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News and information

Extreme childhood leukaemia cluster at Fallon, Nevada

When, in 1983, Yorkshire Television announced its discovery of a pronounced excess of cases of childhood leukaemia in the coastal village of Seascale, adjacent to the Sellafield nuclear complex (formerly Windscale and Calder Works) in Cumbria, there was considerable concern that the current system of radiological protection may be seriously deficient. The Black Advisory Group was immediately established to investigate the ten cases in the village over thirty years, and a whole raft of scientific studies was launched. This concern also led to the creation of the UK Government's independent expert advisory Committee on Medical Aspects of Radiation in the Environment (COMARE) in 1985. That comprehensive assessments carried out by the National Radiological Protection Board could not begin to account for the excess cases in terms of radiation exposure due to radioactive discharges from Sellafield was taken by some as an indication that substantial and fundamental flaws underlie the radiation risk models derived by authoritative bodies such as the International Commission on Radiological Protection. Concern was heightened in 1986 when an excess of childhood leukaemia was reported as having occurred around the Dounreay nuclear establishment in northern Scotland, particularly in the town of Thurso. There followed a number of reports (of varying quality) of raised levels of childhood leukaemia near certain other nuclear installations, but, as at Sellafield, radiological assessments found that radiation exposures were substantially less than would be required to explain the excess cases. Scientific investigations have failed to find errors in these assessments that would be large enough to infer that radiation exposure was the cause of the extra cases. The idea that the risk from radioactive material in discharges, such as plutonium and fission products, might have been grossly underestimated seemed unlikely when studies of the effect of fallout from atmospheric nuclear weapons testing did not find an unexpectedly large rise in childhood leukaemia, and what initially appeared to be an important finding of a statistical association with occupational irradiation of fathers before the conception of their children was not confirmed by subsequent studies.

Despite the failure of scientific investigations to find serious shortcomings in the radiological assessments, many have been reluctant to dismiss radiation as playing a role in the excesses of childhood leukaemia, particularly in the cluster of cases at Seascale. It just seemed that this role must be a complex one that remains to be understood. Indeed, in the absence of an alternative explanation, this position has its attractions. However, in 1988, Professor Leo Kinlen proposed that childhood leukaemia is a rare response to a common, but unidentified, infection. When substantial numbers of infected and susceptible individuals come into contact, as when urban and rural populations mix, localised epidemics of the infection can occur giving rise to additional cases of the rare response, childhood leukaemia. The areas around Sellafield

Items for inclusion in this section are welcomed and should be sent to the Deputy Editor, Jim Gray, at the address given at the front of this issue.

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and Dounreay are certainly isolated and remote, and have experienced influxes of large numbers of 'outsiders'; but it was the confirmation by Kinlen and his colleagues of significant excesses of childhood leukaemia in each recent instance of large-scale population mixing in Britain that provided the most striking support for this hypothesis (see Kinlen 2000 *Radiol. Prot. Bull.* **226** 9–18). This evidence is supported by the findings of studies carried out in other countries, most recently by those conducted around La Hague in France (Boutou *et al* 2002 *Br. J. Cancer* **87** 740–5) and in isolated rural counties of the USA (Wartenberg *et al* 2004 *Br. J. Cancer* **90** 1771–6). The evidence for an infective process underlying childhood leukaemia is compelling.

Now, a remarkable observation of an exceptional cluster of childhood leukaemia in the USA may lend further weight to the idea that population mixing increases the risk of childhood leukaemia. In remote and sparsely-populated Churchill County, Nevada, 11 cases of childhood leukaemia occurred during 1999–2001 when less than one case would be expected (Steinmaus *et al* 2004 *Environ. Health Perspect.* **112** 766–71). The nominal Poisson probability associated with this excess ($p = 4.3 \times 10^{-9}$) makes this cluster the most extreme ever to have been observed anywhere in the world by a considerable margin—a cluster this extreme would only occur by chance in the USA once in every 22,000 years! The extreme rarity of the cluster would be even greater were attention confined to the small town of Fallon, where many of the cases occurred. Of special interest to the population mixing hypothesis is the nearby Fallon military airbase, which, since the mid-1990s, has specialised in training. In 2000, a staggering 55,000 persons attended Fallon airbase for training, coming from many parts of the world. Given the background evidence for the impact of population mixing upon the risk of childhood leukaemia, the large numbers of people of diverse origins passing through the Fallon airbase is an attractive explanation for the childhood leukaemia cluster in its highly rural vicinity.

