 percent of them have decayed and disappeared from the environment after 54 days.

The estimations of the thyroid doses received by exposed populations are based partly on thyroid spectrometric measurements of approximately 400,000 people performed in the three countries in the weeks after the accident (22, 79, 91–93). These measurements, involving only iodine-131 and not short-lived iodine isotopes, were not taken in a standardized way (93). Estimations of individual thyroid doses in a given territory vary by up to four orders of magnitude (22, 79, 91). In addition, they are two to 10 times higher in children than in adults living in areas of equivalent contamination (22, 79, 91–93). This is because children have a smaller thyroid mass and greater iodine uptake; therefore, the thyroid dose is higher in children than in adults after the incorporation of the same quantity of radioactive iodine (14). Children are also likely to consume relatively more milk, which was in most cases the principal exposure pathway for iodine-131.

In the Ukraine, among inhabitants evacuated from the town of Pripyat, the average individual thyroid dose is estimated as 2.8 Gy for those aged 0 to 7 years at the time of the accident, and as 0.4 Gy for other age groups (93) (figure 3). Estimations for the population of Kiev are lower (22).

In Belarus, in the most contaminated zones, the

average individual thyroid dose is estimated at 0.1 to 0.3 Gy for the population as a whole and at 0.4 to 0.7 Gy for children aged less than 8 years at the time of the catastrophe (19) (figure 3).

In Russia, in the region of Bryansk in the zones contaminated by more than 0.6 MBq/m², the average thyroid dose, depending on the district, is estimated at between 0.07 and 2 Gy for children younger than 7 years and between 0.014 and 0.05 Gy among adults (74). For the region of Kaluga, 25 percent of the children and adolescents are thought to have received thyroid doses between 0.03 and 2 Gy, while approximately 2 percent are thought to have received more than 2 Gy (74).

Incidence of childhood thyroid cancer in Belarus, the Ukraine, and Russia. The incidence of thyroid cancers among children aged less than 15 years (at the time of diagnosis) began rising in Belarus in 1990 and continued to do so through 1994 (figure 4) (81, 94–96). Half of the registered cases came from the especially contaminated Gomel region. In the Ukraine, an increase in incidence, evident from 1990 onward, has been reported among children less than 15 years and among adolescents (15–18 years); more than half the cases came from the five regions most exposed to fallout from the accident (73, 96, 97). Lastly, an increase among children under 15 years of age was reported later in Russia for the regions of Bryansk and

Kaluga (74, 98). The majority of cases came from the region of Bryansk, and the increase was first detected only in 1992.

Between the period 1981–1985 and the period 1990–1994, the incidence of childhood thyroid cancer was multiplied by 100 throughout Belarus as a whole (by 200 for Gomel alone), by seven for the Ukraine as a whole (by more than 100 for the five most contaminated zones of the Ukraine), and, finally, by eight for the period 1986–1991 for the Russian regions of Bryansk and Kaluga (96).

In absolute terms, these figures represent 300 new cases of thyroid cancer among children younger than 15 years in Belarus, more than 200 in the Ukraine, and more than 20 in the Russian region of Bryansk (98). Furthermore, in the Ukraine, roughly 100 new cases were observed among adolescents (15–18 years) between 1986 and 1993 (73).

The characteristics of the cancers observed in Belarus (79, 82, 98–101) and in the Ukraine (102) among children younger than 15 years (80 to 120 cases examined, according to the series) have been analyzed in detail. The diagnosis of thyroid cancer was confirmed in more than 90 percent of the cases. These cancers were primarily papillary (96.5 percent from a series of 93 cases diagnosed in Belarus between 1986 and 1991) (99), and two thirds of them were little or moderately differentiated. In the above-mentioned se-

