NUCLEAR POWER *and* LEUKAEMIA

...a review of the research

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Author

Malcolm Grimston is Energy Issues Adviser at the United Kingdom Atomic Energy Authority.

Introduction

Leukaemia

1. Leukaemia is a generic name for certain cancers of the bone marrow and lymphatic system, and it manifests by the rapid multiplication of abnormal white blood cells in the marrow. The blood stream therefore becomes flooded by immature white cells which are not capable of the normal functioning of mature cells. There are several different types of leukaemia, and of the closely related diseases, lymphoma. In addition the excess cancerous tissue in the bone marrow affects the production of red blood cells and platelets, causing anaemia and bleeding.

2. Leukaemia is relatively rare, affecting about 1 in 1,800[1] live births by the age of 15, or about 500 children per year in the UK. Leukaemia kills more children between the ages of 2 and 15 than any other disease, but progressive improvements in treatment mean that recently the cure rate for childhood leukaemia is better than 60%. Childhood leukaemia accounts for about 10% of all leukaemias.

3. Of the various forms of childhood leukaemia, acute lymphoid leukaemia is the most common. This is a rapidly progressive cancer of the lymphocytes, which are cells responsible for recognising infection.

4. Apparent excesses of leukaemia over short periods of time in small areas have been reported for over 50 years, since before nuclear fission was discovered[2]. However, excesses do occur entirely by chance in any random process, and leukaemia does not seem to 'cluster' naturally[3,4]. (By this it is meant that there is little evidence to suggest that local excesses occur more often than would be expected by chance.)

5. However, leukaemia rates in different parts of the country do seem to vary, with Somerset in particular having rather higher levels than expected at all ages, and for most leukaemia types[5].

6. In contrast to many childhood diseases, leukaemia seems to be especially associated with individuals of high socioeconomic status[6]. This has led to leukaemia sometimes being called a 'middle class disease'.

Possible causes

7. It is believed that leukaemia can start with damage to the DNA of a single primitive blood cell in the bone marrow, although cells disrupted in this fashion are almost always dealt with by the body's defence mechanisms.

8. Several agents are known to cause damage to DNA, such as ionising radiation, ultraviolet light, chemicals such as benzene, and some viruses. It is believed that most of these can also cause some forms of leukaemia.

9. In addition, it is thought that hereditary factors may be involved in the development of leukaemia. People with Down's Syndrome, for example, have a twenty-fold increase in their risk of developing acute leukaemia[7].

10. Also implicated in childhood leukaemia may be certain chemotherapeutic drugs, maternal smoking during pregnancy[8], garden pesticides[9], and chickenpox[10] and influenza[11] during pregnancy, but none of these is yet fully accepted.

Ionising radiation

11. It is well established that large doses of ionising radiation to the body can increase the risk of developing leukaemia. This information derives from studies of radiologists early this century; from people treated with large doses of X-rays to the spine for ankylosing spondylitis; and from the survivors of the atom bombs at Hiroshima and Nagasaki, among whom there has been an excess of about 80 cases of leukaemia in a population of just over 90,000[12].

12. It is also established that doses of radiation delivered to the foetus in utero can increase the subsequent risk of the child developing leukaemia[13].

13. In the UK the average annual dose of radiation is about 2.5 mSv (milliSieverts). In Cornwall, owing to high levels of radon gas, the average dose is 7.8 mSv. A few thousand houses in the UK deliver annual doses of more than 50 mSv[14]: a few tens may be delivering doses above 500 mSv[15].

14. It is not generally thought that high levels of radon are associated with leukaemia[16], although one recent study did suggest that there may be such a link[17].

15. Between them, in utero X-rays and ionising radiation are unlikely to account for more than 8% of all childhood leukaemias[18], with another 3% associated with well-defined genetic abnormalities. Hence more than 80% of childhood leukaemia is unexplained.

