Some Recent Issues in Low-Exposure Radiation Epidemiology

by Brian MacMahon*

Three areas of activity in the field of low-level radiation epidemiology have been reviewed. They concern the questions of cancer risk related to antenatal X-ray exposure, occupational radiation exposure, and residence in areas of real or supposed increased levels of radiation. Despite the a priori unlikelihood of useful information developing from studies in any of these areas, such investigations are being pursued, and the results are proving to be stimulating. Much important information will be forthcoming in the near future.

Introduction

There is probably no topic in medical biology that has been reviewed more thoroughly or more frequently than the health effects of ionizing radiation, particularly its neoplastic effects. Nor, probably, has there been any subject of more frequent speculation than the level of carcinogenic risk, if any, associated with low levels and/or very low exposure rates of radiation.

A majority of investigators would probably agree that reliable estimates of these effects are most likely to come from understanding the mechanisms of radiation carcinogenesis, and a great deal of experimental work has been directed to that end. A question that is more controversial is whether empirical observations of humans exposed at levels or rates below those at which effects have already been observed would be useful. It is beyond debate that such observations would be useful, if they could be obtained easily, cheaply, and accurately. They would provide information on the consequences of human exposure in the area of the frequency curve where most human exposures occur and could serve as tests of predictions made from biologic or mathematical models.

The problem, of course, is that such observations, generally speaking, cannot be obtained either easily, cheaply, or accurately. A great deal of noise is to be expected in any observation of human populations, and this is a situation in which the noise is vastly more powerful than the anticipated signal. To take the easiest case, leukemia, by extrapolation from high exposure observation, this disease might occur in a population exposed to 5 rads with a frequency of 5 to 10 per million per annum as a result. That same population will, however, typically also be experiencing indistinguishable but etiologically unrelated leukemias at a rate of about 100 per million per annum. The difficulties are two: first, that of accumulating exposed and unexposed populations of sufficient size and following them over a sufficiently long time that meaningful confidence intervals can be put around differences of the order of 5% or so in a disease that is relatively uncommon. The second difficulty is that of establishing that any difference observed is not attributable to errors of selection or observation, confounding, or any of the other hobgoblins that afflict attempts to observe free-living human populations.

The prevailing scientific opinion has been that little is to be accomplished from attempts to observe populations exposed to less than 5 rads. After an extensive review of human candidate populations on behalf of the U.S. Nuclear Regulatory Commission, Dreyer et al. could recommend “no outstanding candidate population” for studies of low-level radiation (1). Even if the largest identified and available populations were studied, these investigators considered the chance of finding a definitive result to be very small. Low-level radiation was defined as a single exposure of 5 rem (whole-body) or chronic exposures that accumulate at the rate of less than 5 rem per year (1). An Interagency Scientific Review Group established by the NRC and EPA accepted this general conclusion (2). The group went further and noted the hazards that may accompany large, low-exposure epidemiologic studies. They state “When studies having low power to distinguish between real increases in disease rates and chance occurrences are conducted they may, merely by chance, yield estimates that have statistical but not real significance. The likelihood is that such estimates will be biased, that is, result in over-estimates of the true underlying risks, and that this bias will not be readily appreciated or understood” (2). The reasoning here is not

---

*Department of Epidemiology, Harvard School of Public Health, 677 Huntington Avenue, Boston, MA 02115.
entirely clear to me, but it is apparent that low-dose studies are being discouraged.

One of the major problems is that exposure to ionizing radiation is not a uniform event. The types of ionizing particles and ways in which humans can be exposed to them are so heterogeneous and ever-changing that opportunities for replication or the combination of data sets are few. This also seriously hinders the extraction of general, simplifying principles—even in the experience with medium and high exposures. Within many data sets, such as the atomic bomb survivors, there are serious problems of dosimetry (3) and there is a great variety of patterns of response for different tumor types (4). The task of approaching the radiation-careinogenesis issue empirically is an enormous one.

In spite of their pessimism about low-exposure studies, both Dreyer et al. and the Interagency Group recognized that some such studies will be done—for purposes that are not principally scientific, and indeed some have. I will describe the results of a few of these, particularly some which have appeared subsequent to the general review by Kohn and Fry in 1984 (5) and the somewhat earlier reviews of BEIR (6) and Cohen (7), which dealt specifically with the low exposure question.

