REVIEW

Iodide Prophylaxis in Poland After the Chernobyl Reactor Accident: Benefits and Risks

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The accident at the No. 4 reactor of the Chernobyl Power Station took place on April 26, 1986, at 1:23 AM. Like the accident at Three Mile Island No. 2, the immediate cause was operator error, but the much more serious release consequences in the Ukraine can be ascribed to reactor design [1–3]. Two explosions occurred, the first due to steam and a second one due to hydrogen. The explosions expelled fission products and fuel elements to the exterior that accumulated in a cloud reaching to approximately 7,000 m and centered at approximately 4,500 m. Because the graphite ignited, there was a second, more prolonged but less intense, release over a 9- to 10-day period that peaked on May 6, 1986, and dropped sharply on May 11 as the fire was extinguished. The following volatile elements, as well as the noble gases xenon and krypton, constituted the most abundant released material: iodine, cesium, and tellurium. In this review, we will deal primarily with iodine isotopes as they affected Poland. Although iodine isotopes other than ^{131}I are present with higher core inventories [2,4], their short half-lives make them important primarily in the first days, and near the reactor. Spectroscopy of the environmental isotopes was not possible under the emergency conditions prevailing, but it was found that approximately 28% of the air radioactivity was present as short-lived isotopes of iodine as measured in Warsaw on April 28. Thus, some inhalation of short-lived iodine isotopes occurred during the earlier exposure period. Nevertheless, the timing was such that the protective actions were directed at ^{131}I.

Initial Russian estimates of the amount of ^{131}I released from a core inventory of approximately 63 MCi were 7.3 MCi [5]. More recent measurements and calculations have raised that estimate to approximately 60% of the inventory and total releases of 36 to 46 MCi ^{131}I (1.3 to 1.7 ExaBq) [2,4,6,7]. In Poland, increased air radioactivity was first detected on the night of April 27 and 28 [7,8] and amounted to 504 Bq of radioiodines/m^3 air with 1.55- to 3.0-times higher values in northeast Poland. By 10 AM on the 28th, all Polish monitoring stations reported air, soil, and water contamination and were placed on 24-hour emergency alert. Spectra showed that the early air samples were approximately 80% iodine isotopes. Radioiodine depositions on the ground and grass in the provinces varied, but due to local rains, they were from 3.5 to 9 times higher than in Warsaw. Local sources (from research reactors) for the contamination could be ruled out and a serious accident to the east was suspected; this was confirmed by a brief report of the Tass News Agency on the evening of April 28, but its importance was minimized by the agency. Because of the environmental findings, 18 children received neck measurements at the Center for Radiological Protection, where sophisticated counting facilities were available. Thyroid counts amounted to 500 to 1,300 Bq by 11 AM, April 29. During the night of April 28, a governmental commission was called upon to assess damage potential and to recommend protective measures. Because reliable information was not available from Russia, decisions had to be based on a worst case scenario. After study of published response plans [9–14], and the ministerial recommendations [15], the following intervention levels were recommended by the commission on the morning of April 29:

(1) Whole body committed dose should not exceed 5 mSv/y (0.5 rem).

(2) Thyroid committed dose should not exceed 50 mSv/y (5 rem) in children (16 years and under) and 500 mSv/y (50 rem) in adults. The tumorigenicity of radiation to the thyroid has been calculated from external radiation, and it was believed that in children the risk decreases with increasing age. This has now been demonstrated in several studies [16–18]. Even though no similar data are available for internal radiation from ^{131}I, and the effectiveness factor has been estimated to range from 1 to less than 0.1, it was decided to adopt the very conservative dose commitment of 50 mSv as the intervention level for children.

(3) Thyroid content in children 16 years or under should not exceed 5,700 Bq at any one moment.

Considering the high radioiodine uptakes in the population, and assuming continuing contamination, the commission concluded that, in eastern Poland, the annual committed thyroid dose in children under 16 might well exceed the 50-mSv limit, and that, therefore, prophylactic potassium iodide (KI) should be considered. Some of the estimated contamination levels of the environment are summarized and compared with preaccident levels in **Table I.**

