

Juvenile Hypothyroidism among Two Populations Exposed to Radioiodine

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We found an epidemic of juvenile hypothyroidism among a population of self-defined "downwinders" living near the Hanford nuclear facility located in southeast Washington State. The episode followed massive releases of ¹³¹I. Self-reported data on 60 cases of juvenile hypothyroidism (<20 years of age) among a group of 801 Hanford downwinders are presented, as well as data concerning the thyroid status of approximately 160,000 children exposed to radioiodine before 10 years of age as a result of the 26 April 1986 Chernobyl explosion in the former Soviet Union. These children were residents of five regions near Chernobyl. They were examined by standardized screening protocols over a period of 5 years from 1991 to 1996. They are a well-defined group of 10 samples. Fifty-six cases of hypothyroidism were found among boys and 92 among girls. Body burdens of ¹³⁷Cs have been correlated with hypothyroidism prevalence rates. On the other hand, the group of juvenile (<20 years of age) Hanford downwinders is not a representative sample. Most of the 77 cases of juvenile hypothyroidism in the Hanford group were diagnosed from 1945 to 1970. However, the ratio of reported cases to the county population under 20 years of age is roughly correlated with officially estimated mean levels of cumulative thyroid ¹³¹I uptake in these counties, providing evidence that juvenile hypothyroidism was associated with radioiodine exposures. Because even subtle hypothyroidism may be of clinical significance in childhood and can be treated, it may be useful to screen for the condition in populations exposed to radioiodine fallout. Although radiation exposure is associated with hypothyroidism, its excess among fallout-exposed children has not been previously quantified. *Key words:* Chernobyl, downwinders, exposed children, ¹³¹I contamination, ¹³¹I/¹³⁷Cs body burden, Hanford, hypothyroidism, radiation, radioactive fallout, TSH, thyroid, thyroid-stimulating hormone. *Environ Health Perspect* 107:303–308 (1999). [Online 15 March 1999] <http://ehpnet1.niehs.nih.gov/docs/1999/107p303-308goldsmith/abstract.html>

Hypothyroidism is a potential environmental hazard associated with ingestion, physiological uptake, and concentration of radioiodine by the thyroid. Congenital hypothyroidism is well known. Acquired hypothyroidism in childhood (<20 years of age) is uncommon, though dependent on natural environmental iodine levels. Its onset is insidious and the importance of prompt recognition of the condition is related to its association with impairment of physical and mental development, as documented by the initial findings in an exposed Marshall Island population (1). Because hypothyroidism can easily and successfully be treated, its detection is clinically important. Therapeutic high-dose radiation exposure to the head and neck is a known risk factor and the association of delayed hypothyroidism following treatment of hyperthyroidism with ¹³¹I has long been recognized (2).

We present data about hypothyroidism in children exposed to fallout from Chernobyl in the former Soviet Union, as well as data about hypothyroidism in juveniles exposed to radioactive emissions from the Hanford, Washington, plutonium manufacturing plant.

Materials and Methods

Hanford area. The Hanford nuclear site in eastern Washington State was established in 1943 as part of the Manhattan Project. It produced ²³⁹Pu for use in nuclear bombs. The original reactors became operational in 1944. In 1986 it was officially revealed that there had been releases of large quantities of gaseous and particulate radionuclides, especially between 1944 and 1952, of which ¹³¹I (half-life 8 days) was a major component. Shorter- and longer-lived isotopes of radioiodine such as ¹³²I (2.3 hr), ¹³³I (21 hr), ¹³⁵I (0.28 days), and ¹²⁹I (17 million years) were also released.

Although there is considerable uncertainty about the amount of radioactivity released, an estimate of 550,000 Ci in 1945 and 166,000 Ci of ¹³¹I during 1946 through 1952 has been reported (3). The Hanford Environmental Dose Reconstruction (HEDR) project found strong evidence that thyroid glands of large numbers of individuals, particularly children, were likely to have been exposed to doses in the range of several hundred rad depending on where they lived and what they ate and drank (3).

Many residents of the counties potential-ly affected (mainly in eastern Washington,

northeastern Oregon, and Idaho—west of the Rocky Mountains) (Fig. 1), who call themselves "Hanford downwinders." These citizens reported a lack of interest in their chronic and serious health complaints and denial of possible associations with radioactive fallout by both their physicians and federal and state public health agencies. The Hanford downwinders also experienced rejection of possible accountability by appropriate state or federal public health agencies.