Prenatal Diagnostic X-Rays

As late as 1984, it was still respectable to believe that a small proportion of childhood cancers ["perhaps 5% or less" (8)] were produced by exposure of the fetus through diagnostic X-ray examination of the mother's abdomen during pregnancy. This is one of the few facets of this general area with which I have been involved personally, and it falls within my timeliness criterion by virtue of a 1985 contribution to the debate: a study of Connecticut twins by Harvey et al. (9). That a statistical association between this type of radiation exposure and cancer risk exists is probably broadly accepted. The uncertainty relates to its interpretation: whether it is an indication of carcinogenicity of radiation exposures of the order of 1 rad or whether it results from some other characteristic of these pregnancies that both makes them more likely to be X-rayed and is associated with increased cancer risk in the offspring (10).

Harvey et al., following an earlier suggestion of Mole (11), examined the question in a series of twins, the idea being that twin pregnancies were X-rayed principally because they were twins and one can therefore exclude a mysterious third factor that could have been responsible for both the X-ray and the cancer. By cross-linking the Connecticut twins and cancer registries, these investigators identified 31 incident cases of cancer in twins and 109 unaffected comparison twins matched on sex, year of birth, and race. Information on X-rays during pregnancy was sought from a variety of record sources by persons blind as to whether the information related to a cancer case or to a control. The odds ratio associated with prenatal exposure was 2.4, with 95% confidence limits 1.0 to 5.9. Low birth weight was the only other variable found to be associated with cancer risk, a birth weight less than 2.27 kg being associated with a relative risk adjusted for X-ray exposure of 2.3 and a confidence interval of 0.9 to 5.7. A curious and unexplained feature of the data is that the radiation risk was virtually restricted to the children of mothers who had had a previous pregnancy loss. For such children the relative risk was 7.8 (1.2-50.4), and for children whose mothers had not had a previous loss it was 1.4 (0.5-4.3).

It was pointed out by de Swiet that there is no obvious reason why the susceptibility of the human organism to radiation should suddenly change at birth (12), indeed, animal evidence suggests that it does not (6), and that critically ill infants are exposed to X-rays postnatally, possibly accounting for the inverse association of cancer risk with birth weight (12). Twins may indeed experience the double jeopardy of increased frequency of X-ray exposure while in utero and more direct exposures postnatally. This speculation would fit nicely with the fact that the point estimate of the risk ratio found in twins (2.4) is rather higher than overall impressions of the order of the risk ratio in single births (about 1.5). However, the point estimate from the Connecticut data, as noted above, has a rather broad confidence interval.

Overall, the Connecticut data would seem to support the hypothesis of a causal relationship of these exposures to cancer risk. There remain, however, the three longstanding objections to this hypothesis:

a) The lack of increased cancer risk among Japanese children in utero at the time of the atomic bombings and who currently are thought to have received average exposures several times those of the diagnostically exposed fetuses. Conceivably, revision of the atomic-bomb exposure estimates, together with consideration of the possibility that infants exposed prenatally are, or used to be, also more frequently exposed postnatally (e.g., twins), may lessen or remove this inconsistency, but that remains to be seen.

b) The approximately 10-fold difference, for which there is no biologic explanation or precedent, between the absolute risk coefficients for infants exposed prenatally and children exposed before the age of 10 (14). Since the coefficients for children 0 to 9 years of age are based essentially on the atomic-bomb data, this inconsistency also may be modified by revision of the Atomic Bomb Casualty Commission exposure estimates.

c) The fact that in the prenatally exposed infants the leukemias and all the major groups of solid tumors appear to be increased almost equally in relative terms, a situation quite uncharacteristic of any other human or animal exposure.

In addition, the data of Harvey et al. raise a further interesting question. I have suggested on another occasion (prematurely, as the appearance of the data of Harvey et al. would suggest) that data resources may no longer be available for further direct studies of the cancer risk associated with radiation. However, being a twin may itself be a strong surrogate for being X-rayed prenatally, and if the association is causal twins as a group, regardless
of history of X-ray exposure, should have an increased incidence of childhood malignancy (15). The Connecticut data suggest that the incidence of cancer in twins was lower than in single births (14), an observation that would be inconsistent with a causal role for radiation. However, as the authors point out, uncertainties about the completeness of ascertainment, the mortality of twins, and other factors make the conclusion uncertain in these data. The problem of differential mortality of single and twin births could be overcome by limiting comparisons to children 1 year or older. Such data may be forthcoming from an ongoing study based on matching in Swedish registries (J. D. Boice, Jr., personal communication). And so, it appears that an issue which in 1980 I believed to be moribund (15) is still alive and kicking.

