EDITORIAL

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Childhood leukaemia and nuclear installations: the long and winding road

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The findings of Bunch *et al* (2014), published in this issue of *BJC*, provide the latest twist in the long-running tale of childhood leukaemia and nuclear installations. The saga effectively started 30 years ago when the Independent Advisory Group (Chairman: Sir Douglas Black) (1984) confirmed a media report of an ∼10-fold excess incidence of childhood leukaemia over three decades in the village of Seascale on the Cumbrian coast of Northwest England. Attention naturally focused on the possible role of the nearby Sellafield nuclear complex, particularly on the risk of exposure to ionising radiation from radioactive material discharged into the environment, although chance could not be confidently excluded as an explanation for this *post hoc* observation of a cluster of around half a dozen cases. It is beyond reasonable doubt that briefly delivered moderate and high doses of radiation can cause childhood leukaemia (Wakeford, 2013), but a detailed radiological risk assessment carried out for the Independent Advisory Group (1984) found that the doses estimated to have been received by children in Seascale from Sellafield discharges were generally less than those received from natural background radiation and were less than 1% of the dose required to account for the excess cases of childhood leukaemia in the village.

Inevitably, doubts were expressed about the accuracy of the radiological risk assessment: whether the discharge data and dose estimates were accurate, and whether the radiation-induced leukaemia risk model used was appropriate for these exposure circumstances. These concerns were reinforced by the subsequent need to revise the Sellafield discharge chronology (although this did not materially affect the assessed risks because environmental monitoring results had been used whenever possible) (Committee on Medical Aspects of Radiation in the Environment (COMARE), 1986), and by the results of some rather over-enthusiastic epidemiological studies presumably driven by the idea that a dramatic error in conventional radiological risk assessment methodology was awaiting discovery (Wakeford *et al*, 1989).

However, it became clear that the incidence of childhood leukaemia near the Dounreay nuclear establishment on the northern coast of Scotland was also unusual, particularly in the western part of the town of Thurso (Committee on Medical Aspects of Radiation in the Environment (COMARE), 1988). Following the observation at Seascale, this finding naturally increased uncertainty in the accuracy of the radiological risk assessments. Nonetheless, the risk assessment conducted for children living in the vicinity of Dounreay found that the doses received from radioactive discharges were less than those in Seascale and ∼0.1% of the level needed to explain the excess cases, so any error in the risk estimates must be large and therefore amenable to identification through appropriate scientific studies (Committee on Medical Aspects of Radiation in the Environment (COMARE), 1988).

One of the recommendations of the Independent Advisory Group (1984) was the establishment of the independent expert Committee on Medical Aspects of Radiation in the Environment (COMARE) to advise the UK Government, and this was done in 1985. The Committee on Medical Aspects of Radiation in the Environment (COMARE) (1988) considered that 'some feature' of the nuclear installations was likely to be responsible for the excess cases at Seascale and near Dounreay, but did not conclude that this 'feature' was necessarily related to radiation exposure. This caution was seemingly justified by increasing evidence by the end of the 1980s that no errors were present in the radiological risk assessments of a magnitude that could account for the excess cases (Stather *et al*, 1988; Wheldon, 1989).

It was in 1990 that an explanation for the Seascale cluster in terms of radiation exposure seemed to have been found, but not exposure of the affected children themselves, but rather of their fathers while working at Sellafield prior to the conception of their offspring. This suggestion arose from a case–control study of young people in West Cumbria (Gardner *et al*, 1990) and received substantial publicity. However, the finding was based on a very small number of cases, was not capable of explaining the absence of a marked excess of cases among children born to the great majority of Sellafield workers living outside Seascale, had little biological

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basis, and was not confirmed by studies using independent data (including, for example, a case–control study of young people near Dounreay); the hypothesis has now, in effect, been abandoned (Doll *et al*, 1994; Committee on Medical Aspects of Radiation in the Environment (COMARE), 2002; Wakeford, 2003).

