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Editorial Comment

Thyroid cancer following Chernobyl

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The explosion on 26 April 1986 at the Chernobyl nuclear power station in northern Ukraine caused a massive release of radioactive material into the atmosphere. The most heavily contaminated areas nearest to Chernobyl were in what are now the three independent countries of the Ukraine, Belarus and the Russian Federation; some children in these districts received doses of radiation to the thyroid in excess of 1 Gray (Gy) [1,2]. The radioactive cloud spread over most of Europe, leading in many countries to excess doses of more than 10% of annual natural background radiation [3]. Increased radiation attributable to Chernobyl was even detected in North America [4].

Exposure to ionising radiation is associated with an increased risk of a wide range of cancers. Epidemiological studies of cancer following Chernobyl have so far concentrated on two diagnostic groups, namely thyroid cancer and leukaemia. In countries closest to the site of the accident, studies of thyroid cancer have predominated. Further afield, most attention was given initially to leukaemia, although there has been an increasing amount of research on thyroid cancer.

Indications of a rising incidence of thyroid cancer among young people in the heavily contaminated areas emerged within 4 years of the disaster. There were good reasons to expect that there would be an increase in the risk. Much of the initial deposit of radioactive material consisted of iodine, which is readily taken up by the thyroid gland. The thyroid in young people, and especially in infants, is particularly vulnerable to radiation and there is convincing evidence for a carcinogenic effect even of doses as low as 0.1 Gy [5]. The initial reports of raised incidence of thyroid cancer were, however, met with a great deal of scepticism. Thyroid carcinoma is often a fairly indolent disease which can remain undiagnosed for many years and autopsy studies have revealed high rates of occult thyroid cancer [6]. As the exposed populations were subjected to intensive screening for thyroid disease, it would have been very surprising if the incidence of thyroid cancer had not risen. In addition, there was suspicion that some recorded cases, particularly if without histological confirmation, were in fact non-malignant or even non-neoplastic. While the implied relative risks were already substantial, the actual case numbers in the early years were still small and it seemed possible that earlier diagnosis and more efficient ascertainment, together with some misdiagnosis and the play of chance might between them account for any excess. Before long, however, it was clear that there was a real and probably very large increase in the occurrence of thyroid cancer among the younger members of the most heavily exposed populations. On the assumption that all thyroid carcinomas diagnosed before 1991 were unrelated to Chernobyl, screening may itself have been responsible for an increase in incidence by a factor of 1.5–3. In the most severely affected areas of Belarus, the Ukraine and Russia, recorded incidence rose by a factor of 7–9 between 1986–1990 and 1991–1995 [2,7,8], as shown in Table 1.

The sheer size of the increase could hardly be accounted for by screening alone and it is now accepted that a large part of the rise in incidence is attributable to radiation exposure from Chernobyl. Young people with thyroid cancer in the regions of highest incidence have become one of the most intensively studied groups of cancer patients in the world, to the extent that there have been rumours of a market in tumour tissue [9].

Even though many of the thyroid cancers in the high-incidence regions have been detected by screening, they have been shown to be more aggressive than thyroid carcinomas in western Europe that were presumed not to be radiation-induced. The largest comparative study included 472 patients diagnosed before the age of 21 years in Belarus, representing nearly 98% of cases in the country from May 1986 to December 1995, and 369 consecutive patients of the same age from three major treatment centres in Italy and France [10]. In the

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Table 1
Thyroid cancer incidence among young people in the years following Chernobyl: annual rates per million in the most highly contaminated regions of Ukraine [2], Belarus [7] and Russia [8]

	Ukraine Age 0–14 years Six northerly regions	Belarus Age 0–14 years Gomel	Russia Age 0–17 years Bryansk
1986–1990	1.8	10.5	2.1
1991–1995	12.8	97.0[a]	17.1

[a] 1991–1994.

Belarus series, only 5% of tumours were of the less malignant follicular subtype, compared with 15% in Italy and France. Extension outside the thyroid was markedly more frequent in Belarus (49% compared with 25%) and lymph node metastases were somewhat more common (65% compared with 54%). More than half of post-Chernobyl thyroid cancers in Belarussian children have exhibited rearrangements of the *ret* oncogene, with some evidence of a higher frequency of *ret*/PTC3 rearrangements in tumours with shorter latent periods [11].

Allowing for the screening effect, the excess absolute risk of thyroid cancer has increased year on year until at least 1995. In both Belarus and Russia, the risk has been found to be highest among those who were youngest at the time of the accident [12,13]. This is consistent with the results of studies of thyroid carcinoma following irradiation from other sources [5]. In addition, young age at the time of the accident has been associated with greater severity of disease as indicated by extrathyroidal tumour extension, lymph node involvement and distant metastases [14].