**Occupational Exposures**

So, indeed, is the question of carcinogenicity associated with low-level occupational exposures? The recent literature is reviewed by Wilkinson et al. in the introduction to their own study of workers at a plutonium weapons facility (16). The picture resembles somewhat the inside of an old and forgetful gardener’s potting shed. A batch of melanoma here, pancreas cancer there, a little multiple myeloma and lung langer scattered around the floor, together with scraps and pieces of what could be almost anything. The compilation by Wilkinson et al. is a very useful one, for it brings out clearly the total lack of pattern to this body of observations. Some heterogeneity should of course be expected, since not all occupational exposure is to the same form of radiation and not all is by the same route of exposure. However, the picture in this potting shed is much more suggestive of random meandering than of meaningful purpose.

Wilkinson et al.’s own study is a cohort study of 5413 white males employed for at least 2 years in a plutonium weapons facility between 1952 and 1979. Two measures of radiation exposure are employed: body burdens of plutonium estimated from urine bioassays, and external exposures as measured by film badges. For the cohort as a whole there were 656 deaths expected and 408 observed [standardized mortality ratio (SMR) 62, 95% confidence limits (CL95) 57–68]. There were 135 deaths from cancer expected and 95 observed (SMR 71, CL95 59–84). Only cancer of the lung showed a statistically significant difference between expected and observed deaths, there being fewer deaths from the cause than expected (47 expected, 30 observed, SMR 64, CL95 46–87).

Person-years experienced prior to the point when workers accumulated the lowest limit of detection of body plutonium (2 nCi) were compared with those after more than 2 nCi had been accumulated, separate analysis being conducted allowing for 2-year, 5-year, and 10-year induction time. No single cancer site showed a significant difference between observed and expected deaths in any of the three analyses. The category “all lymphopoietic” neoplasms showed a significant excess in the 2-year and 5-year induction time analyses, but it comprised four deaths, each a different diagnostic member of the category. None of these four deaths fell into the 10-year induction period category. There was no clear exposure-response relationship within the exposed group for this or any cancer site.

Comparing person years prior to the accumulation of 1 rem external radiation with those after the accumulation of 1 + rem, there was no cancer or group of cancers for which the risk differed significantly. Again, there was no clear dose-response relationship within the exposed employees.

While admiring of the care and competence with which this study was carried out, and the thoroughness of the analysis, I must confess to some disagreement with the authors over the interpretation of the data. I see this as a distinctly negative study insofar as observation of any effects likely to be attributable to radiation exposure are concerned. The authors, on the other hand, express the interpretation in phrases such as “To our knowledge, these comprise the first epidemiologic findings that suggest an association between exposure to plutonium and untoward health effects in humans” and, in their abstract, “these findings suggest that increased risks for several types of cancer cannot be ruled out at this time for individuals with plutonium body burdens of < 2 nCi” (16). The latter statement will of course always be true, but its use in this context implies that the authors believe that some effects have been observed. If so, I believe that too much is being made of some rather inconsequential and insignificant differences and some observations that are difficult to interpret in terms of radiation effect (e.g., variation in overall SMRs with exposure levels and induction times). No increases of cancer were found in those sites, such as bone and liver, where plutonium is known to concentrate and which might have been expected a priori to be affected if a plutonium effect were to be observed.

On the occupational front we should note also the case-control study of Stern et al. (17), which failed to find association between leukemia and occupational exposure to radiation at Portsmouth Naval Nuclear Shipyard, supporting the inference from the earlier cohort study in the same shipyard that found no excess of leukemia or other cancers among the radiation workers (18) [an earlier proportional mortality study notwithstanding (19)]. Results from a study of several hundred thousand such workers in shipyards across the nation should be available within a matter of months (G. Matanoski, personal communication). Mole (20) has recently summarized the presently inconclusive data on radiation workers in the U.K. and U.S. and commented on the possible effects of dose fractionation in occupational exposures.

**Place of Residence**

Studies that use place of residence as a surrogate for low-level radiation exposure constitute the third and final area of investigation that I shall review briefly. One category of such studies about which there has been much speculation but in which, to my knowledge, there
has been little activity recently, are those where the concern is with residence in areas of relatively high levels of natural background activity.