Nuclear establishments and leukaemia

16. In 1983 James Cutler, a journalist with Yorkshire Television, while researching a programme on the 1957 Windscale Fire, noticed an excessive number of cases of juvenile leukaemia in the town of Seascale, three miles south of the Sellafield nuclear complex. His findings, broadcast in the programme *Windscale, the Nuclear Laundry*, suggested that there had been seven cases of leukaemia in people under the age of 25 (five of these in children under 10) in Seascale between 1954 and 1983, when less than one case would have been expected by chance.

17. The Sellafield complex includes the early Windscale military piles (one of which caught fire in 1957), Calder Hall power station, and one of the world's two largest reprocessing operations. Reprocessing is a chemical process which separates spent nuclear fuel into reusable uranium, plutonium, and waste products. Because of this operation Sellafield discharges more radioactive material into the environment than does a nuclear power station.

18. As a result of Cutler's claims, a committee of enquiry was set up under Sir Douglas Black, a former president of the Royal College of Physicians of London. The Committee reported in 1984[19], confirming the excess in leukaemia rates in the area but saying that more research was necessary before any link with Sellafield could be confirmed or denied.

19. At the Black Report's recommendation, the Department of Health and Social Security set up the Committee on the Medical Aspects of Radiation in the Environment (COMARE), and further epidemiological studies were proposed.

Epidemiology

20. Epidemiology is the study of disease in relation to populations. Its main procedure is statistical analysis, for example observing rates of a disease near nuclear power stations and comparing them to the rates in a 'control'

area which has a similar population but no nuclear power station.

The interpretation of statistical findings can be difficult, as strictly speaking, epidemiology does not prove causes, but demonstrates correlations (although often it produces such overpowering evidence that deduction of causation is inescapable, as in the case of smoking and lung cancer).

For example, cancer mortality rates in towns such as Eastbourne and Bournemouth are significantly higher than the national average. However, this cannot be taken to indicate some deadly environmental factor in these areas: seaside towns attract many senior citizens, among whom deaths from cancer are more common than among younger people.

21. When dealing with a very small number of cases, the statistical picture is even more complicated. For example, if one area is more efficient at registering leukaemia, perhaps because it is a local issue, this can significantly distort the apparent incidence of the disease. It is also difficult to match the study group with a control group which has the right age profile, social group mixture and local environment to avoid the introduction of bias.

22. Further, in the case of leukaemia we have the problem of prior knowledge. If, without having any theory in the first place, we detect an area with an apparent excess of leukaemia, it is not surprising that this excess is sometimes found to be statistically significant.

The effect can be demonstrated with the football pools. On 1st September 1990 there were 15 score draws out of 58 matches. It is quite likely that three of these will be in consecutive matches on the coupon. In fact, matches 53, 54 and 55 were score draws. If we now ask 'what are the odds of matches 53, 54 and 55 all being score draws' we discover the probability is less than 1.5%.

This can now be described as a significant cluster! 58 was also a score draw, and there were 4 no-score draws, including numbers 52 and 57. So out of 19 draws, six came between numbers 52 and 58! The probability of this happening is less than 0.25%, or one in four hundred. Yet the numerical distribution of draws on football pools are clearly genuinely random, or someone would have worked out how to win regularly!

23. The rest of this brief should be read with these statistical problems in mind.

The power stations

24. The definitive Office of Population Censuses and Surveys (OPCS) study into cancer near nuclear establishments in England and Wales[20,21] established that overall cancer rates around nuclear stations are below average when compared to matching control areas. However, when discussing leukaemia the study draws a distinction between the pre-1955 sites, which did seem to display excess rates of childhood leukaemia, and the Central Electricity Generating Board (CEGB) - now Nuclear Electric plc - power stations (the first two of which began operating in 1962), which did not.