A group of downwinders sought and obtained support from volunteer scientists and physicians of the Oregon Chapter of Physicians for Social Responsibility. They, together with local downwinders and environmental activists, undertook this survey of serious health problems. These downwinders and volunteers joined to form the Northwest Radiation Health Alliance, which developed a questionnaire covering personal information, information related to likely exposure, and a wide spectrum of health problems. Between 1,500 and 2,000 questionnaires were distributed through an informal network of concerned downwinders (who did not keep records of exact numbers), followed by a return of 801 usable reports. The diagnosis of hypothyroidism (including year of diagnosis) was assigned to all persons who responded that their physicians had diagnosed them as having hypothyroidism and who had been taking thyroid supplements. A follow-up random sampling of informants by telephone established that most of the diagnoses had been based on blood tests and a few had been based on breathing tests for basal metabolic rate. Postthyroidectomy

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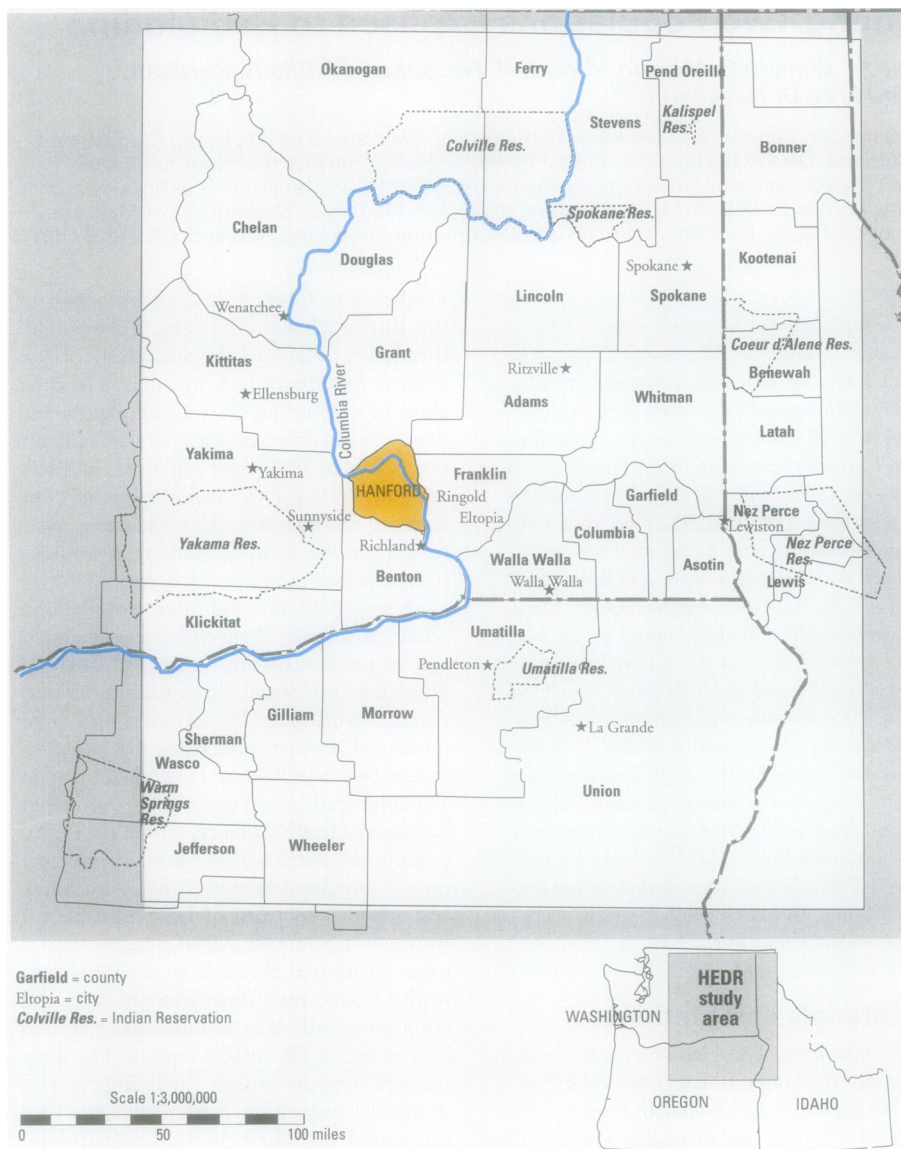


Figure 1. Counties around the Hanford, Washington, plutonium manufacturing plant included in the Hanford Environmental Dose Reconstruction Project (3).

hypothyroid cases taking thyroid were excluded from our counts.