A second group of these studies are those of residents of areas in which there has been fallout from nuclear explosions. We have not heard much in the way of biological effects from Chernobyl yet, although Trichopoulos et al., from an ingenious analysis of trends in births in Greece, have inferred that 23% of early pregnancies at perceived risk in May 1986 were artificially terminated on this account (21). No doubt we will hear more of the fall-out from this incident.

Meanwhile, we are still hearing plenty on the putative effects of fallout from surface tests of nuclear weapons in the Nevada desert in the 1950s. Lyon et al. first noted that deaths from childhood leukemia in the southern counties of Utah increased during the period of testing and then declined when the surface testing ceased (22). Land et al. reanalyzed this situation and concluded that the observations of Lyon et al. resulted from a "possibly anomalous" very low rate of childhood leukemia in southern Utah prior to the testing period (23). The alarming conclusions of Johnson that not only leukemia but also lymphoma, thyroid cancer, and cancer of the breast, gastrointestinal tract, bone, brain, and skin (melanoma) were all in excess in exposed individuals can only be attributed to some quirk in the study methodology which I have not been able to identify. The study was based on interviews with persons identified from church rosters (24).

However, Machado et al., in a reanalysis using slightly different time periods and geographic boundaries, while finding no differences between supposedly exposed and unexposed populations for all other types of cancer, did find a statistically significant excess of deaths from leukemia, with odds ratios of 1.45 (based on 62 deaths) for all ages and 2.84 (based on 9 deaths) at ages 0 to 14 (25). It does appear that something may be afoot in that area. A study now in progress will attempt to assign exposure levels to individuals in the population of the area and may resolve this question (J. L. Lyon, personal communication).

A third group of observations that use geography as a surrogate for radiation exposure are those studies, and sometimes assertions, which link cancer risk to residence near or downwind or downstream from a nuclear power facility. There have been at least six reports of clusters of childhood leukemia and/or cancer around such facilities in the United Kingdom (26-31), the best known being in the village of Seascale, near the Sellafield (Windscale) nuclear fuel reprocessing plant in West Cumbria. Systematic studies of the issue, in the U.K. and in California, have generally been negative (32-34). For England and Wales, the Office of Population Censuses and Surveys has published a report giving age- and sex-specific cancer incidence and mortality rates for all Local Authority Areas (LAAs) with at least one-third of their population living within 10 miles of a nuclear installation. The LAAs were categorized according to proportion of the population living within specified distances (6, 8, or 10 miles) of the installation. Comparable data for matched LAAs without nuclear installations are also provided (35).

A summary of the principal results and conclusion from these data has been published by Cook-Mozaffari et al. (36). These authors conclude that there was "no general increase in cancer mortality near nuclear installations in England and Wales" although "Leukemia in young people [i.e., 0-24 years] may be an exception, though the reason is unclear" (36). The trends appear only for lymphoid leukemia and are more substantial in incidence than in mortality data.

Variations in registration efficiency between areas must be considered, as demonstrated by Wakeford (37) in connection with one specific area (38). As Wakeford also notes, in a report on radiation doses to the public from nuclear installations, the (British) National Radiological Protection Board concludes that "in no way could they (the nuclear emissions and discharges) be responsible for any increased incidence of leukemia amongst children, if such an increased incidence is shown to exist" (39). The statistical problems involved in this problem are complex (40) and, in view of the gerrymandered nature of the clusters, may never be satisfactorily resolved. However, an intriguing biologic twist to the issue has been provided by the observation in the Seascale episode that the excess of leukemias occurs entirely among individuals born in Seascale (observed 5, expected 0.53, relative risk 9.4 with 95% confidence interval 3.0-21.8 (41) and is not seen among children born elsewhere who moved into the parish for schooling (0 observed, 0.54 expected) (42). Further, there is a small but nonsignificant excess of other cancers in the Seascale birth cohort (observed 4, expected 1.07) that is not present in the schools cohort (observed 1, expected 1.18).

These observations inevitably bring us full circle to the first issue discussed in this paper, the prenatal X-ray exposure question, and to ask whether there is indeed something different about the susceptibility of the fetus. I am still inclined to think that this is unlikely, for the reasons given earlier. While the Seascale observations seem most unlikely to be due to chance, the unlikely does occur from time to time. We need either a replication of the observations in a circumstance selected a priori for its similarity to Seascale or an explanation in terms of currently unrecognized exposures—ionizing radiation or possibly something else.