Measures to protect the thyroid gland against envi-

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ronmental radioiodine contamination have been well delineated in the past [9–14]. A salient point from all these studies is that prompt administration of stable iodine is highly desirable because iodide is rapidly concentrated and organified by the thyroid but is then stored for prolonged periods as iodinated thyroglobulin. Although some thyroid uptake had already occurred, stable iodine was still useful to protect the gland against the continuing contamination resulting from Chernobyl. Stores of KI available at Cefarm (the Central Pharmacy Organization) were sufficient for about 90 million doses of 100 mg of KI each. The chief aim of KI prophylaxis is to reduce the thyroid burden to an acceptable level. This could be done either by achieving a nearly total block of radioiodine uptake early, until high levels of contamination subsided, or by intermittent KI treatment after an initial dose according to subsequent contamination levels. This latter maneuver was used in the Polish population. In view of the limited supplies of KI, it was also believed that such a procedure would more readily permit reinstitution of KI prophylaxis if the level of contamination should increase again. Thus, at 12 noon on April 29, the Minister of Health gave orders to prepare KI solution in the centralized pharmacy for distribution to the 11 provinces most affected. This was to be made available through all hospitals, public health centers, schools, kindergartens, and so forth. With the arrival of further contamination data (3 PM), the commission gave the order to implement distribution with droppers or automatic pipettes of a saturated solution of KI, roughly on the basis of weight and the assumption that body iodide distribution and blocking efficiency were similar to that which has been found in adults. The following protocol was used: (1) 15 mg for newborns; (2) 50 mg for children 5 years or under; (3) 70 mg for all others; (4) Because the cancer risk for adults was believed to be low, and some side effects (e.g., in persons with nodular goiter) might be anticipated, iodide prophylaxis was not recommended for adults; (5) Iodide prophylaxis was recommended for pregnant and lactating women, but was not mandatory.

The mass media were used to announce the protective action and to appeal for volunteers to assist in the nationwide distribution (especially in villages).

The following additional protective measures were instituted by the commission:

(1) The feeding of cows on pastures or with fresh fodder was banned countrywide until May 15.

(2) Fresh milk with radioactivity above 1,000 Bq/L was banned for consumption by children and pregnant or lactating women.

(3) All children under the age of 4 were provided powdered milk through numerous distribution centers. Although the decision to substitute powdered milk was made on April 30, the fact that there was a holiday, and the fact that stores were closed on the weekend, delayed effective distribution until May 2.

(4) Approximately 3,000 metric tons of powdered milk were available. Thereafter, powdered milk was imported mostly from Holland.

(5) Children and pregnant or lactating women were advised to eat a minimum of fresh leafy vegetables (until May 16).

A total of 10.5 million doses of KI were given to children and 7 million doses were given to adults. Multiple doses, although not recommended, were taken in a number of cases. In addition, follow-up studies (to be detailed below) revealed that about 6% of the prophylaxis resulted from panic-driven, self-administered tincture of iodine before the KI program was initiated.

By May 3, air contamination had decreased about fourfold and there appeared to be no further radioiodine deposition on the ground; thus it was not considered necessary to distribute a second dose of KI. Direct thyroid radioiodine uptakes [7,13,19] obtained in Warsaw on May 5 showed that the intervention level for thyroid radioactivity in children under 16 was not exceeded as shown in **Table II.** This was not the case in children from areas of high contamination. Despite prophylactic measures, some children exceeded the 5,700-Bq intervention level on May 15 (Table II). Note that these measurements were made 10 days later than those in Warsaw. It is of interest that the Lomza values were in the same range as those in 34 Polish travelers who returned from Kiev between April 26 and May 5 and whose mean thyroid counts were 2,180, 4,471, and 2,125 Bq in children, women, and men, respectively [1]. It is concluded that some regions in Poland would have received (or did receive) enough ^{131}I to exceed the intervention level for dose commitment in a substantial number of children. Due to the failure by the power station management to provide punctual notification of the accident, unprotected intake of ^{131}I occurred that might have been substantially reduced.

The protection program consisted of two phases

TABLE I

Environmental Contamination Before and After the Chernobyl Accident*

Source of Radiation	Units†	Before Accident (Mean)	April 28–May 13 (Maximal)	May 14 (Maximal)
External	mR/h	0.012	0.43	0.028
Air (β)	Bq/m^3	0.1	571	1.2
Milk (β)	Bq/L	42	2,000	220
Water (β)	Bq/L	0.4	111	5.0
Grass (β)	Bq/kg	223	105,000	18,200
Vegetables (β)	Bq/kg	132	253,800	5,600

*Mean of 12 provinces; taken from [7]. Total β radioactivity in air, milk, grass, and so forth, as well as external radiation, was measured over 24 hours in 208 monitoring stations localized countrywide.
†1 Ci = 3.7×10^{10} Bq.

