support the hypothesis, generated by the study of Gardner *et al*, that fathers' exposure to radiation before conception is causal. Unfortunately, in this new study few of the reported radiation exposures have been verified, and no information on dose is available. Also, three of the six fathers of cases who reported prenatal radiation exposure were included in the study of Gardner *et al*.⁴ If these cases are excluded, as would be appropriate for an independent assessment, the evidence suggesting an effect for preconception irradiation is much weaker.

Although the findings from both studies reported in this issue are not incompatible with an effect of paternal preconception radiation exposure of the size described by Gardner *et al*,⁴ neither offers strong confirmatory evidence. Indeed, the findings in the Scottish study indicate that if the cluster of cases around Dounreay truly results from reasons other than chance the excess cannot be explained through paternal exposure to radiation while working at the Dounreay nuclear plant.

As well as radiation McKinney *et al* examined many possible causative exposures. If exposure to ionising radiations before conception really does increase the risk of leukaemia then other mutagenic agents might be expected to have a similar effect, and McKinney *et al* examined exposures before, during, and after pregnancy. They report increased risks associated with several exposures at different periods, including paternal exposure to wood dust, carbon tetrachloride, trichloroethylene, benzene, coal, or graphite and maternal exposure to wood dust. Unfortunately, for none of these is the exposure verified nor the amount of exposure quantified. The strongest link is reported to be with exposure to wood dust before conception in both mothers and fathers. At least some of these findings may be due to chance. The authors made 480 comparisons and a significant result ($p < 0.05$) could be expected in about 10 to 20 by chance alone. At this stage it would therefore be prudent to regard the study of McKinney *et al* as having generated some interesting hypotheses rather than providing strong evidence of new aetiological factors.

The most persuasive evidence that factors before conception influence the risk of childhood leukaemia is provided by the finding of a 20-fold increased risk of leukaemia in children with Down's syndrome. How may we assess the leukaemogenic potential of radiation exposure before conception? The findings from the study of Gardner *et al*⁴ suggesting an effect of paternal preconception radiation may be an important new

lead, but it is important to seek verification of the findings shown in other populations.

Studies are already underway of the children of nuclear workers, but investigation is needed of people who may have conceived children after having been exposed to higher radiation doses than nuclear workers are typically exposed to—in such populations larger effects might be expected. A group of special interest in this respect would be children conceived after their parents had been successfully treated with radiotherapy for malignant or other disease (for example, the children of patients treated with x rays for Hodgkin's disease). This would allow the assessment of the effects of a high radiation dose delivered over a short period. (Relevant to this assessment is the finding that the children of the survivors of the atomic bomb explosions in Japan do not show an increased risk of cancer.¹⁰) If exposure to radiation must occur shortly before conception for leukaemogenesis, as was suggested by the findings of Gardner *et al*, the studies of the children of people exposed to a high radiation dose in a short period are less relevant. A more informative group would be the children of radiologists, especially of those radiologists who were in practice when radiation exposure levels were comparatively high.

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- 1 Independent Advisory Group. *Investigation of the possible increased evidence of cancer in West Cumbria*. London: HMSO, 1984. (Black report.)
- 2 Committee on Medical Aspects of Radiation in the Environment. *Second Report. Investigation of the possible increased incidence of leukaemia in young persons near the Dounreay nuclear establishment, Caithness, Scotland*. London: HMSO, 1988.
- 3 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.
- 4 Gardner MJ, Snee MP, Hall AJ, Powell CA, Downes S, Terrell JD. Results of case-control study of leukaemia and lymphoma among young people near Sellafield nuclear plant in West Cumbria. *BMJ* 1990;300:423-9.
- 5 Gardner MJ, Hall AJ, Snee MP, Downes S, Powell CA, Terrell JD. Methods and basic data of case-control study of leukaemia and lymphoma among young people near Sellafield nuclear plant in West Cumbria. *BMJ* 1990;300:429-34.
- 6 Smith PG. Comments on the case-control study of Gardner *et al* of leukaemia and lymphoma among young people in West Cumbria. *Trop Dis Bull* 1990;65:R1-6.
- 7 Beral V. Leukaemia and nuclear installations. *BMJ* 1990;300:411-2.
- 8 Urquhart JD, Black RJ, Muirhead MJ, *et al*. Case-control study of leukaemia and non-Hodgkin's lymphoma in children in Caithness near the Dounreay nuclear installation. *BMJ* 1991;302:687-92.
- 9 McKinney PA, Alexander FE, Cartwright RA, Parker L. Parental occupations of children with leukaemia in west Cumbria, north Humberside, and Gateshead. *BMJ* 1991;302:681-7.
- 10 Yoshimoto Y, Neel JV, Schull WJ, *et al*. *Frequency of malignant tumors during the first two decades of life in the offspring (F1) of atomic bomb survivors*. Hiroshima: Radiation Effects Research Foundation, 1990. (RERF technical report 4-90.)

Cancer and HIV infection

Bound to increase

Well before the AIDS epidemic began doctors recognised that cancers were commoner in immunosuppressed patients, and male homosexuality had been suggested as a risk factor for cancer a decade earlier. Increasingly frequent reports of malignancy in homosexual men appeared during the 1970s: presumably the social changes that allowed homosexual men freedom of expression also allowed their doctors to identify them.

So when a new immunoparetic disease appeared, initially almost exclusively in homosexual men, it should not have been surprising that there were associated cancers. The surprise has been how few there are. Currently only three are

recognised: Kaposi's sarcoma, non-Hodgkin's lymphoma, and primary cerebral lymphoma.