So, the childhood leukaemia cluster at Seascale may not be attributable to radiation, as initially might have seemed, and the radiological protection community was right to stand its ground. Nonetheless, much good scientific work has been conducted on the basis of the concern about a possible shortcoming in radiation risk assessments, and radiological protection is the stronger for it. But what a contrast between the publicity given to Seascale, next door to a nuclear installation, and that given to Fallon. I suspect that not many reading this will have heard of the Fallon cluster, but all will have heard of the one at Seascale. No doubt this disproportionate media, and consequent public, interest in a possible link between the Seascale cluster and operations at Sellafield has led to a similarly disproportionate level of funding to investigate radiation at the expense of other possible causes. Could be that the money was put on the wrong horse.

Richard Wakeford

COMARE 8th Report

In February, 2004, the Committee on Medical Aspects of Radiation in the Environment (COMARE) published its 8th Report entitled 'Review of pregnancy outcomes following preconceptional exposure to radiation'. This is the second report from COMARE to deal specifically with possible effects on health of the offspring of irradiated parents and follows the 7th COMARE Report which examined the incidence of cancer. The current report extends this to a broader range of transgenerational effects which may result from damage to the genetic material in the ovary and testis including miscarriage, stillbirth, infant death, congenital abnormalities and sex ratio.

An important conclusion of the Report is that studies of human populations exposed to radiation provide little evidence that adverse pregnancy outcomes in general are related to parental exposure to radiation. In coming to this view, the Committee examined 10 human studies comprising atomic bomb survivors, radiation workers, people who had received radiotherapy, medical radiographers and radiologists, and populations living near uranium mines and nuclear reactors. However, differences in design and the endpoints studied make intercomparisons difficult and often only allow broad conclusions to be made. Furthermore, it is recognised that a range of environmental and lifestyle factors can strongly influence adverse pregnancy outcomes and in many studies rates have changed (sometimes markedly) with time. Such factors substantially complicate the interpretation of epidemiological studies.

When considering specific endpoints COMARE concludes that there is no significant evidence that miscarriage or neonatal death is the result of parental irradiation. However, considerable uncertainties remain as to whether there is a relationship between paternal preconceptional irradiation and stillbirth and, while such a link is not established, it cannot be entirely ruled out. The basis of this uncertainty is the study by Parker *et al* (1999 *Lancet* **354** 1407–14) which reported an excess of stillbirths associated with paternal occupational irradiation at Sellafield. This association was primarily driven by three stillbirths with paternal preconceptional radiation doses in excess of 500 mSv. The excess of stillbirths was mainly due to congenital abnormalities and specifically neural tube defects.

The Report further concludes that the overall evidence does not support the idea that a detectable increase in congenital abnormalities in general has resulted from parents' exposure to radiation, but notes that the data are more suggestive than for other adverse pregnancy outcomes. If an association does exist it is likely to be restricted to neural tube defects. The primary source for this continuing concern is again the stillbirth data of Parker *et al*. Support is also drawn from animal studies although it is acknowledged that these were conducted using much higher doses. In addition, the Report refers to an increase in neural tube defects associated with paternal exposure at the Hanford plant based on two cases with paternal preconceptional radiation doses of around 100 mSv (Sever *et al* 1988 *Am. J. Epidemiol.* **127** 226–42). However, a raised incidence was also found in the surrounding population which could not be attributed to occupational exposure at Hanford (Sever *et al* 1988 *Am. J. Epidemiol.* **127** 243–54), and those who conducted these studies concluded that the paternal association was unlikely to be explained by exposure to radiation.

