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Teratogen Update: Radiation and Chernobyl

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ABSTRACT The 1986 nuclear reactor accident at Chernobyl caused nonuniform radiocontamination of air and land, primarily within regions of the former Soviet Union and Western Europe. Major exposure groups included the reactor workers, villagers evacuated from within 30 km of the accident, the "liquidators" who decontaminated the evacuation zone afterward, those in radiocontaminated villages not evacuated, and "others" not in the latter categories. The possibility of being exposed to radiation caused considerable anxiety, especially among pregnant women. Were teratogenic levels of radiation ($\geq$0.1 Gy) exposure attained? To date there is no consistent proof that this level of radiation exposure was received. Nevertheless, thousands of induced abortions were performed. Radioiodine (I-131) caused thyroid cancer in young children in portions of Belarus, the Ukraine, and Russia. It is not known but very possible that I-131 fetal thyroid exposure contributed to this observation. The relationship between mental retardation and radiation exposure has not been confirmed. Leukemia and other cancers, while predicted for the liquidators (mainly males), has not been found in the other exposure groups at this time. Investigations of aborted fetuses and newborns in Belarus showed an increase in the frequency of both congenital and fetal abnormalities in high and low Cs-137 contaminated regions. This study is unreliable due to detection and selection biases. Accident and environmental factors unrelated to radiation doses may have contributed to these observations. Occasional positive teratogenic studies in less contaminated regions of Western Europe are suspect because of the low radiation doses received. There is no substantive proof regarding radiation-induced teratogenic effects from the Chernobyl accident. *Teratology 60:100–106, 1999.* © 1999 Wiley-Liss, Inc.

The worst accident in the history of nuclear power occurred at 1:23 AM on Saturday, April 26, 1986. At this time two explosions destroyed the core and portions of the nuclear reactor building of Unit 4 RBMK at Chernobyl, in the north-central Ukraine (IAEA, '96). This accident subjected the nuclear reactor fuel to very high temperatures (2,000°C), resulting in the release of volatile radionuclides and finely dispersed radiocontaminated material. The resulting plume took several paths over time, resulting in a nonuniform deposition of radioactive material in air and on land.

The fire was extinguished and the releases stopped 10 days after the accident. The quantity of radioactivity released over this time period approximated 1.2E+19 Bq, with 1.5E+18Bq and ~0.09E+18Bq, comprising I-131 (T $1/2_p$ = 8.08 d) and Cs-137 (T $1/2_p$ = 30 y), respectively (Borzilov and Klepikova, '93; IAEA, '96). The radioactive plume exposed unsuspecting individuals to radiation, including pregnant women whose embryos/fetuses were exposed to a proven teratogen.

This report examines and comments on data regarding embryo/fetal radiation exposure associated with the Chernobyl accident.

KNOWN FETAL EFFECTS OF RADIATION

As with other teratogenic agents, the risk associated with irradiating the fetus is a function of both the total dose and postconceptional time. These effects are summarized in Table 1 for a 1-Gy acute dose in rodents and correlated according to human gestational age (Brent, '80). The types of effects following whole-body irradiation are listed in Table 2 (ICRP, '93; Atake and Schull, '93). As stated, the threshold acute dose for malformation of fetal organs is approximately 0.1 Gy, with frank congenital malformations occurring at 0.2 Gy (Jensh and Brent, '87); the risk for severe mental retardation is approximately 30 IQ units per Gy and is not always related to small head size; the risk of fatal cancer is approximately 6% per Gy fetal irradiation (Doll and Wakeford, '97).

