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Thyroid Cancer in the Age Group 0–19: Time Trends and Temporal Changes in Radioactive Fallout

Evis Sala and Jørgen H. Olsen

ALTHOUGH MORTALITY rates from thyroid cancer appears to be decreasing, the time trends for incidence (all ages combined) are increasing in many countries [1–6]. There is a marked female preponderance for this type of cancer; this is most remarkable in the sub-group of papillary carcinomas, which comprise approximately 40–60% of cases [4–7]. In adults, who dominate the picture, the increase has been attributed to widespred use of radiation therapy for benign conditions of the head and neck [8, 9]. Another possible cause of thyroid cancer, also in young patients, is environmental radiation pollution, as the thyroid is highly susceptible to radiogenic induction of cancer [10, 11]. In a cancer registry-based study of childhood cancers (ages 0–14 years) in the Province of Torino, Italy, a downward trend in incidence rates of thyroid tumours was found for the period 1967–1988 [12]. Although statistically not significant and based on only 13 cases, this decrease was reported to parallel dilution of radioactive pollution from nuclear tests carried out in the early 1960s.

The population of Denmark has been covered by complete cancer registration for almost 50 years. As radiation therapy for

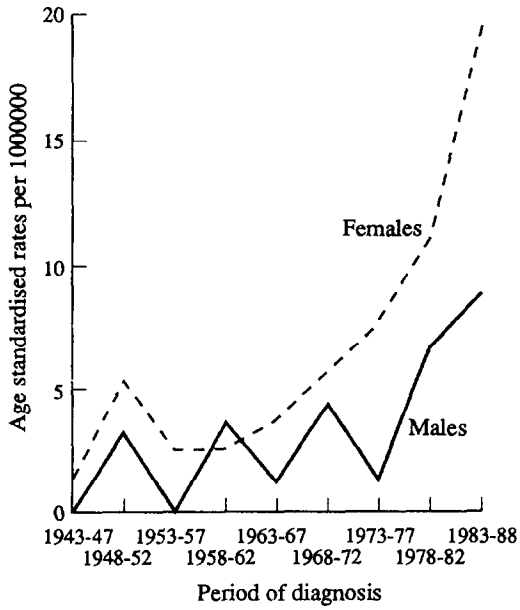

Fig. 1. Age-standardised incidence rates of thyroid cancer in the age group 0–19, Denmark, 1943–1988.

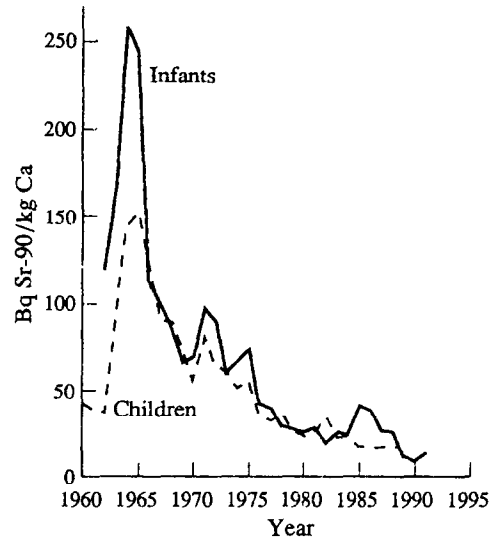

Fig. 2. Strontium-90 levels [sample number weighted mean measured in becquerel (Bq) per kg calcium] in bones of infants (> 1 month ≤ 4 years) and children (> 4 years ≤ 19 years), 1961–1987.

benign conditions of the head and neck has been used only rarely in Denmark [5], the cancer registry was used to follow the trends in incidence of thyroid cancer before and after exposures to fallout from atmospheric testing of nucler weapons during the 1950s and 1960s.

We included all cases of thyroid carcinoma and sarcoma in the age group 0–19 reported to the Danish Cancer Registry, 1943–1988. The diagnoses of cases reported during the period 1943–1977 were reviewed so that all cases could be classified according to the International Classification of Diseases for Oncology (ICD-O). Histopathological slides were not re-examined. Age-standardised incidence rates were calculated and adjusted to the World Standard Population [1], and time trends in incidence rates were tested by linear regression.

A total of 69 cases of thyroid cancer (46 in girls, 23 in boys) were registered during 1943–1988, to give an average of fewer than 2 cases per year. All cases were verified by histopathological examination. Figure 1 shows that the age-standardised incidence rates for this rare cancer increased significantly among girls, from 1.3 per million in 1943–1947 to 19.5 per million in 1983–1988, and among boys from none in the 1940s to 8.9 per million in the 1980s. When tumours were subgrouped according to histopathology [13] 68% of the cases were papillary carcinomas, 6% medullary and 4% follicular carcinomas: about 10% were other specified types of tumour, while 12% remained histologically unspecified in spite of the tissue examination performed. The papillary type was three times more frequent among girls than boys, but boys had a slightly increased frequency of the other histological types combined.