TABLE II

Thyroid Radioiodide in Children and Adults in Warsaw and Lomza*

		No. Examined	Thyroid ^{131}I Content (Bq)		
			Mean	Minimal	Maximal
Warsaw, May 5	Children	171	403	30	1,435
	Women	154	383	67	1,519
	Men	81	425	68	1,360
Lomza, May 15	Children	13	4,668	1,012	14,098
	Women	16	3,907	980	17,770
	Men	7	3,441	878	10,219

*Modified from [7]. Thyroid ^{131}I was measured using two probes with 33 × 25-mm thallium-activated sodium iodide crystals each at 45° from the midline of the neck using the 361-keV photopeak. The device was calibrated with a plexiglass thyroid-neck phantom (150 × 150 mm) with a 32 × 52-mm hole for a standard ^{131}I solution. The calibration factor (cps/Bq) was determined at two geometries and was 5.87×10^{-3} and 7.94×10^{-3} for children and adults, respectively. Uncertainty due to placement in these factors was 20% at the 2 standard deviations confidence level. Counting time was 10 to 15 minutes and the lower limit of detection was 30 Bq in the thyroid. Subjects had their hair washed and neck wiped before counting. Between April 29 and June 27, 1,500 subjects were measured [13,19].

that had relatively little overlap in time. The first phase, initiated on the fourth day of the accident (i.e., April 29) and virtually completed by May 2, was the distribution of KI to greater than 90% of the children under the age of 16 and about a quarter of the adults. Because of diminishing air contamination, the KI prophylaxis was not repeated. In the second phase, ingestion of ^{131}I became the dominant source and powdered milk was made available to all children under 4 years of age. All milk with more than 1,000 Bq/L was banned. This program started effectively on May 3 and was associated with a warning to restrict leafy vegetables. Nevertheless, the main protective measures, KI administration and milk and vegetable withdrawal, effectively protected many children against radioiodine.

PILOT STUDY

After the acute protective phase was terminated in June 1986, it became desirable to initiate a follow-up program with the following objectives:

(1) To obtain more reliable thyroid burden estimates for children and adults in different regions of Poland and to evaluate possible functional and morphologic effects of thyroid irradiation from the Chernobyl accident.

(2) To evaluate the degree of protection achieved during the acute phase, and to obtain accurate information on the incidence of side effects to the single dose of KI.

(3) To evaluate thyroid function of newborns exposed *in utero* and to assess KI effects on this population.

(4) To evaluate the effect of the single dose of KI on subjects with a previous history of thyroid disease.

(5) To obtain estimates of the incidence of adverse reactions to KI.

The program, denoted MZ-XVII, was divided into two phases. The first phase, lasting from October 1987 to December 1988, was intended to establish study populations and methods of study. Pilot studies were carried out with an initial number of 12,600 questionaires. Of these, only 6,082 (48%) persons responded satisfactorily. This was considered to be an inadequate degree of compliance and attempts were made to increase the fraction of responders. In some areas, we found that compliance was markedly improved only by examination and blood collection in the subjects' homes (see below). With these measures, total compliance was increased to 66%.

An epidemiologic software system was devised to provide uniform data collection and storage for the different study regions and to control implementation. A great deal of effort went into the training of personnel in order to obtain uniform medical and laboratory examinations and questionnaire handling. Assay kits were tested and selected for use in the various regional centers [20]. Quality control involved checking of assay kits, provision of standardized reference sera to be used in the five centers, and measurements of every 320th sample in Warsaw.

The study regions were selected on the basis of high, medium, and low estimated ^{131}I thyroid dose commitments and the presence of medical centers in such areas able to carry out population studies, preferably with previous epidemiologic experience in the thyroid field. This led to the selection of Bialystok and Krakow for the high-contamination regions, Poznan and Wroclaw as moderately contaminated regions, and Szczecin as an area nearly free of contamination.

The pilot study showed that the first questionnaire was too detailed and that certain questions could be deleted. This was also true for the medical examination form. These were therefore simplified. Analysis of the efficiency of the data entry into the computer system revealed that as much as 11% of the data from the questionaires and medical examinations was lost during this procedure. Therefore, the software was revised so as not to accept incomplete entries.

FIELD STUDY

On statistical grounds, it was estimated that about 30,000 subjects would be needed for the follow-up study. To attain this goal, and because of the poor compliance in the pilot study, 52,092 persons were questioned and 34,491 completed the study. The compliance was 66.2%, and we attribute this increase to additional efforts to locate subjects in their homes. The group studied represented 0.09% of the total population of Poland; 32% of these lived in villages and 68% in towns—a distribution typical for Poland as a whole. The age and regional distribution for the study cohort is shown in **Table III.** Children to age 16 (12,641) accounted for 36.65% of the group, with 6,137 girls and 6,504 boys. Among the adults (20,578), there were 12,374 women and 8,204 men.