The internalization of I-131 for the first 8 weeks of conception and Cs-137 in the entire pregnancy would represent a risk to the fetus only if the whole-body threshold dose of $\geq$0.1 Gy were reached. The mother would have to ingest 1.39 GBq (early) to 0.37 GBq (late) of I-131 to produce a 0.1-Gy fetal dose (Russell et al., '97). The primary concern for I-131, however, would be the fetal thyroid radiation dose after week 8, with secondary concern for the whole body. With Cs-137, a muscle seeker, the required radioactivity would be 8 kBq (early) to 12 kBq (late) (Caywood et al., '97). With I-131, irradiation of the fetal thyroid gland after weeks 8–12 would create an added risk (Fisher, '75). Mental retardation secondary to fetal hypothyroidism has been

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TABLE 1. Risk associated with irradiation during fetal development (Brent, '80)*

	Preimplantation	Organogenesis	Early fetal	Midfetal	Late fetal
Postconception time (weeks)	1	2–7	8–15	16–25	>25
Effects					
Lethality	+++	+	+	−	−
Gross malformations	−	+++	+	+	−
Growth retardation	−	+++	++	+	+
Mental retardation	−	−	+++	+	−
Sterility	−	+	++	+	+
Cataracts	−	+	+	+	+
Other neuropathology	−	+++	+	+	+
Malignant disease	−	+	+	+	+

*1 Gy acute dose in rodents, correlated according to human gestational age. −, no observed effect; +, demonstrated; ++, readily apparent effect; +++, occurs in high incidence.

TABLE 2. Types of radiation effects following irradiation in utero (ICRP, '93; UNSCEAR, '93; Atake and Schull, '92; Jensh and Brent, '87; Doll and Wakeford, '97)

Time after conception	Effect	Normal incidence in liveborn
First 3 weeks	No deterministic or stochastic effects in liveborn child	
Weeks 3–8	Potential for malformation of organs*	0.06 (1 in 17)
Weeks 8–25	Potential for severe mental retardation**	5.0E − 03 (1 in 200)
Week 4 throughout pregnancy	Cancer in childhood or in adult life***	1.0E − 03 (1 in 1000)

*Malformation of organs appears to be a deterministic effect, with a conservative threshold dose in man, estimated from animal experiments, to be about 0.1 Gy, with frank congenital malformations at 0.2 Gy.
**The risk for severe mental retardation is associated with an observed shift in intelligence quotient (IQ). The shift is estimated as 30 IQ units per 1 Gy in the brain during weeks 8–15 after conception, with lesser IQ shifts during weeks 16–25. At absorbed doses in the brain on the order of 0.1 Gy, no effect would be detectable in the general distribution of IQ in an irradiated group. At somewhat larger absorbed doses, however, the effect might be sufficient to show an increase in the number of children classified as severely retarded. Radiation small-head size has not been demonstrated to be a threshold and, when induced prior to 8 weeks, was not related to intellectual and behavioral impairment.
***The risk of fatal cancers expressed in childhood or in adult life for individuals irradiated in utero may be similar to the risk to individuals irradiated in the first decade of life. For whole-body irradiation of infants and children, the cancer risk is approximately 6% per Gy. The baseline whole population cancer mortality is 1 in 6.7–1 in 4, the difference being a function of country.

reported in children born to mothers who received 0.37 MBq or more of I-131 NaI (Staffer and Hamburger, '76). The maximum fetal thyroid dose occurs at month 6 and approximates 3,108–4,440 cGy/37 MBq of the mother's intake (Stabin et al., '91). Adding to the internal exposure would be that received externally from ambient radiation levels. However, these levels would be attenuated by the surrounding mother's tissue, thus reducing the fetal dose (Ragozzino et al., '86; Wagner et al., '97). The latter, reported to approximate 6 cm from the anterior skin surface, would absorb completely the beta radiation and ~40–50% of I-131 and Cs-137 photons (Johns and Cunningham, '69).

The fetal risks mentioned above are from acute radiation doses, while those received from the Chernobyl accident have been protracted. The latter mode of exposure is believed to incur a smaller risk than the former for a given radiation dose (BEIR, '90). This is especially relevant during the various stages of fetal development.