Outside the immediate vicinity of Chernobyl, where radiation exposure was relatively small, the European Childhood Leukaemia-Lymphoma Incidence Study (ECLIS) was set up to monitor the incidence of these diseases in relation to estimated exposure levels [3]. Childhood leukaemia was chosen because it shows the earliest and largest relative increase in risk following radiation exposure and high quality cancer registration data were most readily available. After 5 years of follow-up, no dose related increase in incidence was detected, a result which was consistent with current estimates of leukaemogenic risk of radiation exposure [3].

Studies of thyroid cancer were initiated in several countries of eastern and southern Europe [15]. When their results were collated after less than 10 years, there were few indications of increasing incidence attributable to radiation from Chernobyl. This was not surprising as exposure levels were relatively low and the duration of follow-up in most studies was less than 7 years.

The article by Cotterill and colleagues (pp. 1020–1026) is the first to present incidence rates for thyroid cancer post-Chernobyl among young people outside the former Soviet Union for a period ending as recently as 1997. Their study region, the North of England, includes the area of the UK that received the heaviest fallout, although this was still considerably lower than in many other European countries. They found a significant increase in the incidence of differentiated thyroid carcinoma among young people aged under 25 years between 1968–1986 and 1987–1997. It is tempting to attribute the increase to radiation from Chernobyl, but this interpretation must be subject to several caveats.

The county with the greatest increase in incidence between the two periods, Cumbria, was the one which received the highest level of fallout. The scale of the increase in Cumbria was largely due to the very low rate in the earlier period, based on a single case. The actual incidence rate in Cumbria since 1987 was not as high as in the city of Newcastle upon Tyne, where the radiation dose was an order of magnitude lower. The extent to which the very low initial incidence in Cumbria reflects low risk in the period before Chernobyl is unknown. Incidence among adults aged 45 years and over during 1968–1985 was slightly below the national average [16]. For men, the former county of Cumberland, covering the North and West of Cumbria, had a significantly low incidence but Westmorland, covering most of the remainder of Cumbria, had one of the highest rates in England; for women, Cumberland again had a lower incidence, but the difference between Cumberland and Westmorland was less marked.

Any increase in thyroid cancer risk related to Chernobyl would be expected to be highest among those who were youngest at the time of exposure. In this study the rate ratio between 1987–1997 and 1968–1986 was slightly higher for children aged under 15 years than for adolescents and young adults aged 15–24 years. It seems unlikely, however, that thyroid cancers occurring before 1991 were a result of exposure to Chernobyl fallout. The incidence among children was actually lower in 1991–1997 than 1987–1990, though based on only 2 cases in each period. In the older age group, however, incidence in 1991–1997 was higher than during the first few years post-Chernobyl. It is not stated whether incidence trends in Cumbria were the same as for the whole region but, as there were only 6 cases in Cumbria during 1987–1997, the result would be virtually impossible to interpret.

Trends in incidence for histological subtypes are not formally presented. While the relative frequencies of follicular/mixed and papillary carcinoma were not significantly different during the two periods, it does appear that the incidence of follicular/mixed carcinoma has remained relatively constant whereas the incidence of papillary carcinoma in 1987–1997 was approximately three times that in 1968–1986. This is consistent with the fact that the much larger increases in the areas closest to Chernobyl have been almost entirely accounted for by

papillary carcinoma. Data on histological subtype by county are not presented, but interpretation would again be rendered very difficult by the small numbers.

As the authors readily admit, a major limitation of their study is the small sample size. There are two ways in which this problem could be addressed. The first is to increase the study population by greatly broadening the geographical coverage to allow for a more powerful investigation of the short-term effects of radiation exposure. This is being done through an international study of thyroid cancer by the European Childhood Leukaemia-Lymphoma Incidence Study (ECLIS) group and the results are eagerly awaited. The second is to study the same population for a much longer period. The risk of radiation-induced thyroid cancer persists for 40 years following exposure, though it does decline after about 30 years [5]. Particularly as adolescents and young adults are among the most mobile sections of the population, true follow-up studies of cohorts living in a specified region would be required, rather than cross-sectional incidence studies that with time would be increasingly compromised by migration. While it would be difficult to identify all people who were resident in the study region at the time of deposition of Chernobyl fallout, it should be relatively straightforward to identify those who were born there over a specified period and study their long-term cancer risk. Researchers in the UK are well placed to carry out such studies through the routine linkage of cancer registrations with the National Health Service Central Registers, which cover virtually the entire national population. Their ability to do so in the future, however, depends on the continuation of the national cancer registration system which is currently under threat from the latest data protection legislation and official guidance on confidentiality.

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