TABLE III

Age Distribution of Polish Population Investigated in Five Regions*

Subjects	Bialystok	Krakow	Poznan	Wroclaw	Szczecin	Total
Children						
1–10 years	2,825	1,255	2,018	825	1,603	8,526
11–16 years	1,163	505	1,069	556	822	4,115
Teenagers						
17–19 years	294	186	460	202	130	1,272
Adults						
20–40 years	3,805	1,655	3,923	1,515	1,182	12,080
>40 years	1,938	1,138	3,390	1,212	820	8,498
Total	10,025	4,793	10,860	4,310	4,557	34,491

*Data taken from [1].

TABLE IV

Predicted Minimal and Maximal ^{131}I Thyroid Committed Doses (mSv) in Poland*

Age of Inhabitants	Contamination					
	High (12 Provinces)		Average (23 Provinces)		Low (14 Provinces)	
	Minimal	Maximal	Minimal	Maximal	Minimal	Maximal
<1 year old	15.5	68.1	5.2	37.7	3.1	23.1
<2–5 years	11.3	40.8	6.3	22.4	3.8	13.7
<6–10 years	10.9	32.4	6.0	18.2	3.7	10.9
Adults	7.1	18.1	3.9	9.9		6.1

*Data modified from [19].

TABLE V

Effect of the Time of KI Prophylaxis on the Committed ^{131}I Dose to the Thyroid*

Age	Date of KI	Inhalation Only			Inhalation + Ingestion		
		Bq	mSv	Reduction %	Bq	mSv	Reduction %
<1 year	None	1,767	2.3	0	13,554	17.5	0
	April 29	664	0.8	64	8,132	10.5	40
	April 30	1,152	1.5	35	10,27	13.3	24
	May 1	1,674	2.1	7	11,310	14.6	17
1–5 years	None	4,550	2.9	0	16,537	10.4	0
	April 29	1,665	1.0	63	10,573	6.6	36
	April 30	2,981	1.9	24	12,335	7.7	25
	May 1	4,247	2.7	7	14,187	8.9	14

*Data modified from [19].

Evaluation of the thyroid committed dose for ^{131}I was done by the direct method [13,19] on the basis of measured thyroid ^{131}I in 1,500 subjects that had been counted in the 5 study areas between April 29 and May 6 for the most part, with some counts up to May 19; and by an indirect method based on the 5-compartment model of iodine metabolism developed by Johnson [21], using measured ^{131}I in air, milk, and other foods, standard values for inhalation rate and milk and food consumption, as well as parameters such as age, sex, thyroid size, and iodine uptakes (**Table IV**). For children under the age of 1 year, the projected mean maximal burden would have exceeded 50 mSv in 12 provinces, with a range of 53.3 to 87.5 mSv. There were a number of "hot spots" in each of the areas wherein the thyroid burden was approximately 6 to 10 times that in the surrounding areas. For children 1 to 5 years old, only one province showed a predicted mean maximal burden in excess of 50 mSv with a range of 47.6 to 55.8 mSv. In none of the older children or adults was the mean maximal burden in excess of this limit, although the spread was considerable and some individuals exceeded the limit.

Anatomic changes in the thyroid were few up to 4 years after the accident. Two children were found to have benign nodules but no childhood thyroid cancers

TABLE VI

Contribution of KI and Powdered Milk to Reduction of Thyroid Burden*

Date of KI Prophylaxis	Dose Reduction Due to KI (%)	Dose Reduction From Milk† and Vegetables (%)	Total Dose Reduction (%)
April 29	40	30	70
April 30	25	30	55
May 1	12	30	42
May 2	8	30	38

*Data are from 11 provinces with higher exposure [7,19].
†Calculated on the assumption that only powdered milk was used and that vegetables were avoided. In children less than 1 year of age, there is an uncertainty as to the contribution of unprotected breast feeding to the thyroid burden.

