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Leukaemia and nuclear installations

Occupational exposure of fathers to radiation may be the explanation

The study of leukaemia and lymphoma in West Cumbria reported today (p 423) was commissioned by the Black inquiry into the raised incidence of childhood leukaemia in the village of Seascale near the nuclear plant Sellafield.[1] The risk of childhood leukaemia was found to be unrelated to various indices of environmental contamination from the Sellafield discharges, such as eating seafood or home grown vegetables or playing on the beach. But the risk was raised if the children's fathers had been employed at Sellafield, particularly if they had had relatively high exposures of radiation before the affected children were conceived. The numbers are small, but the effects are large. The fathers of nine (out of 46) cases and 41 (out of 277) local controls were working at Sellafield when the child was born; but four of the case fathers and three of the control fathers had accumulated exposures to 100 mSv or more of external radiation before the child was conceived. An exposure of 100 mSv or more was associated with a sixfold to eightfold increased risk of leukaemia in the offspring. There was evidence of an increased risk at exposures lower than 100 mSv only when data for the six months before conception were considered, but the numbers were exceedingly small.

When children with non-Hodgkin's lymphoma were included with those with leukaemia the results were similar to those for leukaemia alone. By contrast, Hodgkin's disease showed no association with paternal exposure to radiation. Two control groups were selected—area controls, chosen to permit analysis of the geographical relationship of leukaemia to residence near Sellafield, and local controls, chosen to permit analysis of the relationship to parental occupation. Although each control group served a specific and different purpose the findings are similar regardless of which control group was used. Information for the study was collected by painstaking searching through birth and medical records, by examination of Sellafield employment records, and from postal surveys of parents of the children. Much effort has gone into checking the information collected and making it as accurate and complete as possible (p 429), but with diagnoses dating from as early as 1950 it is inevitable that some data are missing, especially those derived from postal surveys. There are few missing values for paternal employment, and details were obtained from birth certificates and Sellafield employment records, so the data relating to work at Sellafield are likely to be reliable and unbiased.

This study by Gardner and his colleagues' is the first to examine the relation between paternal employment in the nuclear industry and the risk of leukaemia in the offspring. Some comments seem appropriate at this stage even though the children of other nuclear workers need to be studied before firm conclusions can be drawn. Three separate inquiries into alleged increases of childhood leukaemia near different nuclear installations each concluded that there was a real excess but that the increases were too large to be accounted for by radioactive discharges from the plants.[1-3] Each report emphasised that alternative—but as yet unknown—pathways of exposure and mechanisms of carcinogenesis needed to be considered. The results of this study by Gardner *et al* are remarkable not because they offer little support for environmental contamination by radioactive discharges being the cause of childhood leukaemia but because they point to possible alternatives.

According to Gardner *et al* fathers' employment at Sellafield is sufficient to account for the raised incidence of childhood leukaemia in the vicinity. Could paternal employment account for the raised incidence of childhood leukaemia near other plants? The relative risk of childhood leukaemia ranges from 1·4 near Aldermaston and Burghfield to 5 near Dounreay and 10 near Sellafield.[1-3] This range is incompatible with the cause being environmental exposure to radiation: if that were the cause of the childhood leukaemia the relative risks would need to vary more than 1000-fold, since the estimated annual exposure of newborn infants from radioactive discharges ranges from 0·00001 mSv at Aldermaston to 0·005 mSv at Dounreay and 0·3 mSv at Sellafield.[3] The variation in occupational exposure at the plants is much less: the average in radiation workers ranges from 7·8 mSv at Aldermaston to 47·0 mSv at Dounreay and 124·0 mSv at Sellafield.[4-6] Thus the range of occupational exposure and the different mix of nuclear and other workers in the surrounding community is not inconsistent with the range of leukaemia risks observed.

The explanation offered by Gardner *et al* is not, however, without its problems. The only other relevant human data available are on the 7400 children of Japanese men who survived the atomic bomb explosions, and these show no hint of an increased risk of leukaemia in the offspring.[7] And the average exposure to external ionising radiation of the Japanese men was four times higher than that of the Sellafield workers. Some additional explanation will still be required for the children of Sellafield workers. For example, it could be argued that exposure to high levels of radiation at work is a surrogate for exposure to something other than radiation which itself is powerfully leukaemogenic in the next genera-

tion. There is, however, no known substance which increases the risk of leukaemia in offspring of those exposed. It is also possible that the most heavily exposed workers might inadvertently bring radioactive materials home—for example on contaminated clothing. Some studies have found unusually high concentrations of some radionuclides in the dust of workers' homes, but the extent of this domestic contamination was probably not sufficient to explain the excess of childhood leukaemia near Sellafield.[8] Another possibility is that internal rather than external radiation exposure is relevant. If workers were internally contaminated with a radionuclide which was concentrated in the urogenital organs or the semen the doses to the germ cell or the fetus could be greater than those recorded on the worker's externally worn dosimeters or film badges. The risk of prostatic cancer has been shown to be increased in some of the most heavily exposed employees of the United Kingdom Atomic Energy Authority and of the Atomic Weapons Establishment, and it has been suggested that some radionuclides may be concentrated in the prostate.[4 6] In both workforces the risk of prostatic cancer was increased more than 10-fold in the small group of workers with exposures to external radiation of 100 mSv or more, who also had been monitored for possible internal contamination by many different types of radionuclides, including tritium, plutonium, and uranium.[4 6] Information on internal contamination by radionuclides was not available to Smith and Douglas in their analysis of mortality from cancer in the Sellafield workforce[5] or to Gardner and his colleagues in today's report.