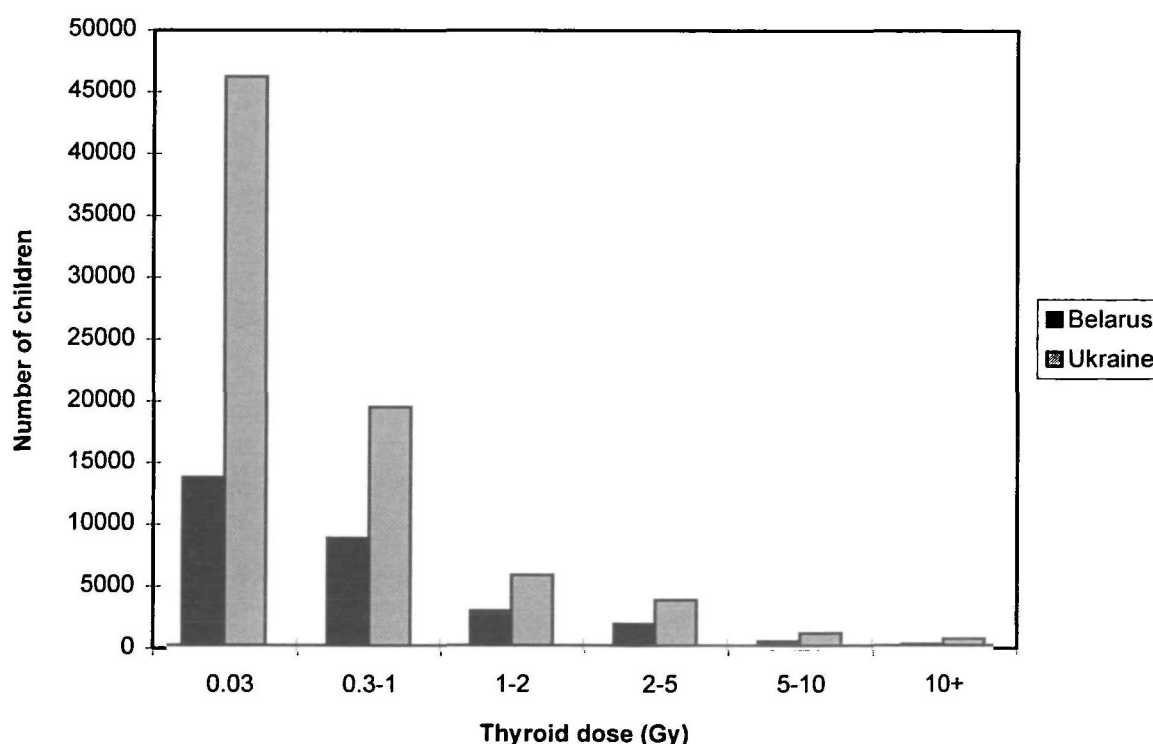


FIGURE 3. Thyroid dose distribution among children with thyroid measurements after the Chernobyl (Ukraine) accident (A. Bouville, US National Cancer Institute, personal communication).

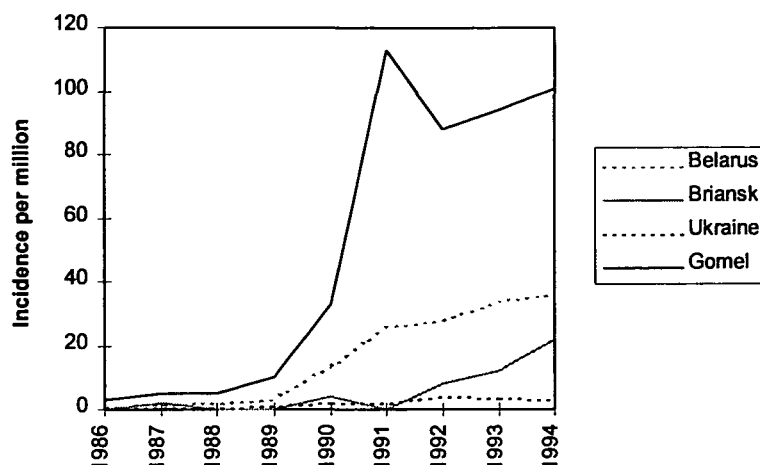


FIGURE 4. Trend of incidence of childhood thyroid cancer in Belarus, Ukraine, and Russia, 1986–1993 (based on references (73), (96), and (97)).

ries, extra-thyroid extension was noted in 60.5 percent of the cases, regional lymphatic metastases in 74 percent, and distant metastases in 7 percent. The tumor size at diagnosis exceeded 1 cm in 88 percent of the cases from a series of 84 diagnosed in Belarus in 1991 and 1992 (100). Similar findings have been made in the other series (99). In the 1986–1991 series, the female-male ratio was approximately 1.3:1; the mean age at diagnosis, 9 years; and the mean age at the time of the accident, 4.6 years (99, 100). What all the studies taken together show is that the younger the age at exposure, the greater the risk and the more likely it is to manifest itself at a younger age (79, 103).

Thyroid cancer among adults in the general population. In Belarus, which has had a cancer registry since 1978, the incidence of thyroid cancer among adults has apparently increased from 2.2 per 100,000 in 1986 to 6.5 per 100,000 in 1993 (81). These data have not been validated.