TABLE VII

Effects of KI Prophylaxis on ^{131}I Thyroid Committed Dose in Children From Warsaw and Ostroleka Province*

No.	Prophylaxis (Date)	Average Dose (mSv)	Range (mSv)	% Dose Reduction
A				
7	None	9.3 ± 4.9	4.8–29	None
18	Yes (April 29)	5.4 ± 3.1	1.7–13.1	45
67	Yes (April 30)	7.0 ± 4.0	1.5–1.9	41
B				
7	None	107	82–133	None
18†	Yes (April 30)	63 ± 6.9	11–218	45
13‡	Yes (April 30)	31 ± 14	13–54	41

A = Warsaw (average contamination); B = Ostroleka Province (high contamination).
*Data modified from [13]. Method as in legend to Table I.
†In villages.
‡In towns.

were found in the study population. It is, of course, too early to make definitive statements regarding thyroid neoplasms and a long-term follow-up study is planned. Comparison of total and nodular goiter prevalence several years before and after the accident showed no significant difference.

PROPHYLAXIS

Approximately 18 million doses of KI solution were distributed primarily, but not exclusively, to children. The bulk of the distribution took about 3 days, with the residual distribution completed on the fourth day, that is, from April 29 to May 2. In certain areas, e.g., Bialystok, about 75% of the population was reached on the first day, but in other areas the bulk of the distribution occurred on the next 2 days. Eventually, 95.3% of children received iodide prophylaxis; 86.7% took a single dose, 2.39% took two or more doses, and a surprising 6.14% were given diluted tincture of iodine by their parents before the start of the program and then took a single dose of KI [1]. This was confirmed by the brisk increase in sales of tincture of iodine in pharmacies. Although not advised to take KI, 23.2% of adults took iodine prophylaxis (19.6% took a single

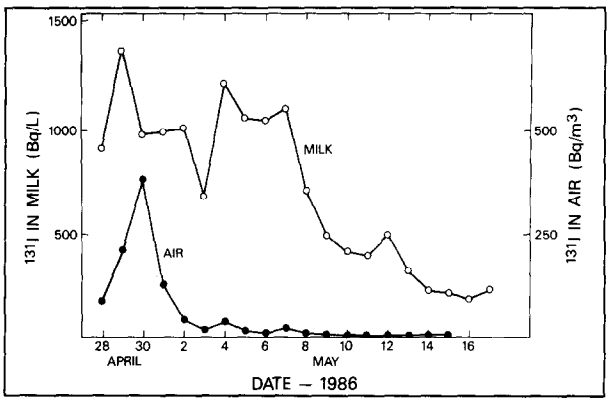

Figure 1. Time course of contamination with ^{131}I in Poland following the Chernobyl accident. ^{131}I in milk was counted twice daily (AM and PM) in 9 milk processing plants in pooled samples from 21 provinces. ^{131}I in air was counted every 6 hours in 49 provinces.

dose of KI, 1.03% two or more doses of KI, and 2.61% took tincture of iodine before the start of the program). This translates to approximately 10.5 million children 16 years old and under, and approximately 7 million adults who received iodide prophylaxis.

The degree of protection afforded children 1 to 5 years of age by the single dose of KI given on different days calculated by the five-compartment model is compared with a comparable total thyroid ^{131}I reconstructed dose commitment for an unprotected population in **Table V.** It is clear that *early* KI administration is, as expected, more effective, and that a single dose of KI will not offer long-term protection against repeated dietary ^{131}I intakes. Had there been prompt warning from the Russian authorites, the 24- or 48-hour gain in time might have provided an extrapolated protection of 53% and 67%, respectively. On the other hand, at later intervals, most of the contamination and hence, potential protection, is related to ingestion. The calculated thyroid ^{131}I dose commitment if all protective measures would have been withheld is also listed in Table V. It is clear that the bulk of the later ^{131}I burden derives from ingested sources (Table V and **Table VI**).

Milk radioactivity varied widely from day to day as shown in **Figure 1,** but as expected, remained elevated long after contamination of the air had subsided. The irregularity in the milk contamination may be partly explained by variable proportions of milk from different regions entering the milk pool that was sampled each day. As shown in Table I, individual maxima often were found to exceed the limit of 1,000 Bq/L by April 30, and it became necessary to supply powdered milk to children. After May 7, the milk radioactivity values progressively declined (Figure 1) and it was judged safe to terminate the powdered milk program on May 16. Together with the restriction of leafy vegetables, the calculated reduction of thyroid burden by food restriction provided an additional 30%