Chernobyl area. Massive emissions of radioiodine (including ^{129}I , ^{131}I , ^{132}I , ^{133}I , and ^{135}I , with half lives of 1.72×10^7 years, 8.0 days, 0.096 days, 0.875 days, and 28 days, respectively) occurred on 26 April 1986, as a result of the explosion of one of the Chernobyl reactors. Emissions of many other isotopes, such as ^{137}Cs , also occurred, but because of the short half-lives of all but one of the radioiodines, it is difficult to estimate the distribution of thyroid doses several years later. Conversely, ^{137}Cs has a 30.2-year half-life and shows gradients both for ground-level contamination and for estimated body burdens for individuals and might, thus, serve as proxy for early radioiodine uptake. With support from the

Nippon Foundation (Tokyo) through the Sasakawa Memorial Foundation (Tokyo), five regional screening centers were established in regions adjacent to the Chernobyl plant, and each was provided with the same equipment, protocol, and staff training for a screening study of children who were up to 9 years of age at the time of the disaster. Thyroid volume was determined by ultrasonography and provided the basis for statistical evaluation of goiter. Goiter prevalence varied from 18% in the Gomel region to 54% in the Kiev region. Whole body ^{137}Cs burden was determined and served as an exposure index, although it was recognized that radiocesium, which follows a different precipitation pattern, was a poor index of exposure to gaseous radioiodine. The ratio of $^{131}\text{I}/^{137}\text{Cs}$ varies nonlinearly

with ^{137}Cs concentrations. The ratio also varies significantly between geographic regions (4). In addition, migration of the population could have distorted the possible association of radiocesium with hypothyroidism.

The plans for the Chernobyl-area study were initiated in 1990 by the Nippon Foundation at the request of the administration of the USSR. The Japanese planning committee developed a protocol for the study and selected the equipment for use in screening. The screening equipment was installed in 1991. The Chernobyl Sasakawa Health and Medical Cooperation Project was completed and a final conference was held 14–15 October 1996 in Kiev, Ukraine. The presentations and data produced were published (5). The data include the following: 1) the number of children studied, by sex and age at the time of the explosion; 2) the year of examination, 3) the place of residence, and usually the district of residence (at the time of the explosion), 4) the results of thyroid examinations by ultrasound and by thyroid function tests, 5) the hematological indices, 6) the results of ^{137}Cs body burden estimations, and 7) the year of examination. The study used both standardized equipment and protocols, thus assuring uniformity in the data and a high level of quality. Hypothyroidism was defined as free thyroxine (T_4) <10 pmol/l and thyroid-stimulating hormone (TSH) >2.9 $\mu\text{IU}/\text{ml}$ as tested by an Amerlite hormone analyzer (Amersham, Tokyo) using an immunometric technique based on enhanced luminescence. We included in our review only those communities with two or more cases of hypothyroidism of either sex.

Table 1 shows the number of individuals who were tested for TSH and T_4 according to sex, age, and residence at the time of the Chernobyl accident.

Results

We present ratios of reported hypothyroid cases per number of respondents alive during 5-year periods, normalized per year and per 100,000 (Table 2, Fig. 2) for Hanford downwinders, whereas rates per 10,000 children at risk are given for the Chernobyl population.

Hanford downwinders. Table 2 shows the number of reported juvenile hypothyroid cases and all juvenile respondents alive, in 5-year time periods during which the condition was diagnosed, as well as ratios per 100,000 per year in our group. For comparison the same information is provided for adults in our study group. Of the 60 cases of juvenile hypothyroidism in our group, 54 were females and 6 males. Figure 2 presents the ratios from Table 2.

The onset of hypothyroidism was strongly associated with the years of reported maximum radioiodine releases, 1944–1949; onset reached a maximum approximately 15 years later in juveniles, then dropped off. The ratios for juveniles after 1960 become rapidly insignificant, perhaps due to the decline in the number of juvenile respondents in our group (Table 2). Most of the juvenile hypothyroid cases were exposed as children <10 years of age. The ratios for adult hypothyroidism appeared to rise more rapidly (Fig. 2), reaching a maximum only 5 years after the heaviest radioiodine releases, and they remained high until the end of our survey in 1997, as compared to pre-1944 values. A separate report about adult hypothyroidism in this group is in preparation.

Table 3 shows the distribution of cases of juvenile hypothyroidism by county (those included in the HEDR study) (3), the population <20 years of age, and the ratio per 100,000 population <20 years of age for the 1950 census (6). These ratios by county are shown in Figure 3 against the background of isopleths of estimated cumulative ¹³¹I thyroid dose (in rad) to a child from exposure to all pathways for the years 1944 through 1951 (assuming milk came from cows on fresh pastures) (3). Keeping in mind that much of the county data are based on small numbers of cases (Table 3), and the large uncertainties in the estimated HEDR doses, there is reasonable concordance between estimated thyroid doses and the case rates.

The downwinders' questionnaire included a question for parents as to whether their child (or children) had reported learning disabilities. Of 136 traceable children without hypothyroidism, 37 had learning disabilities. Of 10 traceable children with hypothyroidism, 4 children had learning disabilities, in contrast to the 2.7 expected.