We also examined the geographical distribution of thyroid cancer in the age group 0–19 according to the east–west axis of the country and after subdivision into coastal and non-coastal municipalities. No differences were found in the incidence.

The steep increase over time in the incidence of thyroid cancer in Denmark, and in other areas with population-based cancer registration, is thus also evident among children and teenagers. Although improved diagnostic procedures and changes in histological criteria may have influenced the subgrouping of tumours over time, there is no reason to believe that the overall increase in thyroid cancer incidence is due to under-reporting of this tumour entity in the past: thyroid cancer is easy to detect and is not subject to misclassification by metastatic spread from other cancers. The finding that the incidence rates among girls are much higher than those among boys is contrary to those for most other childhood tumour types [14]. The increase appears to have begun in the mid-1960s and is particularly steep for girls, in contrast to the observations made in the Italian study of a decrease in incidence rates among children over the same period.

Figure 2 shows the strontium-90 levels in bones from infants and children in Denmark over the period 1961–1987 [15], which reflects the level of radioactive fallout from atmospheric testing of nuclear weapons worldwide [16]. A maximal build-up of strontium-90 occurred in the bones of children during the period 1961–1968. However, all children and most teenagers included in the high incidence period for thyroid cancer (1983–1988) were born after 1968, i.e. among people who were of low-dose generations (Figs 1 and 2).

In conclusion, atmospheric pollution by radioactive material particularly in the 1960s does not seem to explain the increasing trends in thyroid cancer among children and teenagers in Denmark since the mid-1960s. Other environmental factors must be searched for.

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Oestrogen Replacement Treatment and the Risk of Endometrial Cancer: an Assessment of the Role of Covariates

Fabio Levi, Carlo La Vecchia, Cristina Gulie, Silvia Franceschi and Eva Negri

The relationship between oestrogen replacement treatment and the risk of endometrial cancer was analysed in a case–control study of 158 histologically confirmed incident cases below the age of 75 and 468 controls in hospital for acute, non-neoplastic, non-hormone-related conditions conducted in the Swiss Canton of Vaud in 1988–1992. Overall, 60 (38%) cases vs. 93 (20%) controls had ever used oestrogen replacement treatment: the corresponding mutliple logistic regression relative risk (RR) was 2.7 (95% confidence interval, CI: 1.7–4.1). The risk was directly related to duration of use, and rose to 5.1 (95% CI: 2.7–9.8) for > 5 year-use. The RR was still significantly elevated 10 or more years after stopping use (RR = 2.3, 95% CI: 1.2–4.5). When the role of covariates was considered, a significant interaction was observed with body mass index (RR for long-term oestrogen use = 6.0 for lean or normal weight women vs. 2.4 for overweight women). There was also a hint of a negative interaction with oral contraceptive (OC) use, since the RR for oestrogens was higher (or restricted) to women who had never used OC (RR = 5.4, for long-term oestrogen use), as compared with those who had used OC, who showed no significant evidence of association with oestrogens (RR = 0.9 for long-term use). There was no significant interaction with cigarette smoking. Thus, this study confirms the presence of a strong association between oestrogen replacement treatment and endometrial cancer risk, since in the late 1980s or early 1990s about 25% of cases could be attributed to oestrogen replacement treatment in this Swiss population. Further, it confirms the presence of significant negative interactions of oestrogen use with obesity, and, possibly, with OC as well.
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INTRODUCTION

THE RELATIONSHIP between oestrogen replacement therapy (ERT) and the risk of endometrial cancer was originally suggested on the basis of the observation of a substantial rise in the incidence of this neoplasm in the United States in the early 1970s, following the spread of ERT [1]. In 1975, two case–control studies gave direct and quantitative epidemiological support to the association [2, 3].

Since then, at least 20 studies have been published on the topic. Their overall evidence indicates that the risk is about 3- to 4-fold greater in ever-users than in never users, and rises with the dose and duration of use, being up to 10-fold elevated in women who had used high-dose oestrogen for 10 years or more [4].

If the existence of an association is, therefore, beyond any reasonable discussion, there are still some points open to debate. Firstly, it is useful, on a public health scale, to understand the extent to which, if at all, indications from earlier epidemiological studies modified the subsequent patterns of prescription and risk. Secondly, most studies came from North America, and there were only four published investigations from Europe [5–8], where, at least in terms of attributable risk in the population,