25. Reanalysis of the OPCS data has suggested that leukaemia rates in areas near to the CEGB stations seem to be about 15% greater than expected[22]. Discharges of radiation from these plants are extremely low when compared to natural levels of radiation. Further, it seems that leukaemia rates near sites that the CEGB had considered for nuclear stations but rejected, such as Druridge Bay in Northumberland and Luxulyan in Cornwall, are also higher than expected[23]. Hence there may be some other aspect of the type of area in which nuclear stations are built which causes a raised incidence of juvenile leukaemia.

Installations operating before 1955

26. The first COMARE report[24] took into account further discharges from Sellafield, and pointed out that because monitoring practices before 1977 were less sophisticated than today's it was difficult to estimate precise radiation doses from the plant before that date. However, even taking revised estimates of radiation exposure, the report concluded that the leukaemia excess in Seascale was difficult to explain in terms of radioactive discharges.

27. Further investigation revealed another case of leukaemia, in a child born in Seascale who had subsequently left the area, making a total of five fatal cases born in the village[25]. Four of these five cases occurred before 1970. Claims that juvenile leukaemia rates in the rest of West Cumbria are also higher than expected have not as yet been thoroughly investigated.

28. The second COMARE report[26] looked at leukaemia cases which occurred between 1968 and 1984 in the KW postcode area of Caithness, which includes the Dounreay nuclear establishment and the town of Thurso. Dounreay, the location of Britain's research into the Fast Reactor, has on site a variety of facilities, including the

250MW Prototype Fast Reactor and its associated reprocessing plant. This reprocessing operation is much smaller than that at Sellafield.

29. Between 1968 and 1984 there were 12 cases of leukaemia registered within the KW area: five within 12.5 km of Dounreay; one between 12.5 and 25 km; and six more than 25 km away. Furthermore, two cases which had been diagnosed as non-Hodgkin's lymphoma, one within 12.5 km, one between 12.5 and 25 km of the plant, were rediagnosed as leukaemia. Seven of the eight cases living within 25 km of Dounreay had been registered after 1978.

30. The Dounreay pattern differs from the Sellafield one in that it seems to represent a genuine 'cluster': the excess is in a narrow time period as well as a small geographical area.

31. COMARE 2 makes the point that to discover leukaemia excesses near both Britain's reprocessing plants makes it more likely that some common factor associated with these plants is implicated.

32. The third COMARE report[27] found a small but significant increase in leukaemia registration rates within 10 km of Aldermaston and Burghfield. Practically all of the excess is found within 10 km of Burghfield (the discharges from which are minute) in an area which includes Reading, and in children under 5. The report also found a small, non-significant deficit in childhood leukaemias within 10 km of the UK Atomic Energy Authority site at Harwell.

International

33. Recent studies have shown slight (non-significant) deficits in cancer and juvenile leukaemia rates near the French large- scale reprocessing plant at Cap la Hague[28,29], and a study looking at cancer incidence near six French installations which began operation before 1973 finds that leukaemia rates in these areas are slightly lower than would be expected by chance[30].

34. The US equivalent of the OPCS study[20], published by the American National Cancer Institute[31], failed to find any evidence of increased levels of sixteen different types of cancer, including leukaemia, in the 107 US counties surrounding 52 commercial nuclear power stations, nine Department of Energy research and weapons plants and one commercial fuel processing plant. Other studies in

the USA have failed to show any excess of childhood leukaemia near, for example, Three Mile Island[32]; Hanford[33]; Oak Ridge[34]. A recent study does suggest that leukaemia rates (all ages) near the plant at Pilgrim, Massachusetts, may have been higher than expected in the early 1980s, but not subsequently[35].

35. An important international study being conducted at present on the effects of radiation involves the study of the population near to Chernobyl. However, at present there has been insufficient time for useful information to be obtained from that area.

36. In general, however, it does seem that the apparent excess of leukaemia found near nuclear power plants is a British phenomenon which, for some reason, does not occur elsewhere in the world.

Possible causes of leukaemia excesses near nuclear establishments

Radioactive discharges into the environment

37. Perhaps the most superficially attractive explanation of these observations is that some radioactive substance, such as plutonium, released from the establishments is causing the leukaemias. However, this theory has significant weaknesses.