Discussion. The first published reports that thyroid cancer was increasing among children were greeted skeptically for a variety of reasons (104–106). Three questions must be asked: 1) Is the increased incidence real? 2) If so, is it attributable to the accident? and 3) If so, what are the reasons for it?

Several analysts have suggested that this increase may actually be due to the increased detection of occult thyroid carcinomas (tumors only a few millimeters in diameter, asymptomatic, and slow-growing). Their prevalence among adults at autopsy ranges between 2.7 and 35.6 percent, according to the series and country (107). A high prevalence (9 percent) has also been observed in a nonrandom sample of 215 Belarussian adults aged 19 to 88 years who died in 1990 and 1991 (108). There is little documentation of the prevalence of this form of thyroid cancer among chil-

dren younger than 15 years of age (109, 110). The setting-up of screening programs, especially those using ultrasonography, could have contributed to revealing tumors of this type that existed before the accident and which would not otherwise have been detected. In children, the extent of the increase makes it clear that it is not simply the result of increased medical attention, or of more effective diagnostic methods, or both. Furthermore, the tumors observed are mainly invasive and fast-growing (111). It is now generally agreed that the increase in thyroid cancers observed among children and adolescents in the zones exposed to Chernobyl fallout is real (87, 111–113). Conversely, the increase observed among Belarussian adults is more likely to result from more intensive screening because of a relatively high prevalence of occult carcinomas in adults. Cancers may have appeared (or may still appear) in adulthood for the cohort of children exposed in 1986, however.

The role the accident plays in the epidemic of childhood thyroid cancers has also been debated, partly because this increase occurred earlier than expected (106) and partly because the carcinogenicity of iodine-131 has not been established in humans. Three principal points support the attribution of responsibility to Chernobyl's radioactive fallout. The first is, in fact, the distribution over time of the epidemic, the increased risk having been observed among children born before the catastrophe or exposed in utero and not in those born later. The relatively brief time lag between exposure and the increase in incidence is compatible with the available data (84). The second point is the geographic distribution, the highest incidence rates having been found in the zones most contaminated by iodine-131 (the region of Gomel in southern Belarus and parts of northern Ukraine) (97, 100),

while they have increased little or not at all in less contaminated zones (Vitebsk, Belarus, for example) (100). A geographic correlation study in the five most contaminated regions of the Ukraine shows a statistically significant association between the mean doses of iodine-131, estimated at the district level ("raion") on the basis of direct thyroid spectrometric measurements and the age-adjusted incidence of thyroid cancer between 1990 and 1994, for subjects aged between 0 and 18 years of age at the moment of the accident (103). Finally, a dose-response relation (individual thyroid dose) has been observed in a yet-unpublished study (cited by Beebe (114) and A. Bouville, US National Cancer Institute, personal communication, 1995) of Belarussian children aged less than 15 years in 1986 (119 cases and 238 controls).

The respective roles of radioactive agents (external gamma irradiation, internal irradiation by iodine-131 and short-lived iodine isotopes) have not been established, even if it seems probable that iodine-131, the principal component of the thyroid dose after Chernobyl, is important. The dose rate of the short-lived isotopes is high because of their short half-lives; their role was probably greatest in the zones contaminated immediately after the initial radioactivity release (113). In children born more than a few months after the accident, the number of cases drops steeply, suggesting that the causative agent did not persist at high levels in the environment. Williams et al. (102) consider that this fact points strongly to radioactive iodine as the major or even sole cause of this epidemic. Other risk factors may also be important. Iodine deficiency, endemic in the region (75), is believed to be a risk factor for thyroid cancer (113, 115), although mainly for follicular cancers (83). Experimental animal studies have shown that an iodine-deficient diet promotes cancer by its stimulation of thyroid-stimulating hormone secretion and the resulting cell proliferation (88). They have also demonstrated that combined exposure to iodine-131 or x-rays and a promoting agent shortens the latency period of this cancer (88).

Both the tumors and the Belarussian children afflicted by them appear to have different characteristics than those associated with spontaneous tumors (series observed in the United Kingdom); the former include a higher percentage of papillary tumors and, among them, more follicular-solid tumors. The children also have a higher proportion of invasive tumors, a younger mean age at diagnosis, and a lower female-male sex ratio (82, 99). The comparison of these series must nonetheless remain tentative, especially in view of the differences in selection and screening. On-going studies seek to confirm these data and are searching for possible markers indicating the origin of the post-

Chernobyl tumors.

