Cancer in the offspring of radiation workers

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Introduction

It is generally recognised that the irradiation of the abdomen of pregnant women increases the risk of leukaemia in their offspring.\(^1\)\(^2\) It is also known that irradiation of children, like that of people generally, leads to increased rates of leukaemia and of other cancers.\(^3\) This article is about another possibility – that irradiation of parents before the conception of their children can also lead to increased levels of cancer in their offspring.

The reason that this hypothesis (parental preconception irradiation or PPI) became of concern goes back to studies that were undertaken to explore the excess of leukaemia and non-Hodgkin lymphoma (LNHL) in young people near the Sellafield nuclear plant. Gardner and his colleagues\(^4\) carried out a case-control study in west Cumbria to investigate this cluster. They found an association between these diseases and relatively high doses PPI in workers at the Sellafield plant and suggested that this association was causal.

A number of studies were carried out to investigate the PPI hypothesis, in particular the 'record linkage studies' in which the Childhood Cancer Research Group played a major part. In these, cases of childhood cancer and matched controls were extracted from the National Registry of Childhood Tumours and other registries. Identifying information on the parents of cases and controls was obtained and these records were linked to those of radiation workers included in the National Registry for Radiation Workers (NRRW).\(^5\) Analyses were carried out to see whether the risk of childhood cancer increased with the radiation dose that their parents had received or whether the children of radiation workers overall showed a raised risk that was not related to the level of dose that they had received.

Three record linkage studies have been undertaken. The first was a general investigation of possible associations between PPI and childhood cancers. The second examined the question of whether radiation workers carried any risk with them when they left radiation work or whether any risk was confined to the period when they were so employed. The third was an extended investigation of the possibility of effects in the offspring of female radiation workers – there were too few female workers in the first two studies for firm conclusions to be drawn.

The first record linkage study\(^6\)\(^7\)

This included almost 36,000 children in Great Britain who had developed cancer. The parents of these cases and of their controls were matched with about 120,000 radiation workers included in the NRRW. It was found that fathers of children with LNHL were significantly more likely than fathers of controls to have been radiation workers (relative risk = 1.77, 95% confidence interval 1.05 to 3.03) but there was no dose-response relationship for any of the exposure periods studied. The relative risk was most marked for those who were monitored for exposure to radiation but received no doses above the threshold of detection of the dosimeter. No increased risk was found for fathers with a lifetime preconception dose of 100 mSv or more or with a dose in the six months prior to conception of 10 mSv or more, these being the dose categories for which Gardner et al had reported a positive association.

Many fewer mothers of cases and controls linked to the NRRW. In the analysis by dose category, none of the relative risks was significant and there was no trend in relative risk with dose. However, maternal radiation work was associated with a significant increase of childhood cancer (relative risk = 5.00, 95% confidence interval 1.42 to 26.94). This increased risk was not restricted to LNHL. The authors concluded that the numbers of cases and controls were too small for any reliable estimate of risk to be made.

It was concluded that the results did not support the hypothesis that paternal preconception irradiation is a cause of childhood leukaemia and non-Hodgkin lymphoma. The observed associations may have been chance findings or due to some aspect of being a radiation worker other than radiation itself. Perhaps the most plausible of the alternative explanations, at least for LNHL, was that of population mixing. This infection-based hypothesis postulates that at least some childhood leukaemia is a rare response to an unidentified infection and that levels will be increased in situations that promote contacts between susceptible and infected individuals, such as when in- fluxes of people occur in rural areas. Such mixing may occur around nuclear sites, which are usually in rural if not isolated areas.

The second record linkage study\(^8\)\(^9\)

This examined the importance of the timing of paternal employment as a radiation worker on the effects found in the first study. The second RLS used essentially the same set of cases and controls as the first, but took advantage of newly available updated estimates of radiation doses received by study participants. It was found that the elevated risk of LNHL in the children of male radiation workers was limited to those whose fathers were still radiation workers at conception or whose employment also continued until diagnosis. Children whose fathers stopped radiation work prior to their conception were found to have no excess risk of LNHL. This was not what would have been expected if a PPI effect was due to radiation damage to cells from which sperm develop. The authors concluded that the increased risk of LNHL among the children of male radiation workers was possibly associated with an increased exposure to some infective agent consequent on high levels of population mixing.

The third record linkage study\(^10\)\(^11\)\(^12\)

This study was undertaken in order to reassess the earlier finding of an increased risk of childhood cancer among the offspring of UK women radiation workers exposed to ionising radiation before the child's conception. The study involved the collection of new data as well as a pooled analysis of the new and original datasets and used a similar methodology to that in the earlier study. The new study included the mothers of almost 17,000 case children and an equal number of matched controls. When combined with the earlier results, mothers of over 52,000 childhood cancer cases and the same number of controls were included in the pooled analysis.

The new data provided no evidence of an association between childhood cancer and maternal preconception radiation work and analysis of the pooled data showed no statistically significant increase in childhood cancer risk. Considering the pooled data, a weak association was found...
between maternal radiation work during pregnancy and childhood cancer in offspring, although the evidence was limited by the small numbers of linked cases and controls. The authors concluded that, although the numbers of cases and controls remained low, neither the new nor the pooled data supported the earlier suggestion of a raised risk of childhood cancer in the offspring of female radiation workers.

**The conclusions of COMARE**

The Committee on Medical Aspects of Radiation in the Environment (COMARE), in its seventh report, reviewed all the available evidence concerning the incidence of cancer in the children of parents occupationally exposed to radiation prior to the conception of their children.

COMARE concluded that studies from the UK and Germany (but not elsewhere) suggested that the offspring of male radiation workers are about twice as likely to develop childhood leukaemia or non-Hodgkin’s lymphoma as other children but that the balance of the evidence indicated that this excess was not related to radiation dose. COMARE suggested that it might be associated with lifestyle factors, or work practices or population mixing.

**References**