Stillbirths are a diverse and difficult endpoint to evaluate as categorisation of death around the time of birth can be influenced by registration practices and physicians' preferences. Rates have also declined dramatically in recent years, and this is generally thought to be due to improved maternal diet and antenatal care. Moreover, caution should be applied when drawing inferences regarding neural tube defects from purely stillbirth data since this will represent only a small proportion of neural tube defect pregnancies. Reference to data collected by the European Registration of Congenital Anomalies (http://www.eurocat.ulster.ac.uk) indicates that less than one quarter of births with neural tube defects are classified as stillbirths. In addition, since the introduction of antenatal diagnosis in the 1970s, birth prevalence of neural tube defects has dropped markedly. By 1984, five years prior to the cessation of the study by Parker *et al*, 51% of neural tube defect pregnancies in the Northern Region of England, which includes the Sellafield catchment area, were terminated and this increased in the subsequent years (Rankin *et al* 2000 *Paediat. Perinat. Epidimiol.* **14** 104–10). Thus, while the study of stillbirths can provide valuable information, any evaluation of congenital abnormalities should include livebirths plus stillbirths, together with induced abortions, if problems with classification and ascertainment are to be avoided.

COMARE note that the majority of neural tube defects are normally related to maternal factors and warn that there is considerable potential for bias or confounding in the study by Parker *et al*. In addition, there remain concerns that corrections for the very marked temporal trend in stillbirth incidence over the period of study were incomplete and that some residual confounding exists. In light of these concerns, and the caution applied to the interpretation of the negative results obtained from the atomic bomb studies and the studies of offspring of cancer survivors who received radiotherapy, the weight placed on this one study of stillbirths in pregnancies fathered by nuclear workers is perhaps surprising, particularly as the findings were not repeated in the more comprehensive Nuclear Industry Family Study (Doyle *et al* 2000 *Lancet* **356** 1293–9).

Overall, COMARE do not expect that current occupational radiation exposures will lead to a detectable increase in risk of any of the major reproductive outcomes for which data are currently available such as miscarriage, neonatal death, stillbirth or congenital malformations. This should provide reassurance to current workers. Furthermore, if there was an increased risk associated with the higher doses experienced in the early days of the nuclear industry, then this has not been established in the totality of available studies. COMARE have been unable to identify any UK population which might usefully be studied to provide additional information and therefore make no recommendation for further epidemiological work in this area. It is be possible, however, that studies of the offspring of heavily exposed workers in the former Soviet Union may provide further evidence on this subject.

The Report's conclusions are based on the assumption that the aetiologies of the gross health effects covered in the Report encompass a role for conventional genetic mechanisms such as gene mutations, changes in chromosome number and chromosomal rearrangements. However, COMARE also draw attention to recent developments in technology which have identified more subtle radiation-induced changes to the genetic material. These include chromosome microdeletions, changes in DNA repeat sequences and epigenetic changes in gene expression. The implications of such changes for health are currently unknown. Their consequences could fall within the normal range of human variability and thus not be distinguished in the studies examined in this report. Nevertheless, such subtle effects may have public health consequences and COMARE will continue to monitor developments in this area with a view to assessing their implications for human health.

The COMARE 8th Report is available from the National Radiological Protection Board and is also available on the COMARE website (http://www.comare.org.uk).

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New NRPB advice on exposures to electromagnetic fields

In March 2004, the NRPB recommended the adoption in the UK of the guidelines of the International Commission on Non-Ionizing Radiation Protection (ICNIRP) for limiting exposure to electromagnetic fields (EMFs) between 0 and 300 GHz (*Documents of the NRPB* vol 15, no 2). These frequencies include EMFs produced by television and radio transmissions, by mobile telecommunications and by electricity supply and use.

In 1993 NRPB published exposure guidelines for limiting exposure to static and time varying EMFs, and although the guidelines have no statutory force, they have had considerable influence and have had Government endorsement. Since that time there has been a considerable amount of research published and, importantly, ICNIRP has published exposure guidelines covering the same frequency range. The ICNIRP guidelines incorporate two tiers of protection:

one set of values for occupational exposure, which are basically the same as the 1993 NRPB guidelines, and another, more restrictive, set for general public exposure. Several countries have now adopted the ICNIRP guidelines and they provide the basis for a 1999 European Council recommendation on limiting exposure of the general public to EMFs.

NRPB has maintained an ongoing review of scientific evidence and health risk assessment and, at the request of the Department of Health, has now particularly addressed the issues of uncertainty in the science and aspects of precaution. It has obtained advice from UK and international scientific experts and from published comprehensive reviews by expert groups, including its Advisory Group on Non-Ionising Radiation (AGNIR) and a 'weak electric fields group' set up for the purpose. It also ran a public meeting in December 2002 and a public consultation process in summer 2003.

