Original article

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Thyroid disease in northern Italian children born around the time of the Chernobyl nuclear accident

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Background: The Chernobyl nuclear accident of 1986 caused a dramatic increase in the incidence of thyroid cancers in exposed children in Belarus. Airborne radioactivity from the reactor spread over northern Italy, where rainout gave rise to low levels of radioactivity at ground level.

Patients and methods: As the latency between exposure to ionising radiation and development of thyroid cancer is thought to be about 10 years, in 1996/1997 all children born in 1985 and 1986 and attending school in an area of Milan, Italy were examined for thyroid nodules. A total of 3949 children were examined by two physicians blinded to the examination and diagnosis of the other. The children were to be reassessed in 2001/2002.

Results: In total, 1% had palpable nodules. The nodule diagnoses were: Hurtle cell adenoma (one), thyroglossal duct cyst (one), thyroid cyst (four) and thyroiditis (four). The prevalence of thyroid disease in the cohort was indistinguishable from that of populations not exposed to radioactive pollution. Only 10 children re-presented for examination 5 years later; all were negative. The direct costs of the study were estimated at € 21 200.

Conclusion: The high cost of the study in relation to reassuring lack of increase in thyroid nodule prevalence suggests that further studies are not justified.

Key words: Chernobyl accident, childhood, ionising radiation, screening, thyroid disease

Introduction

Thyroid cancer is the third most common solid tumour of childhood, accounting for 0.5% to 1.5% of all paediatric malignancies [1, 2]. Differentiated thyroid carcinoma (DTC), which affects more girls than boys (ratio of 2.4–3.8:1, as in adults), is the most common histotype, and has two well-defined subtypes (papillary and follicular) [1–4]. DTC in paediatric age has an excellent prognosis, even when diagnosed late with distant metastases [5–7]. Although in most cases the first sign is a large neck mass with palpable lymph nodes, and in 5% to 28% lung metastases are present at diagnosis, 10-year survival exceeds 95% in all reports [5, 6, 8].

The only established environmental risk factor for thyroid carcinoma is exposure to ionising radiation [9–11], and the risk, particularly of papillary carcinoma [9–13], is greater the younger the age of exposure [9, 14]. Thyroid tumours caused by exposure to high doses of therapeutic radiation usually develop 6–8 years after irradiation, and can continue to appear up to more than 20 years later, particularly in children [9, 11, 13]. The latency between exposure to low doses of atmospheric radiation and thyroid cancer is expected to be about 10 years [9, 11–13, 15, 16].

Following the explosion of the Chernobyl nuclear reactor in 1986, a dramatic increase in the incidence of benign and malignant thyroid tumours (from 1 per million to 36 per million) was observed in children born or conceived around the time of the accident in a considerable area surrounding the reactor [17, 18]. However, in children born a year later, the incidence had dropped abruptly to the low levels expected in unexposed populations [19–21]. The accident released a radioactive cloud that was carried by the wind in a predominantly westward direction. A few days later it reached western Europe, including northern Italy. In northern Italy in particular, low but significant radioactive contamination was observed on the ground and in the food chain, the main isotopes being the fission products, ^{131}I and ^{137}Cs [17–21].

Around the 10th anniversary of the accident, the mass media in Italy raised the spectre of the risk of radioactive pollution from Chernobyl, renewing concern about the development

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of thyroid cancer in children born in the year of the accident. For this reason we embarked on a study in 1996, 10 years after the accident, to assess the thyroid status in a population of Italian children born in 1985 or 1986. The study aimed to check the children twice, in 1996/1997 and in 2001/2002, to assess, respectively, any increase in the prevalence and incidence of thyroid nodules and cancer. The results of that study are presented here.

Methods

Population

All schoolchildren born in 1985 or 1986 and attending primary schools in Local Health Service area 76 (southwest Milan) were eligible for the study. This area contains the European Institute of Oncology (IEO). In all, 4318 children (2002 girls and 2316 boys) were eligible, but only 3949 were examined.