Quantifying the excess risk associated with different modes of exposure, testing the effect of screening, and examining the role of other possible risk factors all require analytic epidemiologic studies (case-control and cohort). These are now underway, as is the reconstruction of individual thyroid doses. Nonetheless, obtaining precise estimates of individual thyroid doses will be difficult since satisfactory individual spectrometric measurements were not taken during the exposure period (79, 113).

Finally, in the likely hypothesis that this epidemic is radio-induced, we must expect its cumulative prevalence to increase over the next 50 years, like the epidemic already seen among the children treated by external radiotherapy for an enlarged thymus (116).

Leukemia. Because of the doses they received, the evacuated populations and liquidators are likely to be affected by an excess number of leukemia cases (117). Demonstrating this excess, on the other hand, is problematic; it might be difficult to attain sufficient statistical power. That is, even under the most pessimistic estimates of the dose-response relation (117) and dose estimates in the evacuees, we can expect to see approximately 10 additional cases per year for the period 1991–1996. This would represent a threefold increase over the "spontaneous" annual incidence in the region, which is roughly 5 per 100,000 per year (80). A thorough follow-up of these 115,000 people is required to observe these cases, but does not seem to have been arranged. Ivanov et al. (118) have examined the data from the Belarus Childhood Leukemia Register from 1982 through 1994 and observed no increase in the incidence of childhood leukemia cases after the accident, not even in the most contaminated zones, even though case registration probably improved from then on. In the most contaminated regions of the Ukraine and in the 12 regions of the three republics contiguous to Chernobyl, the incidence of leukemia among all age groups shows no significant increase from the trend observed before the accident (119, 120). These data come from an active search for cases, but its practical details are described very sketchily. Moreover, leukemias and lymphomas are combined in the trend analysis, even though no association has been established between lymphoma and ionizing radiation (8). Finally, the size of the populations living in the contaminated zones of the Ukraine is fairly low, making it difficult to demonstrate a weak effect. These descriptive studies are too briefly described and do not allow any definitive conclusion that there is no excess of leukemia.

The European Childhood Leukaemia-Lymphoma Incidence Study (ECLIS) examined data from 36 can-

cer registries in 23 European countries, subdivided into 35 regions by dose level. It collected 23,756 cases of childhood leukemia between 1980 and 1991, for 655 million person-years of observation, and concluded that the incidence after the catastrophe has not been influenced by exposure to fallout (121). Doses from natural irradiation vary in the regions of Europe, we should note (7), and the amplitude of that variation is close to that of the doses due to Chernobyl everywhere except in Belarus, where the doses were highest. Finding evidence of an effect from the Chernobyl accident in these regions was, thus, improbable. Two other studies of childhood leukemia, in Sweden (122) and Finland (123), also failed to show an association with fallout. The follow-up time has, of course, been short, but the result is consistent with the known effects of radiation (14).

Other cancers. Ionizing radiation exposure and the occurrence of cancers in other organs are known to be related. Nonetheless, the expected excess relative risks are markedly lower than for leukemia and thyroid cancer. The latency period is longer (10). Thus, demonstrating an excess risk is problematic. It is hardly surprising that studies conducted among the population of the most contaminated zones of the three republics have thus far yielded negative results (120).

Other cancers in Europe. Under the hypothesis that no threshold level of ionizing radiation is required, the doses received in Europe, outside the states of the former USSR, are or will be responsible for some cases of cancer, in particular, leukemia and thyroid cancer. It is theoretically possible to calculate the number by using estimates of the doses different European populations received. Nonetheless, the additional expected cases are very few and, thus, impossible to verify epidemiologically. One exception, however, is southern Bavaria (Germany) where the doses received may cause an estimated 15 percent excess number of childhood cancers (35), which is at the limit of sensitivity of epidemiologic methods. Elsewhere, calculation of the lifetime external dose depends on precise knowledge of local doses.