At this stage it is impossible to distinguish between the various pathways of contamination and the causal mechanisms which might explain the findings by Gardner *et al*. Despite their preliminary nature the implications are sufficiently important to warrant further investigation. Experimental evidence is sparce, and the finding that irradiation of male mice increases the risk of leukaemia in their offspring needs to be replicated.[9] Case-control studies similar to that of Gardner *et al* are already underway near the nuclear plants at Dounreay and at Aldermaston and Burghfield. Those studies are important, but they too are likely to be plagued by small numbers and large confidence intervals around whatever risk estimates are obtained. Other statistically powerful studies need to be devised, therefore, to discover not only more about the children of nuclear workers but also about the workers themselves. The Committee on Medical Aspects of Radiation in the Environment has already recommended cohort studies of nuclear workers' children.[2 3] Germ cell mutations can cause retinoblastoma and other childhood disorders,[10] and if the increased risk of leukaemia is caused by this mechanism then conditions other than leukaemia should also be studied in the offspring of workers. Highly exposed workers also need to be investigated for possible domestic contamination with radionuclides and also for the possibility that radionuclides might be concentrated in the urogenital organs or seminal fluids.

The results reported today are the first of their kind, and the risks described have large uncertainties associated with them. It would be premature to recommend formal changes to radiation protection limits on the basis of this one study; but until the findings from other studies are available workers need to be counselled and those who have not yet completed their families should be advised to avoid high exposures. The nuclear industry and its workforce have a good record for voluntarily limiting exposure and for collaborating with independent researchers in studying the health of the workers. This needs to continue. The more rapidly the mystery of childhood leukaemia near the nuclear plants can be unravelled the more rapidly steps can be taken to prevent it.

VALERIE BERAL
Director

Imperial Cancer Research Fund Cancer Epidemiology Unit, Radcliffe Infirmary, Oxford OX2 6HE

1 Independent Advisory Group. *Investigation of the possible increased incidence of cancer in West Cumbria*. London: HMSO, 1984. (Black report.)
2 Committee on Medical Aspects of Radiation in the Environment. *Third Report. Report on the incidence of childhood cancer in the West Berkshire and North Hampshire area, in which are situated the Atomic Weapons Research Establishment, Aldermaston and the Royal Ordnance Factory, Burghfield*. London: HMSO, 1989.
3 Committee on Medical Aspects of Radiation in the Environment. *Second Report. Investigation of the possible increased incidence of leukaemia in young people near the Dounreay Nuclear Establishment, Caithness, Scotland*. London: HMSO, 1988.
4 Beral V, Fraser P, Carpenter L, Booth M, Brown A, Rose G. Mortality of employees of the Atomic Weapons Establishment, 1951-82. *Br Med J* 1988;**297**:757-70.
5 Smith PG, Douglas AJ. Mortality of workers at the Sellafield plant of British Nuclear Fuels. *Br Med J* 1986;**293**:845-54.
6 Beral V, Inskip H, Fraser P, Booth M, Coleman D, Rose G. Mortality of employees of the United Kingdom Atomic Energy Authority, 1946-1979. *Br Med J* 1985;**291**:440-7.
7 Ishimaru T, Ishimaru M, Mikami M. *Leukaemia incidence among individuals exposed in utero, children of atomic bomb survivors and their controls, Hiroshima and Nagasaki, 1945-79*. Hiroshima: Radiation Effects Research Foundation, 1981. (RERF Technical Report 11-81.)
8 Goddard AJH, Minski MJ, Thornton I, Culbard EBC. *Household particulate survey. Radioactivity in house dust in West Cumbria and its significance*. London: Department of the Environment, 1986. (DOE Report DOE/RW/8703.)
9 Nomura T. Parental exposure to X rays and chemicals induces heritable tumours and anomalies in mice. *Nature* 1982;**296**:575-7.
10 Knudson AG. Genetics of human cancer. *Annu Rev of Genet* 1986;**20**:231-51.

Bovine spongiform encephalopathy

The safety of beef has not yet been tested and may not be testable

The outbreak of bovine spongiform encephalopathy has caused loss to farmers and continuing public anxiety about possible transmission of infection to humans through beef or milk. Histopathological findings and transmission in the laboratory leave no doubt that the disease belongs to the group of diseases—which includes scrapie, kuru, and Creutzfeldt-Jakob disease—that may be transmitted by unconventional agents.[1 2] Bovine spongiform encephalopathy is scrapie in cattle and is almost certainly acquired from infected sheep products in feed.[3] Similar transmission has occurred in captive deer,[4] in mink,[5] and most recently in studies in mice.[6] The agents and the diseases they can cause have certain characteristics of great importance to the investigation of the present bovine epidemic and its possible consequences.

The agents are extremely persistent and difficult to destroy. Their presence cannot be detected except by evident clinical disease or pathological changes in the brain. The incubation period is long. In man the incubation period after accidental contamination of the brain is about 18 months.[7] Symptoms of Creutzfeldt-Jakob disease after subcutaneous injections of human growth hormone prepared from pooled cadaveric pituitary glands appeared after a delay of 15 to 20 years.[8] Occasional cases of kuru, which is believed to be transmitted solely by cannibalism, still occur more than 30 years after this practice was abandoned.[9] In monkeys the incubation period after oral administration of large amounts of tissue infected with scrapie was 2·5 years.[10] Bovine spongiform encephalopathy develops in cattle some five years after eating