NRPB concluded that levels similar to ICNIRP's are appropriate to prevent adverse health. Recognising the benefits of international harmonisation, it has therefore recommended adoption of ICNIRP guidelines rather than proposing similar but different levels of its own.

The ICNIRP guidelines set restrictions on exposure to prevent adverse health effects for which there is clear evidence and whose mechanisms are understood. Just as with the 1993 NRPB guidelines, these health effects are principally induced electric fields (which can interfere with nerves) at frequencies up to about 100 kHz, and heating above that frequency. The new departure for NRPB is the lower levels for the public, generally by a factor of five. NRPB's reason for this is the extra sensitivity of some groups in the whole publication, specifically infants and children, old people, and people with epilepsy or on certain medications, and the reduced opportunity for administrative or engineering controls. It is described as a 'cautious' approach, where 'increased susceptibility is expected on scientific grounds, but where, because there is a lack of specific scientific data, the degree of susceptibility has not been quantitatively determined'. NRPB now arguably gives a clearer and more detailed justification of this than ICNIRP itself does.

In confining quantitative exposure limits to established adverse health effects, NRPB notes that uncertainties in the science remain, particularly those associated with epidemiological studies. Although these studies do not provide a sound basis for quantifying exposure guidelines, NRPB considers they indicate that further precaution may be appropriate in respect of some EMF exposures. Rather than make proposals itself, it recommends that Government considers this.

Coincidentally, almost simultaneously with the new NRPB advice, the draft European Directive on occupational exposure to electromagnetic fields completed its passage through the European Commission, Parliament and Council and has therefore come into force. It is also based on the values for occupational exposure from the 1998 ICNIRP Guidelines. The HSE now have four years to bring it into force in the UK.

http://www.nrpb.org/publications/documents_of_nrpb/abstracts/absd15-2.htm

NRPB Report on Particle Deposition and Health in the Vicinity of Power Lines

In 1996 and in 1999, a group at Bristol University in the UK, lead by Professor Denis Henshaw, proposed mechanisms whereby power lines could affect human health, not via the magnetic field which has historically been the main concern, but via either the electric field or the corona ions they produce, and the effect of these on existing airborne pollutants. The main ongoing suggestions are that electric fields cause increased deposition of charged pollutants on the skin, and that corona ions transfer charge to pollutants and thereby cause increased deposition in the airways.

The suggestions have been previously criticised by scientists from NRPB and the electricity industry, and the authors have in turn responded. Given the ongoing controversy, NRPB's Advisory Group on Non-Ionising Radiation (AGNIR) decided to investigate the suggestions in detail, setting up an ad-hoc group for the purpose. AGNIR issued its report in March 2004 (*Documents of the NRPB* vol 15, no 1). It concluded that:

> 'Any health risks from the deposition of environmental particulate air pollutants on the skin appear to be negligible ... it seems unlikely that corona ions would have more than a small effect on the long-term health risks associated with particulate air pollutants, even in the individuals who are most affected. In public health terms, the proportionate impact will be even lower because only a small fraction of the general population live or work close to sources of corona ions.'

AGNIR states that the potential implications for the health of the general public of corona ions generated by power lines do not, therefore, provide a strong case for further research in this area.

http://www.nrpb.org/publications/documents_of_nrpb/abstracts/absd15-1.htm

Recent NRPB Publications (February–April 2004)

Documents

None

Reports

New report: Radiological Consequences Resulting from Accidents and Incidents Involving the Transport of Radioactive Materials in the UK—2002 Review
http://www.nrpb.org/publications/w_series_reports/2004/nrpb_w53.htm

Additions and developments to the NRPB website

New document: Particle Deposition in the Vicinity of Power Lines and Possible Effects on Health (Report of an Independent Advisory Group on Non-Ionising Radiation and its Ad Hoc Group on Corona Ions)
http://www.nrpb.org/publications/documents_of_nrpb/abstracts/absd15-1.htm

Updated information on the Advisory Group on Non-Ionising Radiation (AGNIR)
http://www.nrpb.org/advisory_groups/agnir/index.htm

Advice on Limiting Exposure to Electromagnetic Fields (0–300 GHz)
http://www.nrpb.org/publications/documents_of_nrpb/abstracts/absd15-2.htm