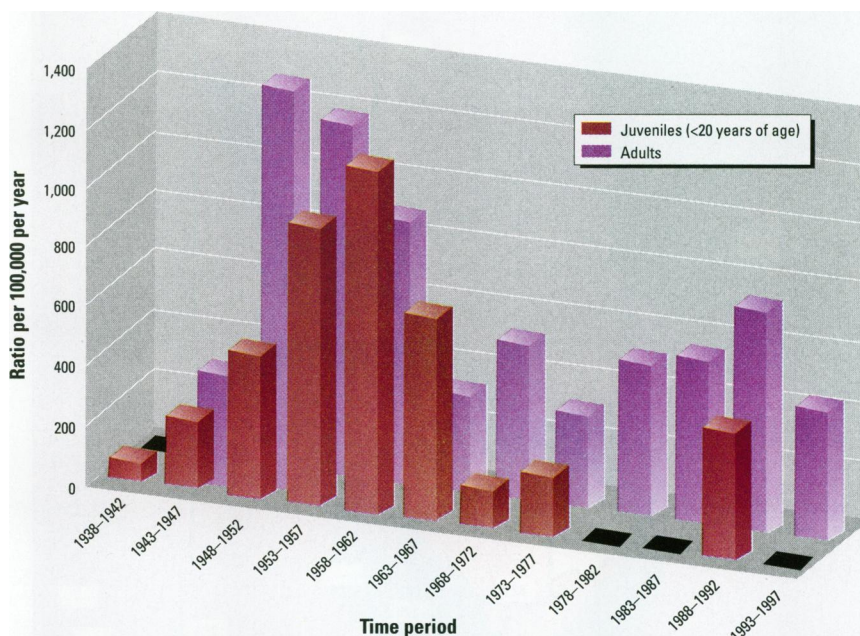


Figure 2. Self-reported hypothyroidism in a group of juvenile (<20 years of age) and adult Hanford downwinders by 5-year periods of diagnosis. Converted to ratio per 100,000/year.

Table 1. Populations^a by age, sex, and location (region), studied by the Chernobyl–Sasakava health and medical cooperation project, who had thyroxin and thyroid-stimulating hormone tests (5)

Age ^b	Gomel		Zhitomir		Mogilev		Bryansk		Kiev	
	Boys	Girls	Boys	Girls	Boys	Girls	Boys	Girls	Boys	Girls
<1	1,390	1,400	1,657	1,691	1,581	1,492	1,092	1,107	1,682	1,651
1	1,372	1,369	1,656	1,708	1,460	1,424	1,165	1,076	1,737	1,824
2	1,285	1,324	1,693	1,785	1,436	1,423	1,254	1,114	1,890	1,839
3	1,246	1,269	1,748	1,904	1,474	1,499	1,168	1,172	1,745	1,792
4	1,139	1,273	1,606	1,835	1,394	1,503	1,188	1,153	1,609	1,700
5	948	1,079	1,659	1,800	1,348	1,463	1,086	1,061	1,505	1,715
6	728	840	1,473	1,607	1,194	1,164	1,100	1,061	1,271	1,522
7	437	472	1,159	1,441	813	878	783	905	977	1,192
8	229	295	710	1,031	518	627	578	737	490	697
9	149	182	271	439	268	360	278	463	203	318
Total	8,923	9,503	13,632	15,241	11,486	11,833	9,692	9,849	13,109	14,250

^aTotal number of children seen, 1991–1996.
^bAt the time of the Chernobyl accident.

Table 2. Diagnoses of hypothyroidism in a group of self-selected Hanford, Washington, downwinders in 5-year periods

Period of diagnosis	Juveniles (<20 years of age)			Adults			Total		
	Reported hypothyroid cases	Subjects alive during period ^a	Ratio per 100,000/year	Reported hypothyroid cases	Subjects alive during period ^a	Ratio per 100,000/year	Reported hypothyroid cases	Subjects alive during period ^a	Ratio per 100,000/year
1938–1942	1	308	65	0	145	0	1	453	44
1943–1947	4	348	230	3	207	290	7	555	252
1948–1952	9	382	471	16	252	1,270	25	634	789
1953–1957	17	366	929	19	320	1,188	36	686	1,050
1958–1962	18	313	1,150	18	406	887	36	719	1,001
1963–1967	8	238	672	8	495	323	16	733	437
1968–1972	1	162	123	15	580	517	16	742	431
1973–1977	1	103	194	10	631	317	11	734	300
1978–1982	0	68	0	17	664	512	17	732	464
1983–1987	0	50	0	18	663	543	18	713	505
1988–1992	1	47	426	24	656	732	25	703	711
1993–1997	0	29	0	14	636	440	14	665	421

^aSubjects alive are all subjects in our group alive during that 5-year period. Variations reflect the net effect of births and deaths during that period. Juveniles alive are all subjects who were <20 years of age in the middle of the period.