Study design

Information. Before starting the study, we informed the local population by publishing articles explaining the aims and methods of the study in local newspapers, and obtained the willing consent of the local health and school authorities. We also convened a meeting of all local general practitioners (GPs) and held parent meetings at the schools, explaining the study and answering questions. All eligible children were given a letter to take home to their parents, again explaining the aims and methods of the study. The parents were requested to fill in a questionnaire asking where the mother was living during the pregnancy and about any family history of thyroid disease. The parents were asked to sign the accompanying informed consent form. Only children whose parents signed the consent form were included in the study and examined. The result of each child's examination was sent to the parents. Whenever a thyroid condition was revealed, we met the parents and family GP to explain the findings and propose additional examinations and treatment where necessary.

First examination. The examinations were carried out during school hours in the school medical room. Parents of children absent from school on that day were informed and invited to bring their children to the IEO outpatient clinic for examination. Each child was examined by two physicians experienced in thyroid examination, one being a surgeon (N.T., L.C., G.G. or F.C.) and the other an endocrinologist or nuclear medicine physician (B.G., G.P., C.D.C. or C.G.). The examination was carried out as specified by the WHO criteria for thyroid disease screening programs [22, 23]. Each physician was blinded to the examination and findings of the other. The findings were classified according to the WHO score as follows: 0 = negative, Ia = enlarged gland without nodules, Ib = palpable nodule. When there was discordance between the two examinations, the disagreement was recorded and the worst diagnosis considered.

If an enlarged thyroid or a nodule was found, an examination programme was proposed. For enlarged thyroid gland (Ia), clinical follow-up was recommended for at least 2 years. For palpable nodules (Ib), thyroid ultrasound examination, blood tests, fine needle aspiration biopsy (FNAB) and in some cases surgery were proposed.

Evaluation 5 years later. Parents and children were informed that a further clinical examination, similar to the initial one, would be available to all 5 years later, to further check for thyroid disease and assess the outcome of any previous condition. A letter was sent out to all parents 4 years after the first intervention, informing them where they should take their children for the second examination.

Table 1. Estimates of equivalent dose to the thyroid (mSv) for people in the Milan area in May 1986

	Protected	Unprotected
Adults	1.9	6.2
Children (1–10 years)	4.5	28.5
Infants (< 1 year)	4.5	39.5

The theoretical probability of developing a radiation induced thyroid cancer for children exposed to radioactive pollution during their first year of life in the Milan area (1986) is in the range $6.75–89.55 \times 10^{-5}$.

Radioactive background and risk evaluation

The radioactive pollution in the Milan area in May 1986 had been monitored daily, and from these data [24] it was possible to estimate the mean quantity of radioactive iodine absorbed by the thyroid and the corresponding dose. The amount of incorporated ^{131}I depended on the age and on the protection measures adopted, which included assumption of levo-tyrosine (Table 1).

According to ICRP Publication 60 [25], for an adult population, the nominal coefficient of probability $P_{1,a}$ of developing a lethal thyroid tumour caused by exposure to ionising radiation over a lifetime is given by:

$$P_{1,a} = 0.08 \times 10^{-2}\text{Sv}^{-1}$$

Mortality for thyroid cancers is low, <10% 20 years after surgery. For this reason, we estimate that the probability P_a of developing a cancer is about nine times greater than the probability of developing a lethal cancer:

$$P_a = 0.75 \times 10^{-2}\text{Sv}^{-1}$$

For children of age 0–10 years, the probability $P_{s,c}$ is two to three times greater [25]:

$$P_{s,c} = (2–3) \times P_a$$

The equivalent dose absorbed by the thyroid of children in this age range as a consequence of inhalation and ingestion of ^{131}I was evaluated as the absorbed equivalent dose [24] and was in the range $[4.9–39.8] \times 10^{-3}$Sv. The probability of occurrence of thyroid tumours in the same population can be evaluated by multiplying the nominal coefficient of probability by the estimated equivalent dose, and is therefore given by:

$$P_{s,c} = [2–3] \times 0.75 \times 10^{-2}\text{Sv}^{-1} \times [4.9–39.8] \times 10^{-3}\text{Sv}$$
$$= [6.75–89.55] \times 10^{-5}$$

By multiplying this probability by the number of children examined (3969), one would expect about one to four cancers (lethal and non-lethal) and 130 nodules (benign tumours, cysts, goitres and inflamed thyroids) in the study population.