However, reports of raised risks of childhood leukaemia near some nuclear installations continued to appear in the 1990s and 2000s, the cluster of cases around the Krümmel nuclear power station in northern Germany being particularly striking (Hoffmann *et al*, 2007). The interpretation of these findings has not been straightforward (Committee on Medical Aspects of Radiation in the Environment (COMARE), 2011), and again, the assessed risks from radioactive discharges were much too small to account for the reported excess cases.

One aspect of exposure to discharges that has been examined in some depth is the risk from internally deposited radioactive materials ('internal emitters'), as it has been proposed that conventional risk estimates derived primarily (but not solely) from exposure to external sources of penetrating radiation (such as gamma-rays from the atomic-bomb explosions over Hiroshima and Nagasaki) are not appropriate for determining the risks from internal emitters, and that these risks have been grossly underestimated (Committee Examining Radiation Risks of Internal Emitters (CERRIE), 2004). However, an investigation of this suggestion has not revealed evidence of serious errors (Committee Examining Radiation Risks of Internal Emitters (CERRIE), 2004). For example, atmospheric nuclear weapons testing in the late-1950s and early-1960s led to global radioactive fallout and exposure to a spectrum of radionuclides very similar to that for releases from nuclear installations, but although doses from internal emitters in fallout were larger (generally much larger) than those from installation discharges, there is no evidence of an impact of fallout on childhood leukaemia risk that is much greater than conventionally assessed (Wakeford *et al*, 2010; Wakeford, 2014).

The periods during which the excesses have been apparent have added to the puzzle: in Seascale the cluster started in the early 1950s and existed until at least the early 1990s (Committee on Medical Aspects of Radiation in the Environment (COMARE), 1996), while around Dounreay the increased incidence seems to have been concentrated in the 1980s (Black *et al*, 1994). Now, Bunch *et al* (2014), after examining leukaemia incidence in young people during 1963–2006, have found that the excesses of cases in Seascale and around Dounreay disappeared in the early-1990s, compounding the problems of interpretation.

What could be the explanation for all of this? Some radical defect in the radiological risk assessments might have been persistently overlooked during the past three decades, but this seems most unlikely given the substantial attention paid to this issue. On the other hand, perhaps there has been over-concentration on just a few pieces of the complex jigsaw that is the aetiology of childhood leukaemia. For example, the remarkable childhood leukaemia cluster at Fallon, Nevada, away from any nuclear installation (Steinmaus *et al*, 2004) and the evidence for a generally non-uniform geographical distribution of childhood leukaemia incidence throughout Great Britain (Committee on Medical Aspects of Radiation in the Environment (COMARE), 2006) suggest that there are important, probably widespread, risk factors that can produce localised aggregations of cases. Perhaps this is the common 'feature' of childhood leukaemia clusters near some nuclear installations?

Of considerable importance in this respect is the evidence that has accumulated over the past 25 years that childhood leukaemia has an infectious basis (Kinlen, 2012). Indeed, it was the Seascale cluster that prompted the hypothesis that childhood leukaemia is a rare response to a common, but unidentified, infection, and that marked mixing of populations from rural communities (with more people susceptible to infection) with those from urban areas (with more people infected) can give rise to subclinical 'mini-epidemics' of the relevant infection and an excess of cases of its rare response, childhood leukaemia (Kinlen, 1988). With various large construction projects at Sellafield, remote rural Seascale has experienced exceptional population mixing over four decades, and its remarkably large proportion of high socio-economic status families may have promoted the impact of any infection (Kinlen, 2011). West Thurso, on the other hand, experienced substantial population mixing in the early-1980s due to the North Sea oil construction industry (Kinlen *et al*, 1993), which may account for the different temporal pattern of excess cases.

The last three decades have witnessed much effort expended on detailed investigations of the risk of childhood leukaemia near nuclear installations. It has proved to be a long and winding road to journey, with a variety of hypotheses involving exposure to ionising radiation coming into, and then going out of, fashion, but it was important to establish that no major errors were present in the scientific basis of radiological protection. However, it may well be that the patterns of incidence found near some nuclear installations are not caused by radiation, but by variations in risk that are much more general (Laurier *et al*, 2014). The journey may have led us to a better understanding of the aetiology of childhood leukaemia.

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