reduction in thyroid committed dose on the assumption of full compliance with the program [13]. The average total reduction in thyroid burden in three fourths of the children (aged 1 to 4) in the 11 provinces treated between April 29 and May 2 was 62%, whereas the remaining fourth of the children received only an average of 40% reduction. As a result of the protective measures, about 90% of children up to the age of 16 had their dose commitment kept below 50 mSv. Both Tables V and VI reemphasize the need for rapid intervention with KI in order to achieve the desired level of protection. Considerable additional protection might have been achieved with early warning. Validation of the reconstructed thyroid burdens was possible from data obtained by direct thyroid measurements in children up to 5 years of age. These are shown for an area of average contamination (Warsaw) and for a heavily contaminated region (Ostroleka) in **Table VII** [19]. All data for thyroid dose were consistent with a lognormal distribution. It is apparent that the degree of protection calculated from such measurements is similar to those derived from dose reconstruction. The overall conclusion, based on both direct and reconstructed dosimetry, is that KI prophylaxis amounted to 40%, 25%, and 12% on April 29 and 30, and May 1, respectively, of the total committed dose to May 30 [22,23].

SIDE EFFECTS OF A SINGLE DOSE OF KI

Intrathyroidal

Quantitative aspects of adverse reactions to iodide have been hampered in the past by the small size of the study groups, selection bias, anecdotal reports, use of very large doses of KI, or limited follow-up [24–26]. One of the chief aims of the field study was an evaluation of the intrathyroidal and extrathyroidal side effects after a known intake of KI in a large population. Some 95% of children received KI [1]. Of 12,084 children in the study group who received KI, 91.4% had normal serum thyroid-stimulating hormone (TSH) levels measured during 1989 to 1990 (mean 1.5 mIU/L) (normal range 0.3 to 3.8 mIU/L), 4.7% had lower TSH values (mean = 0.19 mIU/L), and 3.9% had values in excess of 3.9 mIU/L (mean = 5.7 mIU/L). This should be compared with the values from 557 unprotected children of the same age distribution: 93.1% normal, 3.7% low, and 3.2% high (the respective means are 1.5, 0.2, and 5.1 mIU/L). There are no statistical differences between the protected and unprotected groups. Thus, until 1989, no permanent effect on thyroid function could be detected by this test. These conclusions are confirmed by screening studies for congenital hypothyroidism in Central Poland on 120,000 to 140,000 newborns for the years 1985, 1986, and 1987 [27,28]. The incidence of transiently elevated TSH levels and of confirmed congenital hypothyroidism remained unchanged. Serum levels of thyroxine (T_4), triiodothyronine (T_3), and antithyroid antibodies in these children showed a similar lack of difference between the protected and unprotected groups [20]. Thus, we found no readily detectable long-term disturbance in thyroid function as a result of a single dose of KI in children. Similar conclusions were reached from a study carried out in 1989 of 3,363 women and 1,688 men without previous thyroid disease who had received KI, whose serum T_4, T_3, TSH, and antibody levels were not different from those in 9,344 women and 7,225 men not receiving iodide prophylaxis [1,20].

TABLE VIII

Prevalence of Thyroid Disorders Before and After KI Prophylaxis*

Diagnosis	Without Prophylaxis (1,282 Patients) (%)	With KI Prophylaxis (774 Patients†) (%)
Nontoxic diffuse goiter	429 (33)	384 (49)
Nontoxic nodular goiter	432 (34)	255 (33)
Graves' disease	124 (9.7)	32 (4.1)
Toxic nodular goiter	121 (9.4)	34 (4.4)
Hypothyroidism	44 (3.4)	27 (3.5)
Post-thyroidectomy	129 (10)	40 (5.2)
Thyroid cancer	3 (0.23)	2 (0.26)

*From the Lodz Outpatient Endocrine Clinic [29]. All diagnoses were made before 1986. The course of the disease was ascertained by questionnaire, clinic visits, laboratory tests for T_4, T_3, TSH, and antibodies, and ultrasound scans. Thirty-two patients had side effects with a distribution like that of Table X. Five of these patients consulted a physician.
†Sixty-nine of these patients took more than one dose of KI.

Of 2,521 adults with thyroid disease diagnosed and/or treated before 1986 at the Lodz Clinic [29], a single dose of iodine was taken by 705 patients, and 69 took 2 or more doses. On the other hand, 1,282 did not receive KI. The diagnoses in the treated and untreated groups are listed in **Table VIII.** Although the distribution in the two groups is not identical, their subsequent clinical courses between 1986 and 1990 were identical irrespective of iodide prophylaxis. In none of the patients with nodular goiter was there a single case of induction of thyrotoxicosis, nor was there any exacerbation of preexisting hyperthyroidism or a change in antibody titers or prevalence in patients with Graves' disease.