38. First, and most obvious, are the very low levels of radioactive discharge compared to natural background radiation, and to the levels of radiation observed to be necessary to cause leukaemia among radiologists, spondylitics and atom bomb survivors. The National Radiological Protection Board (NRPB) has calculated that discharges from Sellafield are too low by a factor of 300 to account for the five excess leukaemias, on current dose/response estimates[36].

Discharges cannot be much greater than thought, as the material involved would then have shown up in autopsies carried out in the area in far greater amounts than is the case[37]. Similarly, the susceptibility of children to radiation is unlikely to be much greater than is believed at present, as natural radiation would then cause more leukaemia than actually occurs[37]: there is no difference in radiation damage caused by natural and artificial radioactive materials.

39. The fallout from the atmospheric atom bomb tests carried out between 1958 and 1963 did not seem to cause any worldwide increase in leukaemia incidence. Yet these tests released the same materials, including plutonium, as are discharged from a reprocessing plant. Furthermore, the dose received because of the test fallout by anyone living in Thurso was about the same as that received because of discharges from Dounreay[38]. So if these discharges are to blame, the whole world might have been expected to have suffered from raised leukaemia incidence in the early and mid 1960s, something which did not occur.

40. The excesses near Sellafield, Dounreay, Aldermaston and Burghfield all involve about five to fifteen cases. Yet before the dramatic reductions of recent years Sellafield's discharges were about 15 times greater than Dounreay's, which were in turn about 900 times greater than the minute discharges owing to Aldermaston and Burghfield[39]. Hence the effect seems to be independent of the amount, and type, of radioactive material released by the establishment in question.

This is a very difficult observation to reconcile with present accepted theory. The third COMARE report[27], for example, states, 'In our judgment, the authorised and accidental radioactive discharges from [Aldermaston and Burghfield] are far too low to account for the observed increase in childhood cancer incidence in the area,' and points out, for example, that people living 5 km from Aldermaston receive about twice as much radiation from the coal plant operating on the site than they would have in the peak year of discharges from the weapons operations. The deficit of leukaemias within 10km of Harwell, which discharges rather more radioactive material than Aldermaston or Burghfield, is also puzzling.

41. If radioactive discharges into the environment are to blame, then, it would seem that they must involve an unusual radioactive substance with a specific tendency to cause childhood leukaemia: or there is selective deposition in an organ in which childhood leukaemia is unusually easy to induce. No such pathways or substances have yet been identified. (The target organ may not be the bone marrow, since bone marrow develops relatively late in the human foetus, and in the early stages of foetal development blood cells are manufactured in a variety of sites, such as the liver and the thymus. However, it does seem that most childhood leukaemias do arise in the marrow[38].)

Viral causes

42. At least one virus (Human T-cell Lymphotropic Viruses type 1, and possibly type 2) is known to cause rare forms of leukaemia in man[40], though neither of these viruses is associated with acute lymphoid leukaemia. It is also known that a virus can cause leukaemia in cats[40] and cattle.

43. However, the observation that leukaemia in man does not seem to cluster more than would be expected by chance militates against the theory that leukaemia is a common response to a rare viral infection.

44. There remains the real possibility that leukaemia is a rare response to a common virus, against which people living in stable communities will normally develop immunity[3]. The link between the hepatitis B virus and hepatocellular carcinoma is an example of such a disease[41], but such links are difficult to establish when the supposed agent is unidentified and its commonest manifestation (if any) is unrecognised.

However, excesses of leukaemia might be expected when people from isolated communities come together into areas with high population densities, as this would presumably facilitate the transmission of this virus. Such excesses have indeed been observed in the New Towns of the 1940s, such as Glenrothes, Corby, Peterlee, Aycliffe and Cwmbran[42,43]. These excesses persisted for about the first ten years after the populations of the towns began to undergo significant expansion.

