Juvenile Hypothyroidism among Two Populations Exposed to Radiiodine

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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 radiiodine 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 radiiodine 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 population groups exposed to radiiodine 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/1999/107p303-308/goldsmith/abstract.html

Hypothyroidism is a potential environmental hazard associated with ingestion, physiological uptake, and concentration of radiiodine 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), 135I (21 hr), 135I (0.28 days), and 135I (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 potentially 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...
hypothyroid cases taking thyroid were excluded from our counts.

Chernobyl area. Massive emissions of radioiodine (including 129I, 131I, 132I, 133I, and 137I, with half lives of 1.72 × 107 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 137Cs, 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, 137Cs 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 137Cs burden was determined and served as an exposure index, although it was recognized that radioiodine, which follows a different precipitation pattern, was a poor index of exposure to gaseous radioiodine. The ratio of 131I/137Cs varies nonlinearly with 137Cs 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 137Cs 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 thyroxin (T₄) <10 pmol/l and thyroid-stimulating hormone (TSH) >2.9 μIU/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 T₄ 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 radioactive iodine releases, 1944–1949; onset reached a maximum approximately 15 years later in juveniles, then dropped off. The ratios for juveniles after 1960 became 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 radioactive iodine 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* 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)

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

*Subjects 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.
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 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 Saskatchewan 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 radiiodine 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)

| Region          | Boys | Girls | Rate per 10,000 |
|-----------------|------|-------|----------------|
| Gomel           | 14   | 16    | 15.7           |
| Mogilev         | 27   | 40    | 28.4           |
| Bryansk         | 6    | 11    | 7.9            |
| Zhitomir        | 6    | 10    | 6.2            |
| Kiev            | 26   | 39    | 26.1           |
|                  |      |       | 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                              | 9.2  | 9.0   | 65.9 | 51.9  |                  |
| Novozubkovskii                       | 0.0  | 23.6  | 187.2| 185.0 |                  |
| Zlynkovskii                          | 0.0  | 23.6  | 187.2| 185.0 |                  |
| Remainder of Bryansk                 | 1.9  | 4.8   | 35.4 | 31.8  |                  |
| Gomel                                | 0.0  | 23.6  | 187.2| 185.0 |                  |
| Remanter of Gomel                    | 1.9  | 4.8   | 35.4 | 31.8  |                  |
| Borodyanski                          | 0.0  | 20.0  | 35.4 | 31.8  |                  |
| Brovarskii                           | 0.0  | 23.6  | 187.2| 185.0 |                  |
| Irpenskii                            | 0.0  | 23.6  | 187.2| 185.0 |                  |
| Svyatoshinskii                       | 0.0  | 23.6  | 187.2| 185.0 |                  |
| Mogilev                              | 0.0  | 23.6  | 187.2| 185.0 |                  |
| Remanter of Mogilev                  | 0.0  | 23.6  | 187.2| 185.0 |                  |
| Slavgorodskii                        | 0.0  | 23.6  | 187.2| 185.0 |                  |
| Emlichinskii                         | 0.0  | 23.6  | 187.2| 185.0 |                  |
| Korosten                             | 0.0  | 23.6  | 187.2| 185.0 |                  |
| Korostenskii                         | 0.0  | 23.6  | 187.2| 185.0 |                  |
| Luginskii                            | 0.0  | 23.6  | 187.2| 185.0 |                  |
| Malinskaya                           | 0.0  | 23.6  | 187.2| 185.0 |                  |
| North Volinski                       | 0.0  | 23.6  | 187.2| 185.0 |                  |
| Olevskii                             | 0.0  | 23.6  | 187.2| 185.0 |                  |
| Ovruchskii                           | 0.0  | 23.6  | 187.2| 185.0 |                  |

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

*The 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.

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