Still unexplained, and initially dismissed as harmless, Kaposi's sarcoma may kill or disable by affecting lungs or viscera. It also causes profound psychological distress. The purple blemishes are best treated with local radiotherapy,¹ and if they are caught early a single treatment will give a perfect cosmetic result. Older lesions, however, leak blood into the tissues, causing haemosiderin tattoos that remain after radiation. The radiotherapist is often outstripped by the progress of the disease, and systemic treatment is inadequate. High dose interferon is sometimes effective but may have

intolerable side effects. Many chemotherapy regimens have been proposed; systemic vincristine and bleomycin are the current favourites because they cause little myelotoxicity and no alopecia, nausea, or vomiting.² The response rate is reasonable but remission is short lived; treatment is palliative rather than curative.

More was known about non-Hodgkin's lymphoma than about Kaposi's sarcoma at the beginning of the epidemic, and conventional treatments provide palliation. Patients may die quickly of opportunistic infection or progressive lymphoma, although some do well, with a complete remission sustained for many months of good quality life.³ Primary cerebral lymphoma has a particularly grim outlook, with a short survival, often only days. Radiotherapy of the whole brain will help if given quickly, but an early diagnosis requires a brain biopsy.⁴

We know that the Centers for Disease Control classification may be missing some opportunistic infections.⁵ Is it also failing to identify some opportunistic cancers? Hodgkin's disease is a strong contender, with European reports that this cancer is seen more commonly in seropositive drug addicts.⁶⁻⁸ Hodgkin's disease in people with HIV infection clearly behaves uncharacteristically, and this change in tumour behaviour is probably related to the virus.

Cervical precancers are commonly seen in women infected with HIV.⁹ It is still too early to incriminate the virus as an independent cancer inducer in the few reported patients, some of whom have other strong risk factors for cervical carcinoma. Infection with HIV, however, may adversely affect the complex relation between human papillomavirus and female genital tract epithelium, and it seems more than coincidental that women who have received kidney grafts are at an increased risk of cervical intraepithelial neoplasia.¹⁰ Transplant immunosuppression is also associated with Kaposi's sarcoma and lymphoma, the two tumours that are most closely linked to HIV. Investigations by controlled trials have been called for,¹¹ but the problem of HIV and cancer is likely to be harder to unravel in women than in men, in whom studies of surrogate populations (for example, young never married men aged 20-49 are used as surrogates for homosexual men) have been fruitful.¹² Women with HIV make up a heterogeneous group and cannot be so easily identified by the epidemiologist.

Patients with HIV and cancers such as gliomas and lung cancer are already being seen in oncology clinics. The role of the virus is uncertain: for some patients the infection may be incidental, while for others their tumours will be as unpredictable and aggressive as the other cancers associated with AIDS.

Beyond dispute is the prospect of more patients with HIV and cancer. The population of people with asymptomatic HIV infection is expanding and maturing, and they will be at least as likely to develop cancers as anyone else. In addition, improved survival due to prophylaxis against *Pneumocystis carinii* pneumonia and antiretroviral treatment will allow many more non-Hodgkin's lymphomas to develop.¹³

These patients' demands for intensive management have been met with no change in staffing levels. How long this can continue is one of several urgent questions that the United Kingdom AIDS Oncology Group, set up to coordinate clinical activity, will have to answer.

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- 1 Spittle MF. A simple and effective treatment for AIDS related Kaposi's sarcoma. *BMJ* 1987;295:248-9.
- 2 Levine AM. Lymphoma in acquired immunodeficiency syndrome. *Semin Oncol* 1990;17:104-12.
- 3 Gill P, Rarick M, Bernstein-Singer M, et al. Treatment of advanced Kaposi's sarcoma using a combination of bleomycin and vincristine. *Am J Clin Oncol* 1990;13:315-9.
- 4 Baumgartner JE, Rachlin JR, Beckstead JH, et al. Primary central nervous system lymphomas: natural history and response to radiation therapy in 55 patients with acquired immunodeficiency syndrome. *J Neurosurg* 1990;73:206-11.
- 5 Gilks CF, Brindle RJ, Otieno LS, et al. Life threatening bacteraemia in HIV-1 seropositive adults admitted to hospital in Nairobi, Kenya. *Lancet* 1990;336:545-9.
- 6 Roithmann S, Tourani J-M, Andrieu J-M. Hodgkin's disease in HIV-infected intravenous drug abusers. *N Engl J Med* 1990;323:275-6.
- 7 Serrano M, Bellas C, Campo E, et al. Hodgkin's disease in patients with antibodies to human immunodeficiency virus. *Cancer* 1990;65:2248-54.
- 8 Italian Cooperative Group for AIDS-Related Tumours. Malignant lymphomas in patients with or at risk of AIDS in Italy. *J Natl Cancer Inst* 1988;80:855-60.
- 9 Bradbeer C. Is infection with HIV a risk factor for cervical intraepithelial neoplasia? *Lancet* 1987;iii:1277-8.
- 10 Alloub MI, Barr BBB, McLaren KM, Smith IW, Bunney MH, Smart GE. Human papillomavirus infection and cervical intraepithelial neoplasia in women with renal allografts. *BMJ* 1989;298:153-6.
- 11 Norman S, Studd J, Johnson M. HIV infection in women. *BMJ* 1990;301:1231-2.
- 12 Biggar RJ, Burnett W, Mikl J, Nasca P. Cancer among New York men at risk of acquired immunodeficiency syndrome. *Int J Cancer* 1989;43:979-85.
- 13 Pluda JM, Yarchoan R, Jaffe ES, et al. Development of non-Hodgkin lymphoma in a cohort of patients with severe HIV infection on long term antiretroviral therapy. *Ann Intern Med* 1990;113:276-82.