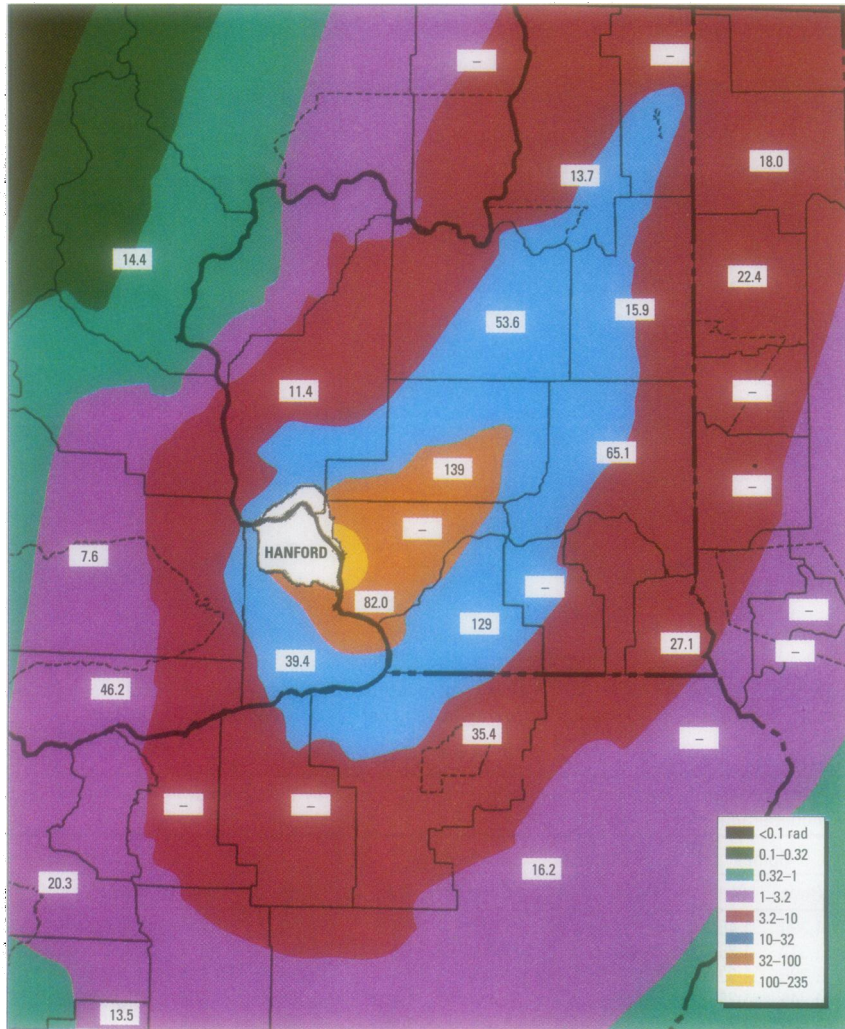


Figure 3. Isopeleths of doses to the thyroid for a child (J) and ratio of self-reported cases of hypothyroidism per 100,000 population under 20 years of age in potentially exposed counties represented in the Hanford downwinder group (Table 3). A dash (-) in Table 3 and on the map indicates that we have no reported cases of juvenile hypothyroidism from these counties among our group of respondents.

Chernobyl study population. Table 4 shows the number of cases of hypothyroidism and rates per 10,000 for boys and girls for each of the five regional screening centers (5). The exposures in Gomel and Zhitomir were greater than those in Mogilev and Bryansk and lowest in Kiev (Fig. 4). The rates of hypothyroidism were appreciably higher in Zhitomir and Gomel, somewhat higher in Mogilev and Bryansk, and lowest in Kiev. The only exception was the female rate in Kiev, which was approximately equal to that in Mogilev.

Using data obtained from individual communities (Table 5), we first selected those communities with two or more cases of hypothyroidism of either sex and averaged the body burden estimates of ^{137}Cs for those communities in relationship to frequency of hypothyroidism. Because of its uniform availability and general stability, we chose to represent the body burden

as the upper 75th percentile of the distribution. We included any community for which there were six or more body burden measurements. The exposure data per community are similar for boys and girls, yet the rates for girls are mostly higher than those for boys.

Figure 5 shows the relationship of body burden of ^{137}Cs with hypothyroidism for boys and Figure 6A and 6B show the same for girls. Figure 5 shows a correlation coefficient of 0.71, which is significant. For girls, even when the communities with exposures above a mean of 60 Bq/kg are omitted (Fig. 6B), the coefficient is only 0.35, which is nonsignificant.