Cancer in the liquidators. Using data from the Registry of Russian Liquidators (annual medical examination), Ivanov et al. (124) observed a significant trend towards increased cancer incidence and mortality (all cancers together) according to external dose. The analysis concerned 1,026 cases of cancers in a cohort of 143,000 liquidators, 114,000 of whom had a documented dosimetry (number of person-years not specified). The authors calculated the relative risk using as the reference the group whose dose was between 0 and 50 mGy. A significantly higher relative risk was seen at exposure over 100 mGy, but the dose-effect relation

is both unclear and untested. The authors do not seem to have taken age into account in calculating the relative risk. These data must be interpreted cautiously, however, for the low level of confirmation of cancers in this registry has been pointed out (125). In Belarus, a similar register contains data for 45,000 liquidators (155 cancer cases for the period 1993–1994) (126). The standardized incidence ratios (SIR) were calculated using the population of Belarus as the reference. The incidence of bladder cancer increased significantly among men (SIR = 219, 95 percent CI 123–361) while that of thyroid cancer was significantly higher among women (SIR = 376, 95 percent CI 122–878). Male liquidators who had worked at least 1 month in the 30 km zone around Chernobyl have a risk of thyroid cancer significantly higher than that of the reference population (SIR = 625, 95 percent CI 129–1,826) as well as a greater risk of leukemia, the histologic types of which have not been specified (SIR = 342, 95 percent CI 126–746). These results, however, are based on a relatively small number of cases and on active follow-up of the liquidators, while cancer registration in the reference population is passive. The incidence of cancer in the reference population may be underestimated. In particular, more intensive screening may explain the reported excess of thyroid cancers and leukemia.

INDIRECT EFFECTS

The effects that we call “indirect” here are those that may be causally linked to the catastrophe without having a direct relation to the action of ionizing radiation.

Psychologic impact

It is now generally agreed that disasters have serious negative consequences to the mental health of affected populations. Their victims can suffer both short- and long-term psychologic consequences, but individual reactions to these events are extremely variable (11, 127). The consequences to psychologic health are one of the primary public health problems arising from the accident at Chernobyl (98).

The International Chernobyl Project study described above (3, 15) also examined this subject in 1990. A nonstandardized checklist (11) was used to ask about sleep problems, various subjective complaints, and alcohol consumption. The high-stress levels shown by residents of the contaminated and control zones did not differ particularly.

In 1993, Viinamäki et al. (128) conducted a cross-sectional study in the region of Bryansk (Russia); 325 subjects lived in a contaminated village (>1,300 kBq/

m²) and 278 lived in a control village (<37 Bq/m²). The survey evaluated the psychologic state of subjects older than 14 years with a version of the General Health Questionnaire. It allows the calculation of a score between 0 and 12 and covers anxiety, depression, self-esteem, and day-to-day difficulties. In both groups, the participation rate was approximately 70 percent. Some sociodemographic features differed between the two groups. They were not taken into account in the analysis. The results, adjusted for age, showed a significantly higher mean score among the exposed group. The analysis also showed that scores rose with age (for women only), with inadequate social support (exposed women and control men), and with money problems. The sampling method is summarily described, and the lack of control for some variables makes it difficult to generalize these results.

Havenaar et al. (129) studied a nonrandom sample of all segments of the population in a highly contaminated region (Gomel, Belarus) and in a socioeconomically comparable region that was much less touched (Tver, Russia). Each subject (1,617 in the first region, 1,427 in the second) completed a self-reported questionnaire (General Health Questionnaire). In both regions, approximately half the respondents report unsatisfactory health or psychologic well-being. The authors calculated odds ratios adjusted for age, sex, civil status, and education. The risk of psychologic distress was higher (OR = 2.0, 95 percent CI 1.8–2.4) in the contaminated zone, as was the use of medication (OR = 1.4, 95 percent CI 1.2–1.6). A high score on the General Health Questionnaire was predicted for mothers with children and evacuees, but not by the level of contamination of the residence area. In the next phase, a stratified sampling of each group (322 in the exposed group, 284 in the other) underwent a standardized physical and psychiatric examination (*Diagnostic and Statistical Manual of Mental Disorders: DSM III-R* criteria). The two groups did not differ significantly.

Results similar to those in the two preceding studies (increased risks for mothers of young children and those with low social support) were also observed after the accident at Three Mile Island (Pennsylvania, United States) among the local population, which had received very low exposure to ionizing radiation (130, 131).

A 1993 opinion poll surveyed a sample of 3,067 people selected by the quota method in Belarus, Russia, and the Ukraine. These subjects lived in different zones: contaminated, non-contaminated adjacent to contaminated, relocation, forbidden, and control. The degree of psychologic distress related to the accident, evaluated on a scale from one to five, was generally

high. People in the contaminated and resettled areas, as well as the 30 km zone, rated themselves more highly than respondents in the control and nonrestricted areas. The best predictor of personal distress due to the accident was fear of health effects to oneself and one's family. Between 25 and 50 percent of those questioned said they used sedatives; the highest percentage lived in the relocation zones (132).