The very peculiar nature of the population mixing at Seascale and Thurso when the plants at Sellafield and Dounreay were established, would lead one to expect a similar effect to be observed there.

45. However, in its initial form this theory does not seem to be able to explain excesses at Aldermaston and Burghfield (established in highly-populated Berkshire), or the cases at Dounreay between 1980 and 1984, which happened too long after the site was opened in 1950.

Other site factors

46. The possibility remains that leukaemia may be caused by some chemical released by the plant, or the chemical behaviour of a rare radioactive substance. As yet no such agents have been identified in discharges from nuclear plants.

47. It has also been suggested that stress because of the very presence of the plant might be causing suppression of the immune system. However, there is little direct evidence of this, and anyway it seems an unlikely cause in the UK. There is no reason to believe that local people feel such stress because of the establishments, nor is there any suggestion of raised leukaemia levels near other 'stressful' plant outside the nuclear industry (though few studies have been done on such establishments).

Paternal radiation exposure

48. As a further result of the Black Report recommendations, a study was launched, under the leadership of Professor Martin Gardner of the Medical Research Council's Epidemiology Unit at the University of Southampton, to examine a collection of possibilities, including that of a link between juvenile leukaemia and paternal radiation exposure. COMARE 2 had noted that in many of the Dounreay leukaemia cases one or other parent had worked at the plant.

49. The Gardner Report[44] showed a statistical association between paternal occupation and leukaemia. Men working in the nuclear reprocessing industry in Cumbria apparently ran raised risks of fathering leukaemic children, as did men working in the iron and steel, chemicals and farming industries.

50. The fathers of four of the five leukaemia cases born and diagnosed in Seascale are known to have worked at Sellafield, and had received cumulative radiation doses of at least 97 mSv prior to conceiving. Professor Gardner also suggested that there is statistical connection between increased leukaemia incidence in children and paternal doses greater than 10 mSv in the six months prior to conception, although this possibility has yet to be tested thoroughly. The risk of fathering a leukaemic child in either of these exposure groups was said to be raised by a factor of about 6 to 8, that is, about 1 in 300 children born to this group of men had developed leukaemia.

51. Gardner's study showed no link between environmental radiation and leukaemia. For example, the report considered people who play on the beach, eat fish or shellfish, grow vegetables etc, and could find no associated risk. If Gardner's findings are correct they lend strong support to the view that environmental discharges are far too low to be causing any health problems.

52. However, the association between paternal radiation and subsequent juvenile leukaemia was surprising. For example, there was no excess of leukaemia among children born to male survivors of Hiroshima or Nagasaki, who received average radiation doses of 492 mSv[45]; nor among men who received significant abdominal doses of X-rays[46]. The absence of a significant excess of testicular cancer among Sellafield workers suggests no accumulation of radioactive material in the testes[47]. It is known that plutonium tends to deposit in the skeleton and

liver: it is estimated that only about 0.035% of ingested plutonium concentrates in the testicles[48].

53. Further, acute doses of more than 4,000 mSv are necessary to double the chromosomal mutation frequency in human sperm[49]. The lack of any evidence of other inherited diseases in the vicinity of Sellafield presents a further problem for interpreting Gardner's findings[50].

54. It has been suggested that any chromosomal alteration which would cause leukaemogenesis would be inconsistent with the viability of the early embryo, and so could not be inherited[49].

Conclusion

55. Despite the intensive study of childhood leukaemia in recent years, particularly near British nuclear installations, the small number of cases, low levels of exposure and lack of evident pathways or mechanisms make it extremely difficult to interpret the findings.

The 1990 Gardner Report does seem to suggest that people living near Sellafield but without direct connection with the plant are at no risk: if paternal exposure to radiation is the cause, clearly discharges from the plant into the local environment are unlikely to be relevant. But we are still some way away from a thorough understanding of what is the mechanism causing childhood leukaemia.

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