Supported by a grant to the Kresge Center for Environmental Health, Harvard School of Public Health, from the National Institute of Environmental Health Sciences (5 P13 ES00002).

REFERENCES

1. Dreyer, N. A., Kohn, H. I., Clapp, B. W., Covino, S. J., Jr., Fahey, F. H., Friedlander, E. R., and Loughlin, J. E. The Feasibility of Epidemiologic Investigations of the Health Effects of Low-level Ionizing Radiation. Final Report. NUREG/CR-1728. U.S. Nuclear Regulatory Commission, Washington, DC, 1980.

2. Goldsmith, R., and Parsont, M. A. Report of the Interagency Scientific Review Group. Attachment to The Feasibility of Epidemiologic Investigations of the Health Effects of Low-level Ionizing Radiation. Final Report. NUREG/CR-1728. U.S. Nuclear Regulatory Commission, Washington, DC, 1980.
3. Fry, R. J. M. New dosimetry of atomic bomb radiation. Lancet ii: 845–848 (1987).

4. Cohen, B. L. Alternatives to the BEIR relative risk model for explaining atomic-bomb survivor cancer mortality. Health Phys. 52: 55–69 (1987).

5. Kohl, H. L. and Fry, R. J. M. Radiation carcinogenesis. N. Engl. J. Med. 310: 504–511 (1984).

6. Committee on the Biological Effects of Ionizing Radiations. The Effects on Populations of Exposure to Low Levels of Ionizing Radiation. National Academy Press, Washington, DC, 1980.

7. Cohen, B. L. The cancer risk from low-level radiation. Health Phys. 39: 659–678 (1980).

8. Doll, R., and Peto, R. The Causes of Cancer: Quantitative Estimates of Avoidable Risks of Cancer in the United States Today. Oxford University Press, Oxford, 1984, p. 1252.

9. Harvey, E. B., Boice, J. D., Jr., Honeyman, M., and Flannery, J. T. Prenatal x-ray exposure and childhood cancer in twins. N. Engl. J. Med. 312: 541–545 (1985).

10. MacMahon, B. Prenatal x-ray exposure and twins. N. Engl. J. Med. 312: 576–577 (1985).

11. Mole, R. H. Antenatal irradiation and childhood cancer: Causation or coincidence? Br. J. Cancer 39: 196–208 (1974).

12. de Swiet, M. Prenatal x-ray exposure and childhood cancer in twins (letter to the editor). N. Engl. J. Med. 312: 1574 (1985).

13. Jablons, S., and Kato, H. Childhood cancer in the relation to prenatal exposure to atomic-bomb radiation. Lancet ii: 1000–1003 (1970).

14. Harvey, E. B., and Boice, J. D., Jr. Prenatal x-ray exposure and childhood cancer in twins (letter to the editor). N. Engl. J. Med. 312: 1575 (1985).

15. MacMahon, B. Childhood cancer and prenatal irradiation. In: Cancer Achievements, Challenges and Prospects for the 1980's, Vol. 1 (J. H. Burchenal and H. F. Oettgen, Eds.), Grune and Stratton, New York, 1980, pp. 223–228.

16. Wilkinson, G. S., Tietjens, G. L., Wiggs, L. D., Galke, W. A., Aquavella, J. F., Reyes, M., Volez, G. L., and Waxweiler, R. J. Mortality among plutonium and other radiation workers at a plutonium weapons facility. Am. J. Epidemiol. 123: 231–250 (1986).

17. Stern, F. B., Waxweiler, R. A., Beaumont, J. J., Lee, S. T., Rinsky, R. A., Zumwalde, R. D., Halperin, W. E., Bierbaum, P. J., Landrigan, P. J., and Murray, W. E., Jr. A case-control study of leukemia at a nuclear naval shipyard. Am. J. Epidemiol. 123: 980–992 (1986).

18. Rinsky, R. A., Zumwalde, R. D., Waxweiler, R. J., Murray, W. E., Jr., Bierbaum, P. J., Landrigan, P. J., Terplak, M., and Cox, C. Cancer mortality in a naval shipyard. Lancet i: 231–233 (1981).

19. Najarian, T., and Colton, T. Mortality from leukemia and cancer in shipyard nuclear workers. Lancet i: 1018–1020 (1978).