Acute, thyroid-related reactions were, however, seen in 0.37% of newborns who received KI prophylaxis on the second day of life. Despite the fact that these infants received up to 5 times the mg KI/kg body weight that adults received, only 12 of 3,214 infants showed a transient increase in serum TSH levels and had decreases in their serum free T_4 (**Table IX**). This transient thyroid inhibition has had no known sequelae to date, but these findings point to the need for careful observation in case more prolonged periods of iodide prophylaxis are required.

TABLE IX

Intrathyroidal Side Effects Seen in Newborns After KI Administration During the First Days of Life*

Time of Examination	3rd–5th Day of Life	16th–20th Day of Life
No. of examined	3,214	3,214
No. (%) with elevated serum TSH	12 (0.37)	None
Mean serum TSH (mIU/L)	83.5 ± 35.2	6.4 ± 2.3
No. (%) with decreased serum free T_4	12 (0.37)	None
Mean serum free T_4 (nmol/L)	126.0 ± 9.4	116.1 ± 19.6

*Modified [28]. Normal range of serum TSH (very young children) 2.5–11.0 mIU/L. Normal range of serum free T_4 (very young children) 90.1–153.0 nmol/L.

TABLE X

Extrathyroidal Side Effects After KI Prophylaxis*

Symptoms	Children		Adults	
	No.	%	No.	%
None	11,482	95.4	4,833	95.5
Iodine mumps	0		0	
Parotitis	0		0	
Headache	22	0.18	35	0.69
Stomachache	43	0.36	32	0.63
Diarrhea	23	0.19	6	0.12
Vomiting	286	2.38	43	0.85
Shortness of breath	13	0.11	32	0.63
Skin rashes	129	1.07	63	1.24
Others	42	0.35	10	0.20
Total taking prophylaxis	12,040		5,061	

*Data modified from [1]. Includes patients who took one or multiple doses of KI or tincture of iodine.

This caution also applies to KI administration to women in the second half of pregnancy. In addition, there were four cases of thyroid pain in adults (0.08%) and none in children. These subsided spontaneously and were not followed up to ascertain the possibility of iodide-induced thyroiditis.

The thyroid status of children born in 1986 and examined in the second to third year of life was compared with that in an age- and sex-matched group born in 1987, when radioiodine was long gone from the environment. No significant differences existed between these two groups [27].

Extrathyroidal

Nonthyroidal side effects of KI occurred after a very small fraction of the total number of doses administered; they were, nevertheless, somewhat more common than expected (**Table X**). Vomiting was the most common. It is not clear to what extent this was due to maladroitness in the administration of KI. We were alerted to this possibility by the finding that those children receiving diluted tincture of iodine had about twice the incidence of vomiting as the remainder of the group. Similarly, a few cases of diarrhea and gastric complaints were noted in both children and adults, but it remains unclear to what extent this can be related to the iodide administered. There were no complaints of iodide mumps occasionally described in the literature after single-dose iodide administration. Skin rashes were reported in a surprising number—approximately 1%—of both children and adults. These were of a minor nature and there is no record that a dermatologist was consulted in any of them. A number of subjects with adverse reactions (18% of children and 22% of adults) consulted a physician for these reactions. In turn, approximately 80% of these visits were judged not to require further medical attention; thus it can be estimated that about 4% of all adverse reactions reported were medically significant. It should be pointed out that control values for these side effects in a population not receiving KI are not available. Also, the relation of some of these complications to iodide rather than to the panic conditions is uncertain at present. Nevertheless, we suggest an estimate of approximately 0.2% of the population studied had medically significant adverse reactions to KI. Two adults with chronic obstructive lung disease and known sensitivity to iodides nevertheless took KI out of fear of radiation and promptly developed acute respiratory distress that required hospitalization. This was not seen in any of the other patients.

COMMENTS

A number of studies have shown unambiguously that radioiodine uptake (burden) can be effectively blocked by KI administration provided this occurs before or within a few hours of exposure to the isotope [11,23,24,30,31]. The extent of protection and its duration are dose-related but even a large single dose (i.e., greater than 100 mg I^-/d) will not protect for much longer than approximately 36 hours. On the other hand, continuing radioiodine contamination could still be protected against, and the ability to respond as quickly as 24 to 48 hours after the decision to intervene had been made testifies to the value of well-organized pharmacy and distribution systems. In many other countries, such centralization does not exist, which emphasizes once again the need for storage of KI tablets in various critical locations that can demonstrably provide rapid distribution in case of an accident. During actual accident conditions, radioiodine contamination is likely to occur over extended periods, as was the case in Poland after the Chernobyl accident. Thus, even delayed KI prophylaxis will provide partial protection—the extent depending on the nature of the exposure versus time curve.