EARLY INTERVENTION, FALLOUT PATTERNS, AND RADIATION EXPOSURES

Early intervention

Early human intervention concentrated on fighting the fire within the reactor building. The death toll within 3 months of the accident was 31 of the 200 individuals (the majority were male) who suffered acute whole-body external radiation effects from 100–1,500 cGy as members of the reactor operating staff and fire-fighting crew (Mettler et al., '96). Based on numerous tests of air, water, and soil, a 30-km zone was established from which 116,000 individuals were evacuated 1–11 days after the accident (UNSCEAR, '88). Their average protracted external and inhalation radiation dose was estimated to range between 0.01–38.3 cGy (Likhtarev et al., ’94).

Fallout patterns

The release of radioactive material beyond the 30-km zone was determined primarily by wind direction and rainfall. The latter enhanced the ground deposition of radioactive material. This resulted in nonuniform ground deposits throughout Eastern and Western Europe. The ground deposition of radionuclides was expressed as activity/area with units of MBq/m^2. Initially, areas of Belarus, the Ukraine, and Russia showed I-131 levels of 0.2–40 MBq/m^2 (Balter, ’96). Later, Cs-137 levels up to 1.5^+ MBq/m^2 dominated the landscape in these countries (Ivanov et al., ’96). As of 1996, no measurable I-131 remained, and about 85% of the Cs-137 was still present (Dreicer and Alexakhin, ’96). The highly contaminated area encompassed approximately 20% of Belarus, 8% of the Ukraine, and 0.5–1% of Russia, an area about the size of Kentucky (IAEA, ’96). To put the “activity/area” unit in proper perspective, consider the following example regarding naturally occurring radioactive material. Uranium-238 (T $1/2_p$ = 4.5E+9y) in igneous rock represents a ground concentration of 0.81 MBq/m^2 (Shapiro, ’90). This radionuclide plus its decay products represent an external annual dose equivalent of 0.24 mGy/year at 1 meter above the ground (Shapiro, ’90). The annual cumulative dose equivalent at 1 meter from ground contamination (1 cm depth) of Cs-137 at 1.5 MBq/m^2 and I-131 at 40 MBq/m^2 would approximate 5 mSv and 8 mSv, respectively (Golikov and Balonov, ’93). Residual radioactive material in the global environment as of 1996 consisted primarily of Cs-137 (6.8E+16Bq)(Dreicer and Alexakhin, ’96).

The liquidators

Besides the on-site respondents, 600,000–1 million persons, mostly adult males, participated as liquidators within the 30-km evacuation zone. Greater than 85% of this group received an external radiation dose over 2 months of 0.1 Sv, with 10% receiving 0.25 Sv and the remaining individuals up to 0.50 Sv (IAEA, ’96). This group has been difficult to follow after completing their liquidation tasks. However, it is improbable that pregnant individuals took part in this highly risky cleanup.

Controls/exposure in the three republics

The 270,000 inhabitants of areas within Belarus, the Ukraine, and Russia where ground contamination was at least 0.6 MBq/m^2 of Cs-137 were subjected to strict radiation safety controls, while those in less contaminated areas of 0.04–0.6 MBq/m^2 experienced more relaxed restrictions in this regard (IAEA, ’96). The controls included shelter, evacuation, and control of food and water consumption, as well as the issuance of KI, when appropriate (Bolanov, ’93; Mettler et al., ’96; Kondrusev, ’89; Jaworowski, ’86). While maternal exposure to pharmacologic quantities of iodides may harm the fetal thyroid (Mandel et al., ’94), it will also protect the fetal thyroid against radioiodine (Noteboom et al., ’97). Transfer factors from fallout to the thyroid would also be important (Beno et al., ’92). The estimated effective radiation doses, which will be received over 70 years for those in the contaminated areas, will range up to those received from natural environmental radiation for this time period (IAEA, ’96).