Discussion

Although the self-selected nature of the Hanford sample precludes any effort to estimate the rate of incidence of hypothyroidism in the population in general, the large

Table 3. Self-reported cases of juvenile hypothyroidism by county in a group of Hanford, Washington, downwinders and ratios per 100,000 of county population <20 years of age (1950)

State, county	No. of cases	Population <20 years of age	Ratio per 100,000
Idaho			
Benewah	0	2,253	-
Bonner	1	5,564	18.0
Kootenai	2	8,916	22.4
Latah	0	7,179	-
Lewis	0	1,610	-
Nez Perce	0	7,940	-
Oregon			
Deschutes	1	7,402	13.5
Gilliam	0	908	-
Morrow	0	1,703	-
Umatilla	5	14,131	35.4
Union	1	6,164	16.2
Wallowa	0	2,525	-
Wasco	1	4,917	20.3
Washington			
Adams	3	2,157	139
Asotin	1	3,691	27.1
Benton ^a	3	7,616	39.4
Chelan	2	13,892	14.4
Columbia	0	1,620	-
Ferry	0	1,651	-
Franklin	0	4,684	-
Grant	1	8,740	11.4
Klickitat	2	4,328	46.2
Lincoln	2	3,733	53.6
Pend Oreille	0	2,756	-
Spokane	11	69,257	15.9
Stevens	1	7,277	13.7
Tri-Cities ^b	13	15,852	82.0
Walla Walla	16	12,382	129
Whitman	7	10,750	65.1
Yakima	4	52,778	7.6
Total, HEDR area^c	77	294,376	26.2

^aExcluding urban areas of Kennewick and Richland.

^bUrban areas of Kennewick, Pasco, and Richland.

^cData from the Technical Steering Panel of the Hanford Environmental Dose Reconstruction Project (3).

number of cases, their apparent congruence with estimated but uncertain average doses to the thyroid for the counties of residence, and their onset shortly after massive emissions of ^{131}I suggest their description as an epidemic phenomenon related to emissions of ^{131}I .

We recognize that a small cluster of cases could be the result of the diagnostic criteria of a single practitioner, but the spread of cases over a wide region makes this unlikely. Although knowledge of heavy exposure to radioactive emissions could have encouraged doctors to look for hypothyroidism, the massive emission of ^{131}I was not admitted by the government until 1986 and the diagnoses for the juveniles in our group had been made decades earlier. The link of juvenile hypothyroidism among Hanford downwinders with emissions of ^{131}I is supported by the apparent congruence of ratios of cases per 100,000 population <20 years of age and the rough estimates of thyroid doses for children when

the data are examined by county. If the age distribution of children who were living at the time of maximal emissions in 1945 are examined, most of them were exposed at <10 years of age. In fact, the only two children who were older than 10 years of age at the time of maximal exposure developed hypothyroidism very quickly in the years between 1945 and 1947.

The Marshall Island population exposed to the Bravo nuclear bomb test on 1 March 1954 also showed an unexpected development of hypothyroidism in children exposed prior to 10 years of age. According to Cronkite et al. (8),

Anthropometric measurements...revealed that beginning a few years after exposure, some of the exposed children, particularly boys less than 10 years of age, lagged in growth. Growth deficiencies were the result of hypothyroidism and were corrected by thyroxin therapy.... In 1966 on the advice of a panel of thyroid experts the exposed Rongelap (later the Ailinginae) group were put on lifetime thyroxin therapy, in the hope of reducing the development of thyroid tumors.... The thyroxin treatment has not been completely successful. Some people on therapy developed tumors.

Although the marked excess of thyroid cancer in young children from the Chernobyl area is well known, little attention has been paid to the even greater increase in childhood hypothyroidism in this population. Because of its scope and standardization, the Chernobyl Sasakawa Health and Medical Project findings indicate that there is a significant association, at least for boys, with the range of exposures to ¹³⁷Cs. For girls, there seems to be some protective mechanism for the upper levels (>60 Bq/kg) of exposure. Quastel et al. (9) have shown a significant shift in the TSH distribution toward higher TSH values for girls immigrating to Israel from the more heavily contaminated region of Gomel, as compared to those for girls emigrating from Kiev. However, any interpretation of a dose-response relationship must remain tentative, as current (1991-1996) levels of ¹³⁷Cs body burden cannot be expected to be closely related to the unmeasured radioiodine exposures in 1986. Not only is there no reliable estimation of thyroid dose available for these five regions, but the 5-year hiatus of observations from 1986 to 1991 makes it impossible to document the initial rise in frequency of hypothyroidism among the Chernobyl population, as was observed among our group of Hanford downwinders. Although the lack of these important data is unfortunate, the major strengths of the Japanese monitoring data are the study size, the representativeness of the samples, and the standardized approach.