Many children under the age of 1 year in the 12 provinces would have received greater than 50 mSv in the absence of any protective measures. The calculated thyroid burden in some children up to 5 years of age also exceeded this limit. The protective measures of a single dose of KI and milk substitution lowered the burden to less than 50 mSv in most of the children at risk. The effective reduction in thyroid burden amounted to approximately 40%; this might have been increased to 60% to 70% with earlier prophylaxis, particularly with respect to inhaled ^{131}I. Continuing high levels of contamination would, of course, mandate repeated KI distribution.

The present program involved the largest population ever studied after a single pharmacologic dose of KI. Of the approximately 34,000 respondents to the questionnaire, 12,040 of 12,641 children received iodides, and 5,061 of the adults took iodides. No acute intrathyroidal sequelae were seen except for the transient thyroid blockade in newborn infants. Moreover, in adults with thyroid disease diagnosed before 1986, the 4-year follow-up showed the course of these disorders not to be affected by KI prophylaxis. There were a surprising number of mild gastrointestinal disorders both in children and in adults. The available literature [24,26], although very incomplete, does not reveal this to be a problem at the KI doses used. The bulk of these gastrointestinal complaints did not require medical attention, and we are uncertain at present whether they were due to psychologic factors, inept methods of KI administration, or intrinsic toxicity. We suspect that the number of these reactions would have been substantially reduced if KI had been available in tablet form. It should also be mentioned that in case of difficulties with the administration of KI to infants or children, there have been good results with syrup of hydriodic acid [32]. Similar uncertainties apply to some of the other side effects listed in Table X, but the approximately 1% skin rashes must be considered significant. There were no serious adverse reactions among the approximately 18 million doses of KI given except for the two adults with known iodide sensitivity who had severe reactions following KI; this serves as a warning that such patients must be identified, educated about their sensitivity, and excluded during prophylactic programs of this sort. Finally, the incidence of medically significant, but not serious, reactions to this single dose of KI was low enough (0.2%) to make us believe the KI distribution was the correct and safe response.

The response to a widespread accident like the Chernobyl "meltdown" is as much a social problem as a medical or scientific one. It requires rapid organization of large numbers of people and facilities, and for this the highly centralized structure of the Polish government of the time was very suitable. This is exemplified by the prompt mobilization of local health centers and volunteers, the efficient preparation and distribution of KI through a centralized pharmacy system, a nationalized powdered milk system, and so forth. This permitted the rapid initiation of response measures that likely would have taken substantially longer in less centralized systems. Since speed is of the essence, it follows that a well-planned emergency response and protective mechanism must be in place *before* an accident occurs and preferably tested by some sort of mock alert. This involves a protocol for dosimetry including an agreement on the intervention level, arrangements for evacuation in near-field regions, and storage of readily available KI (probably in a number of places in a large country). We believe that current shelf-life estimates for KI are underestimates, and that with suitable protection from light and moisture (i.e., foil-wrapped), shelf life can be extended for many years. Furthermore, a loss of 20% from a tablet of 130-mg KI will leave sufficient iodide for adequate protection. This is an argument for providing somewhat greater than minimal KI doses [31]. Another argument is the longer duration of protection after a larger KI tablet in case of a missed dose. Equally important is the identification of supplies of uncontaminated foods and milk, and, perhaps most important of all, a decision as to who will be in charge.

In addition to the above recommendations, the present study brought to light some tactical suggestions for future investigations.

(1) Compliance with questionnaires requires active supervision.

(2) Compliance with a powdered milk program is hard to evaluate in rural communities with their own milk supplies.

(3) Pregnant and lactating women will have to be vigorously recruited for programs designed to prevent ^{131}I ingestion.

(4) Dosimetry standards and equipment must be in place before accidents and should be available in several centers or in mobile units.

(5) Data required for dose reconstruction should be collected at the time of the accident to the extent possible, especially where direct measurement capability is limited. Obviously, as many direct thyroid radioactivity measurements as possible are desirable, but certainly enough such measurements should be available to validate dose reconstructions. "Hot spots" should be identified wherever possible to avoid skewing of exposure data.

(6) Control values for some of the side effects were not available for the present study and should (ideally) be sought during a panic situation of a different sort where KI is not involved. Moreover, control values for goiter and thyroid tumor prevalence within a national registry are indispensable for any subsequent evaluation of radiation effects.

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