The remaining combined population (~280 million) in the three republics, where Cs-137 contamination levels were less than 0.04 MBq/m^2, received approximately 0.26 mSv during the first year (IAEA, ’96). The effective dose equivalent from external gamma radiation was estimated for various villages in the Bryansk region of Russia from 1986–1991 (Golikov and Balonov, ’93). For one town with a terrestrial Cs-137 contamination level of 0.73 MBq/m^2 in 1986, the cumulative radiation dose was determined to be 0.96 and 1.84 mSv for individuals living in large buildings and wooden houses, respectively. This amount of radiation dose is less than the worldwide average natural background radiation of 2.4 mSv (UNSCEAR, ’93). In a 1986 study, the average monthly effective dose to inhabitants of a Russian settlement with a Cs-137 contamination level of 1.56 MBq/m^2 was 0.86 mSv/month, which approximates the ambient natural background of 0.744 mGy/month (Erkin and Lebedev, ’93; Golikov and Balonov, ’93). This exposure level resembles the 0.50 mSv/month allowed for a radiation worker’s developing fetus (NRC, ’91). The latter two examples serve to illustrate that the ambient radiation exposure for a majority of contaminated villages away from the exclusion zone represented little risk to the developing fetus. The radiation exposure would also be a function of working and living conditions. The exposure would be less for those working indoors and living in brick houses and greater for those working outdoors and living in wooden houses (Erkin and Lebedev, ’93).

While living within a radiocontaminated environment increases the risk for carcinogenic effects, an increase for deterministic effects can only occur if the threshold dose for the effect is surpassed (Table 1). The Cs-137 body burden was measured for 1,228 men, women, and children who had emigrated from the Ukraine, Belarus, and Russia to Israel (Quastel et al., ’97). These authors reported a maximum back calculation of 6 Bq/kg (0.75 kBq) Cs-137. Women and children had considerably lower Cs-137 body burdens because of lower muscle mass and faster excretion than adult males. All Cs-137 body burdens were too low for any concern regarding the health of the emigrés (Quastel et al., ’95).

Western Europe

Lesser quantities of radioactive material deposited in regions distant from the reactor site and remnants of the plume were measurable over the entire northern hemisphere. Material released into the atmosphere dispersed according to the prevailing winds, and a portion was accumulated on the ground via wet and/or dry deposition. While many radionuclides were released, I-131 (T $1/2_p = 8.08$ d) and Cs-137 (T $1/2_p = 30$ y) dominated. The contamination levels in Western Europe ranged from 0.001–0.04 MBq/m^2, with a reported 50-year cumulative effective dose of 0.03–2 mSv (UNSCEAR, '88). Thyroid bioassays of European travelers returning to the United States shortly after the accident exhibited miniscule I-131 uptakes (Castronovo, '86). Two pregnant travelers in this group, who hiked in the rain in Bavaria and north/south Germany, had thyroid uptakes of 111–148 Bq of I-131 (Castronovo, '87). Thus, it became apparent that individuals who visited several European countries were slightly contaminated with radioactivity by the accident. The Chernobyl-related radiation doses to populations in countries within the northern hemisphere during the first year averaged just 0.80 mSv (IAEA, '96). Nevertheless, widespread fears regarding fetal effects prompted many countries beyond the exclusion zone to investigate this topic. A cluster of 12 cases of trisomy 21 occurred in West Berlin 9 months after the accident, when 2–3 cases were expected (Sperling et al., '91, '94). The authors reported a "several-fold increase" above the natural radiation dose during the 9-day exposure period (Sperling et al., '94). These data differ from other negative reports where radiation exposures were much higher (Little, '93; Williams, '94). A summary of these reports is given in Table 3.