Studies on this subject have also been performed among patients hospitalized for acute radiation sickness after the accident (133) and among liquidators (134). The articles provide few if any details about the selection conditions, the methods of data collection, and the diagnostic criteria. Furthermore, the nosography is different from that used in the West. It is therefore difficult to interpret these data.

Different analyses (132, 135) underline the multiplicity and interrelation of the stress factors: an initial public policy marked by secrecy and by authoritarian administration of protection measures; the absence of public confidence in the authorities, in medical professionals, and in the media; major political and economic transformations since 1989 in what was the USSR; the perception of risks linked to the accident; and a lack of confidence in the future.

Other problems

The 2,400 tons of lead poured on the melted core of the reactor were partly vaporized. According to Burkart (136), this caused a marked increase in levels of lead in the blood of children in the area, but this statement has not been documented. No increased levels of lead were detected in sampled populations (15). Another issue, apparently not studied at all, is the consequences of the restrictions on food products in the controlled regions (micronutrient deficiencies or subdeficiencies).

Voluntary abortions

Western Europe saw an increase in voluntary abortions. In Switzerland, in June 1986, there were 60 percent more voluntary abortions than expected, based on the trend between 1984 and 1988 (137), and similar reports came from northern Italy (138) and Greece (139). This undue choice of voluntary abortions may be considered a consequence of the stress to women who were pregnant at the moment of the catastrophe. It also reflects the inadequacy of the medical profession's knowledge of the risks linked to ionizing radiation. Irgens et al. (47) did not observe such an increase in six counties in Norway where the declaration of elective abortion is a legal obligation. On the other hand, Burkart (136) indicates, without mentioning the

source of the data, that Belarussian doctors were recommending abortions during 1987 and pointed out that this advice may have been justified to the extent that these doctors suspected, without being able to verify, that their patients had received high doses of radiation.

Fecundity

In the three contiguous republics, birth rates fell in the months following the accident nationally as well as in the contaminated zones (3). This observation is also true for numerous regions of the former Soviet Union (45). The number of pregnancies also decreased in Sweden (44), Norway (47), and Italy (138) in the early years after the accident. The demonstration of a causal link with the accident is problematic.

CONCLUSION

The increase in thyroid cancer in children and adolescents of the three contiguous republics of Belarus, the Ukraine, and Russia is well-documented and the causal relation with the accident is now undisputed. Uncertainty remains about the relative contributions of various radioactive agents and other risk factors and about the future extent of the epidemic, depending on age group at exposure. Research needs to concentrate on screening cases, so that early treatment can be provided, and on investigating the dose-response relation in this particular epidemiologic situation.

The risk of leukemia is expected to increase moderately among those who were relatively highly exposed (i.e., liquidators) or in the more radiosensitive groups (such as children). Both descriptive and analytic studies should be carried out. Despite the unlikelihood of a detectable increase of other cancer types, careful monitoring is needed among all population groups for verification purposes and because of the great public concern.

As expected from previous scientific knowledge, no excess in congenital malformations has been shown; nonetheless available data should be validated.

The existence of a post-accident psychologic impact is reasonably certain, although its nature, extent, and specific risk factors remain to be determined.

Different articles have reported increases in various physical disorders. These claims originate from ecologic studies, so that no causal link can be established with the accident. These claims often appear in non-scientific reports and their basis in fact cannot be ascertained (no specification of diagnostic and selection criteria, poor or no characterization of control groups, no consideration of confounding factors such as age and sex, superficial analyses, and paucity of

preaccident reference data). Many reports appear to concern artificial increases corresponding to a better screening. In addition, some of these pathologies have not been previously related to ionizing radiation (changes in female reproductive functions and neonatal health, vegetative dystonia, endocrine and respiratory effects), or only at doses much higher than those resulting from the accident (immunologic, cardiovascular, neurologic, and digestive effects, lens changes). Lastly, some likely effects of social changes (e.g., nutritional) in the three republics have not been examined or documented. Epidemiologic studies are needed on all these topics and should start with accurate descriptions.

Many epidemiologic studies have begun or are being planned in the three countries of the former USSR most touched by the accident. These studies are intended to answer, insofar as possible, the questions posed above about thyroid cancer, and to verify whether any other chronic disorders can be discerned. They involve many international partners and are being conducted among the general population as well as among the liquidators (140).

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