Table 4. Juvenile hypothyroidism by region, community, and sex in the vicinity of Chernobyl (5)

	Gomel		Mogilev		Bryansk		Zhitomir		Kiev	
	Boys	Girls	Boys	Girls	Boys	Girls	Boys	Girls	Boys	Girls
Cases	14	27	6	7	6	10	26	39	4	9
Rate per 10,000	15.7	28.4	5.2	5.9	6.2	10.2	19.1	25.6	3.1	6.3

Gomel and Mogilev are in Belarus; Bryansk is in Russia; Zhitomir and Kiev are in Ukraine.

Table 5. Community rates (per 10,000) for hypothyroidism by sex, with estimated exposures in Chernobyl-affected regions (5) based on body burdens of ¹³⁷Cs (Bq/kg)

Community (city or surrounding area)	Region	Rates		Estimated dose	
		Boys	Girls	Boys	Girls
Klintsy	B	9.2	9.0	65.9	51.9
Novozybkovskii	B	0.0	14.6	172.7	141.7
Remainder of Bryansk	B	(2.2) ^a	4.8	-	-
Zlynkovskii	B	0.0	23.6	187.2	185.0
Gomel	G	32.5	22.7	38.4	37.5
Gomelskii	G	11.0	27.7	44.8	47.8
Rechitskii	G	(11.6)	56.7	43.0	50.4
Remainder of Gomel	G	13.9	24.6	-	-
Borodyanskii	K	0.0	20.0	39.4	39.1
Brovarskii	K	24.6	0.0	33.4	28.8
Irpenskii	K	(3.5)	6.8	30.5	31.8
Svyatoshinskii	K	0.0	23.8	25.9	23.7
Mogilev	M	(1.8)	3.5	28.3	29.1
Mogilevskii	M	13.3	(6.8)	30.7	30.1
Remainder of Mogilev	M	4.8	4.6	-	-
Slavgorodskii	M	(36.2)	69.7	71.8	47.7
Emilchinskii	Z	19.8	33.8	69.0	52.1
Korosten	Z	8.1	20.1	43.5	39.9
Korostenskii	Z	28.5	18.5	59.0	56.3
Luginiskii	Z	27.2	63.5	105.7	106.2
Malinskya	Z	(8.8)	49.8	40.0	38.2
North Volinskii	Z	(6.2)	23.3	36.4	34.6
Olevskii	Z	36.6	(7.5)	131.8	99.1
Ovruchskii	Z	56.1	39.7	117.4	83.3

Abbreviations: B, Bryansk; G, Gomel; K, Kiev; M, Mogilev; Z, Zhitomir.

^aThe data shown in parentheses are based on a single case.

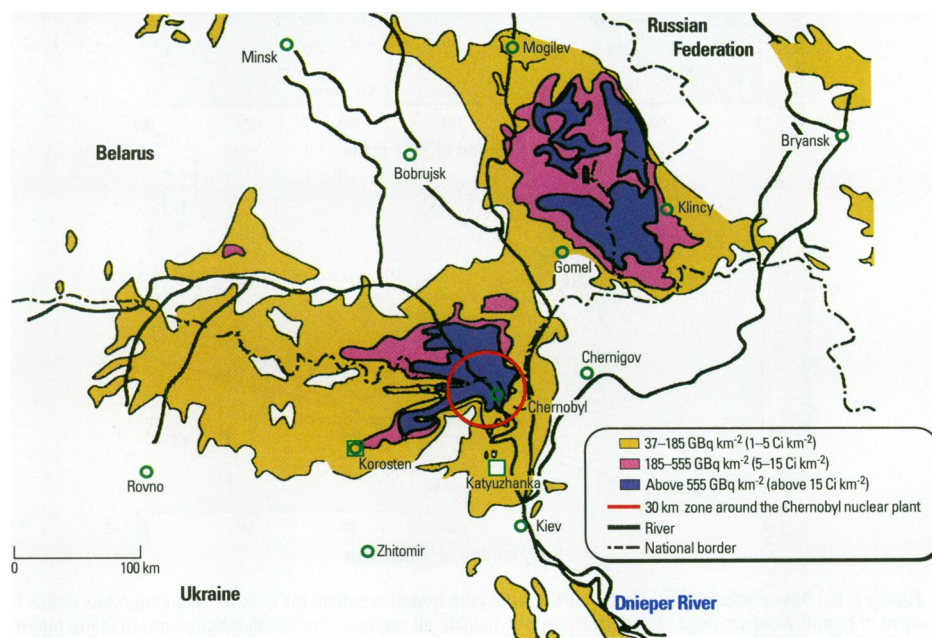


Figure 4. Isopleths of ¹³⁷Cs surface contamination in regions around Chernobyl. Adapted from the International Advisory Committee (7).

The upper normal limits of serum TSH used to define hypothyroidism for the Chernobyl children (5) seem somewhat lower than those generally used clinically. On the other hand, no laboratory data were available for the group of Hanford downwinders.