A significant increase in perinatal mortality in 1987 was reported in Germany after background equivalent exposures (Korblein and Kuchenhoff, '97). A response to this report held any such excess to be due to factors other than radiation (Rossi, '97). Similarly, it is difficult to accept in utero radiation from the Chernobyl accident as the causative agent for reported increase in leukemia in Greek and German children because more severely affected Belarus did not exhibit a similar trend (Ivanov et al., '96). Estimates of the maximum adult effective dose in Western Europe during the first year after the accident were reported to be 1.7 mSv (DeWals and Dolk, '90). At these low doses, teratogenic effects have never been observed and are thus highly unlikely.

PREGNANCY TERMINATIONS

A well-documented health consequence of the Chernobyl accident was the dramatic increase in pregnancy terminations both near and far from the accident site. There was widespread concern following reports of environmental and food contamination. The resulting anxiety regarding possible fetal radiation effects was amplified by lack of information and official guidance, and a persistent "nuclear phobia." This led to an increase in abortions, delays in planned conception, and a greater demand for prenatal screening (DeWals and Dolk, '90; Rojas-Burk, '92). During most of May 1986, there was panic among expectant mothers who thought they had a high risk of giving birth to an abnormal child. Countries outside the exclusion zone reporting a reduction of births included Italy (Spinelli and Osborn, '91), Denmark (Knudsen, '91), Norway (Irgens et al., '91), Hungary (Czeizel, '91), and Greece (Trichopoulos et al., '87).

Fetal studies in Belarus and the Ukraine

A descriptive analysis of birth defects and malformations was performed in Belarus to assess whether such rates correlated with areas having different levels of Cs-137 contamination. A stereomicroscopic examination of ~21,000 5–12-week-old legal abortions from 1980–1991 showed all types of congenital malformations for zones containing at least 0.6 MBq/m^2 Cs-137 when compared with controls from Minsk from 1980–1991 (Lazjuk et al., '93, '94, '97). In these latter studies, however, no conclusions could be reached regarding radiation-induced teratogenesis because the blinding of the pathologists to zone and time period was not stated and the time periods were not matched, suggesting a possible selection bias. The prevalence of all types of congenital malformations among live births from 1979–1991 increased for both contaminated and control zones, also suggesting a selection bias. In addition, it has not been possible to correlate individual radiation doses with the incidence of congenital malformations because not one pregnant woman received more than 0.1 Gy threshold dose during the entire pregnancy (Lazjuk et al., '93). Down syndrome was not increased in frequency. The observed congenital malformations, if real, could have been caused by nonradiation factors, e.g., defective nourishment, chemical contamination, and psychological stress (Lazjuk et al., '93). Of the evacuees from the Ukraine, 100 children were born at 6 months with no reported birth defects (Mould, '88). A retrospective analysis of the birth archives of Kiev's two largest obstetric hospitals between 1969–1990 showed no pronounced changes for spontaneous miscarriages, congenital anomalies, and perinatal mortality (Buzhievskaya et al., '95). The Kiev Institute reported a nonteratogenic maximum of 11.1 kBq of Cs-137 internalized by pregnant women 1–3 months after the accident (Mould, '88). A brain damage-in utero study involving ~4,500 children born within 1 year of the accident or to mothers evacuated from the 30-km zone showed no correlation between mental retardation and radiation exposure (Kreisel, '95). Radiation exposures did not approach those necessary for mental retardation as reported previously for atom bomb survivors (Otake and Schull, '84). Other cancers and leukemia, to date, have not been at statistically greater than normal levels (Prisyazhniuk et al., '95; Ivanov et al., '96; Parkin et al., '96).