Cost analysis

We estimated the direct costs of the study by summing secretarial costs, postage, stationery telephone calls, physicians' time and the costs of the ultrasound examinations and blood tests. Secretarial costs were calculated from the salary of the secretary and the hours spent on the study. The physicians' time was calculated from the average salary of all the physicians involved. Each doctor nominally spends 48 h a week at the hospital; we therefore calculated the value of 1 h by dividing the monthly salary by

192 and then multiplying this value for the hours spent by each doctor in the schools visiting the children. Costs of imaging and blood tests were calculated as the prices paid by the Italian Health Service. We did not consider any other costs.

Results

The information program

This started in October 1995 and lasted 8 months; during this period, we published local newspaper articles. From January 1996 to May 1996, meetings with parents and GPs were held; at least one adult member of all the children's families participated. It emerged that the great majority were favourable to the study, although the majority wanted no imaging or blood tests in the baseline evaluation, but agreed that their children should undergo further tests if a nodule was found.

Baseline intervention

This lasted 9 months (September 1996 to May 1997). Of the 4318 children (2002 girls and 2316 boys) eligible, 3949 underwent clinical examination at school, 369 (8.5%) did not. Of the latter, 171 refused and 198 were not at school and did not present at the IEO outpatient clinic (Table 2).

The findings of the baseline examinations are shown in Table 3. Thirty-seven (1%) children were classified as Ib (palpable nodule), and were proposed for thyroid ultrasound scan and blood tests. However, seven refused further examination, in all cases because their condition was known and they were being followed elsewhere. Of the remaining 30 children (Table 4), the four with thyroiditis were given therapy and checked twice a year. The five children with thyroid cyst or thyroid duct cyst all refused treatment but consented to follow-up, and were programmed for clinical and ultrasound examination twice a year. The only child with a solid nodule underwent hemithyroidectomy and isthmusectomy; her histological diagnosis was Hurtle cell adenoma. She is being examined at 6 monthly intervals by ultrasound, blood tests and physical examination, and at last check-up was free of disease.

Table 2. Study population

	Total	Boys	Girls
Eligible	4318	2316	2002
Refused	171	104	67
Absent	198	122	76
Examined (%)	3949 (91.5)	2090 (90.2)	1859 (92.9)

Table 3. Clinical diagnoses [*n* (%)]

WHO Class	Total	Boys	Girls
0/negative	3421 (86.6)	1878 (89.8)	1543 (83.0)
Ia/enlarged thyroid, no nodule	491 (12.5)	192 (9.3)	299 (16.1)
Ib/palpable nodules	37 (0.9)	20 (0.9)	17 (0.9)

Table 4. Ultrasound diagnoses of Ib thyroid nodules

Diagnosis	No. of cases
Adenoma (Hurtle adenoma by histology)	1
Thyroglossal duct cyst	1
Thyroid cyst	4
Thyroiditis (+ increased blood antibodies)	4
NED	20
Total	30

NED, enlarged asymmetrical hypertrophy of the thyroid gland with no evidence of disease.

Table 5. Direct costs of study

Item	Hours	Cost (€)
Secretary	140	1400
Physicians	740	14 400
US examination and blood tests	10	5000
Telephone, postage, stationery		1000
Total	890	21 200

US, ultrasound.

The remaining 20 children had asymmetrical hypertrophy of the thyroid gland but no evidence of disease; none developed further thyroid pathology. No relationship was found between family history of thyroid diseases and thyroid nodules in children.

Incidence evaluation

All the families of the children who underwent baseline evaluation were further invited by letter to participate in the second part of the study in October–December 2001, but only 10 answered positively and underwent this second visit. All were negative. A renewed invitation was sent in May/June 2002, but there was no further response.