20. Mole, R. H. Radiation, cancer risk, and the new dosimetry (letter to the editor). Lancet ii: 1403–1404 (1987).

21. Trichopoulos, D., Zaritsanos, X., Koutis, C., Drogari, P., Preobrazhenskaya, C., and Petridou, E. The victims of Chernobyl in Greece: Induced abortion after the accident. Br. Med. J. 295: 1100 (1987).

22. Lyon, J. L., Klauber, M. R., Gardner, J. W., and Udall, K. S. Childhood leukemias associated with fallout from nuclear testing. N. Engl. J. Med. 300: 397–402 (1979).

23. Land, C. E., McKay, F. W., and Macado, S. G. Childhood leukemia and fallout from the Nevada nuclear tests. Science 225: 139–144 (1984).

24. Johnson, C. J. Cancer incidence in an area of radioactive fallout downwind from the Nevada test site. JAMA 251: 230–236 (1984).

25. Machado, S. G., Land, C. E., and MacKay, F. W. Cancer mortality and radioactive fallout in southwestern Utah. Am. J. Epidemiol. 125: 44–61 (1987).

26. Black, D. Investigation of the Possible Increased Incidence of Cancer in West Cumbria. Report of the Independent Advisory Group, Her Majesty's Stationery Office, London, 1984.

27. Heasman, M. A., Kemp, I. W., Mackachen, A. M., Trotter, P., and Hole, D. J. Incidence of leukaemia in young people in west of Scotland (letter to the editor). Lancet i: 1188–1189 (1984).

28. Barton, C. J., Roman, E., Ryder, H. M., and Watson, A. Childhood leukaemia in west Berkshire (letter to the editor). Lancet ii: 1248–1249 (1985).

29. Heasman, M. A., Kemp, I. W., Urquhart, J. D., and Black, R. Childhood leukaemia in Northern Scotland (letter to the editor). Lancet ii: 266 (1986).

30. Urquhart, J., Cutler, J., and Burke, M. Leukaemia and lymphatic cancer in young people near nuclear installations (letter to the editor). Lancet ii: 384 (1986).

31. Beral, V. Cancer near nuclear installations (letter to the editor). Lancet ii: 556 (1987).

32. Enstrom, J. E. Cancer mortality around the San Onofre nuclear power plant, 1960–1975. Am. J. Public Health 73: 83–92 (1983).

33. Baron, J. A. Cancer mortality in small areas around nuclear facilities in England and Wales. Br. J. Cancer 50: 815–824 (1984).

34. Hole, D. J., and Gillis, C. R. Childhood leukaemia in the west of Scotland (letter to the editor). Lancet ii: 524–525 (1986).

35. Cook-Mozaffari, F. J., Ashwood, F. L., Vincent, T., Forman, D., and Alderson, M. Cancer Incidence and Mortality in the Vicinity of Nuclear Installations, England and Wales, 1950–1980. Studies on Medical and Population Subjects No. 51. Her Majesty's Stationery Office, London, 1987.

36. Forman, D., Cook-Mozaffari, P., Darby, S., Davey, G., Stratton, I., Doll, R., and Pike, M. Cancer near nuclear installations. Nature 320: 499–505 (1985).

37. Wakeford, R. Childhood leukaemia incidence around nuclear installations (letter to the editor). Lancet ii: 309 (1988).

38. Roman, E., Beral, V., Carpenter, L., Watson, A., Barton, C., Ryder, H., and Aston, D. L. Childhood leukaemia in the West Berkshire and Basingstoke and North Hampshire District Health Authorities in relation to nuclear establishments in the vicinity. Br. Med. J. 294: 497–498 (1987).

39. Dionian, J., Wan, S. L., and Wrixon, A. D. Radiation doses to members of the public around AWRE Aldermaston, ROH Burghfield and AERE Harwell. National Radiological Protection Board Report No. R202. Her Majesty's Stationery Office, London, 1987.

40. Dunster, H. J. Leukaemia and lymphatic cancer in young people near nuclear installations (letter to the editor). Lancet ii: 384–385 (1986).

41. Gardner, M. J., Hall, A. J., Downs, S., and Trell, J. D. Follow-up study of children born to mothers resident in Seascale, West Cumbria (birth cohort). Br. Med. J. 295: 822–827 (1987).

42. Gardner, M. J., Hall, A. J., Downs, S., and Trell, J. D. Follow-up study of children born elsewhere but attending schools in Seascale, West Cumbria (school cohort). Br. Med. J. 295: 819–822 (1987).