CONCLUSIONS

The scientific information available now shows no evidence that the radiation exposures of pregnant women from Chernobyl produced any harmful effects. Perceptual competition has come from the lay press,

TABLE 3. Several examples of embryo/fetal studies throughout Europe and Asia Minor

Country	Comment
Austria	No significant changes in the incident of birth defects, abortion rate, or counseling rate at pregnancy termination clinics were observed (Haeusler et al., ’92).
EUROCAT	The teratological impact potential of radiocontamination from the Chernobyl accident was evaluated in relation to central nervous system and eye defects in 18 regional registries in nine countries of Western Europe. Observed frequencies of the six classes of anomaly in the exposed cohorts were compared with expected frequencies for 1980–1985. The only significant increase was neural tube defects in Odense, Denmark (0.9 expected/4 observed). The results did not show a general increase in the frequency of malformations (EUROCAT Working Group, ’88).
Finland	The amount of radioactive fallout that Finnish people were exposed to after the accident at Chernobyl was not high enough to cause fetal damage in children born at term. The higher incidence of premature births among malformed children in the most heavily contaminated areas, however, remains unexplained (Harjulento et al., ’89).
Germany	An increase in the rate of trisomy 21 was observed (2–3 E/12O) in Berlin (West) exactly 9 months following the Chernobyl accident (Sperling et al., ’91, ’94). For the latter cluster, fallout was present during the time of affected meiosis, whereas another cluster in Nuremburg preceded the radioactivity by 1 month (Burkart and Schoetz, ’97). These data differ from negative reports frim higher exposure (Little, ’93; Williams, ’94). No evidence that Chernobyl caused an increase in congenital malformations was reported from Bavaria (Irl et al., ’95).
Greece	All childhood leukemia cases diagnosed throughout Greece since January 1, 1980 have been recorded. Infants exposed in utero to radiation from the Chernobyl accident had 2.6 times the incidence of leukemia compared to unexposed children (Petridou et al., ’96).
Hungary	The frequency of different types of isolated and multiple malformations did not change (DeWals and Dolk, ’90).
Norway	Prospectively collected data on all newborns who were conceived in the period May 1983–April 1989 were used to assess possible dose response relations. A positive association was observed between total radiation dose and hydrocephaly, while a negative association was observed with Down syndrome. Potential sources of bias are discussed (Terji Lie et al., ’92).
Scotland	A study of Down syndrome for 1978–1989 in Lothian revealed a significantly higher-than-expected incidence of cases in 1987. Given the reported levels of radioactive fallout resulting from the Chernobyl accident, there is no plausible explanation to link the two events (Ramsay et al., ’91).
Sweden	No major effects on pregnancy outcome were seen, but the indicated increase in Down syndrome and childhood leukemia, if not random, could be the result of radioactive exposure (Ericson and Kallen, ’94). No increase was seen in the occurrence of malformations among infants born after the accident (DeWals and Dolk, ’90).
Turkey	Neural tube defects apparently increased in some regions (Mocan et al., ’92). First-year average dose was 0.19 mSv, compared to the natural annual dose of 2 mSv (UNSCEAR, ’88).
Ukraine (Kiev)	This investigation determined the frequency of adverse pregnancy outcomes in Kiev during the period surrounding the Chernobyl accident. Spontaneous miscarriages, congenital anomalies, and perinatal mortality varied during 1969–1990 without any pronounced changes in direction. The average dose equivalent for Kiev inhabitants was 8.05 mSv (Buzhievskaya et al., ’95). In the contaminated region of Zhytomyr an increased incidence of pathologic deliveries, anemia, toxemia, and hemorrhages was reported (Ponomarenko et al., ’91).

with newspaper reporters playing up anecdotal stories of children with birth defects and leukemia (Kotz, ’95). In addition, the population of the former Soviet Union was subject to haphazard radiation and chemical disposal techniques which gave little thought to health of the people or the land (Burkart, ’96). Taking such vast environmental contamination into account when attempting to ferret out possible Chernobyl-related radiation effects is indeed a challenge (Serykh, ’96; Zaykovskaya, ’96; Balter, ’95; Edwards, ’94). The former Soviet Union will undoubtedly become a source for documenting radiation effects, provided the necessary studies are properly implemented (Davis, ’99). Nevertheless, no excesses in teratogenesis have been attributed to the Chernobyl accident, which agrees with what has been stated previously (Little, ’93; Bard et al., ’97).

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