We believe that these Hanford and Chernobyl data, along with the data from the Marshallese study (10) and the increase in thyroid autoantibodies found among children and adolescents from Belarus following the Chernobyl accident (11), suggest that screening tests for juvenile hypothyroidism

can be beneficial among populations exposed to radioiodine.

Conclusion

The massive emissions of ^{131}I in 1945 from the Hanford plutonium manufacturing plant appear to be associated with the subsequent occurrence over the next 20 years of an epidemic of juvenile hypothyroidism among children living downwind. There is general congruence of the estimated cumulative thyroid dose and the numbers of cases per 100,000 juveniles by counties. In 1945, most of the children were younger than 10 years of age. The finding of a community rate associated with exposure for children living near Chernobyl suggests that for any community with large radioiodine exposures, hypothyroidism in children is a likely occurrence, and if found, it can easily be treated. Therefore, screening tests may be beneficial for such populations.

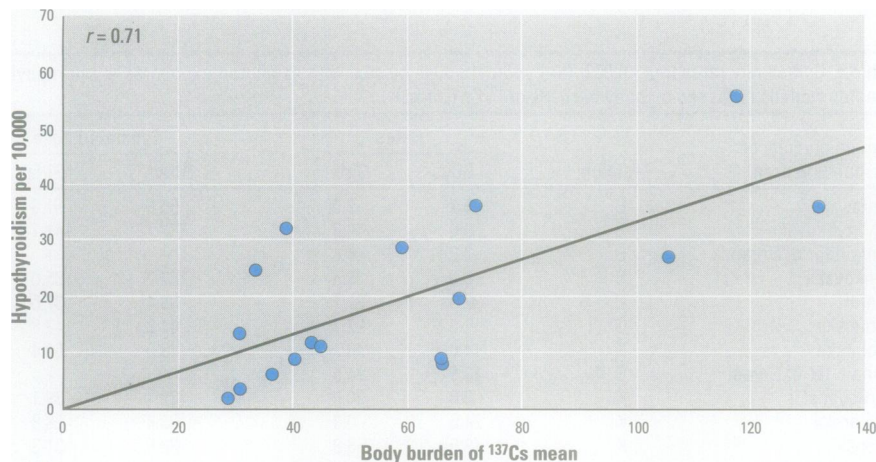


Figure 5. Association of mean ^{137}Cs body burden with hypothyroidism per 10,000 for boys near Chernobyl, by community. ^{137}Cs is the mean of 75th percentile for all ages and all years with six or more cases observed.

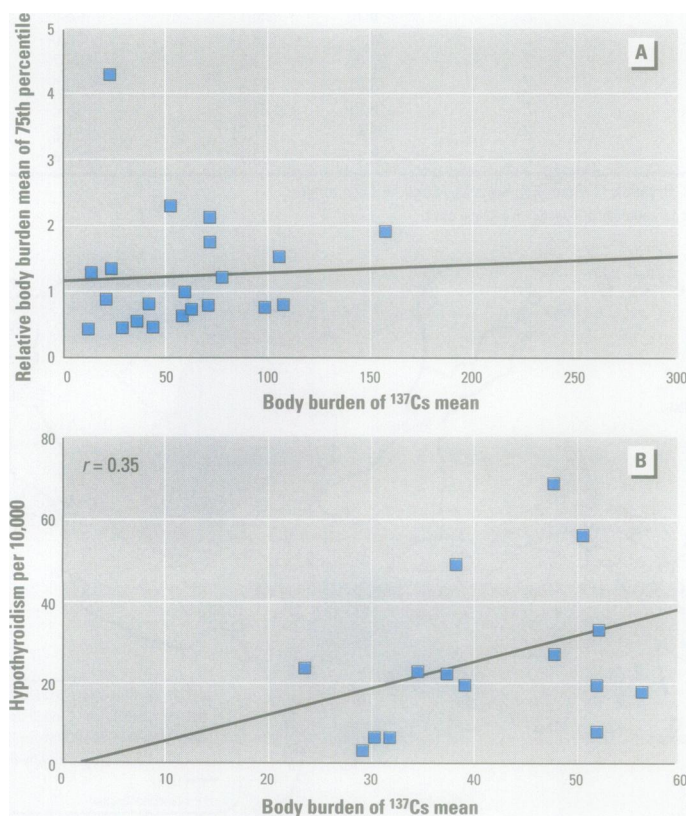


Figure 6. (A) Association of ^{137}Cs body burden rate with hypothyroidism for girls from communities with >1 case of hypothyroidism near Chernobyl (rate per 10,000), all regions. The relative body burden is the mean of the 75th percentile. (B) Association of mean ^{137}Cs body burden <60 Bq/kg with hypothyroidism for girls near Chernobyl (rate per 10,000). ^{137}Cs body burden is the mean of 75th percentile for all ages and all years with six or more cases measured.

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