Cost evaluation

Direct costs are shown in Table 5. We calculated that one secretary worked for at least 1 month on the study (writing letters, calling schools and families, arranging visits to schools and the IEO, and arranging tests after the clinical examinations).

Twenty hours per week of physicians' time was spent examining the children at their schools over a period of 36 weeks (total 720 h). Based on the average monthly salary of all physicians involved, this came to € 14 400. The cost of phone calls, stationery and postage was estimated at € 1000 and the cost of the ultrasound and blood examinations at € 5000.

It proved impossible to calculate indirect costs which included the time spent by doctors and teachers in meetings to arrange the study, meetings with parents, and time spent by parents accompanying children to the IEO.

Discussion

Ultrasound examinations carried out before the Chernobyl incident had found no differences in the incidence of cysts, nodules or autoimmune thyroiditis in children from areas of the former USSR that became contaminated compared with those that remained uncontaminated [10, 19]. The incident caused a dramatic increase in the incidence of thyroid cancers in children in a considerable area surrounding the reactor [19–21]. Furthermore, many children in contaminated regions of the Ukraine were found to have radiation dose-dependent increases in serum thyroxine levels, but no overt clinical thyrotoxicosis. The effect was most marked in the youngest children, but in all cases levels had returned to normal 12–18 months later [14, 21]. The suspicion arises that this finding may portend future thyroid disease, especially because mild dietary iodine deficiency characterises the region, suggesting the need for continued monitoring of these children.

The westward spread of radioactive contamination from Chernobyl across much of the European continent caused concern, although the reactions of national authorities varied widely: no measures, recommending iodine supplementation, intensification of normal monitoring programs, and banning the sale of fresh vegetables and milk products [18, 26].

Our estimates of local radioactivity levels and of absorbed dose indicated only a small increase in the risk of cancer and other thyroid diseases that would not show up in a population of around 5000. It would have been necessary to assess around 50 000 children to see such an increase, and such a large study would not have been justified by the high cost in relation to the expected small excess of cases. In fact, the criteria of Wilson and Junger were not fulfilled [27, 28], so a screening programme for thyroid cancer was not justified. Nevertheless, we considered it useful to determine the prevalence of thyroid diseases in the children of a circumscribed area born at the time of Chernobyl; apart from the scientific interest, there was worry about the consequences of the accident in Italy at the time of the 10th anniversary of the accident. We carried out a population study avoiding the possible bias of a volunteer group.

The prevalence of thyroid disease in our population was found to be indistinguishable from that in populations not exposed to radioactive iodine. Furthermore, we found no relationship between a family history of thyroid disease and the prevalence of thyroid nodules in the children studied. The relatively high incidence of symmetrically enlarged thyroid glands without nodules in girls of around 10 years of age may be linked to the physiological growth spurt that occurs at this age [23, 29].

We carried out only clinical screening on our population because the parents did not want instrumental examinations. Use of ultrasound and blood tests in suspicious cases provided an opportunity to assess the sensitivity of the clinical methodology, although such techniques are not part of normal screening.

Notwithstanding our calculations, it is not possible to predict with certainty the future incidence of thyroid cancer following exposure to low doses of ionising radiation; we therefore consider that we were prudent in carrying out our study, particularly since those exposed to even very low radioactivity at young age may be at increased risk [9, 11, 13]. Environmental monitoring at the time of the accident showed that the Milan area received low amounts of radioactivity, whereas in neighbouring areas, levels of radioactivity were considerably higher. The area covered by the Lombardy Cancer Registry was one such area but no increase in thyroid cancers has been observed there [2].

Compliance to the first phase of the study was very high (~ 90%) perhaps in relation to the prominent media coverage of the incident on the 10th anniversary of its occurrence. In contrast, only 10 of the 3949 invited children underwent the second examination. This disappointing second response meant we could not evaluate the incidence of thyroid conditions in our population. We surmise that in our healthy study population there was no longer any fear of cancer arising from what was by then a distant and half-forgotten event. The high costs of this study in relation to the finding of no increase in thyroid disease indicate that further population studies in areas that received only low radiation are not justified.

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