

Childhood Cancer

3. Possible causative factors – ionising radiation

There is a well-established link between exposure to ionising radiation and cancer. Ionising radiation can be either natural background radiation such as radon, or man-made such as X-rays or nuclear weaponry. It also includes ionising radiation used for medical diagnosis and treatment.

A paediatrician in Germany explained in very clear terms why children may be more at risk than adults when exposed to ionising radiation, even low grade (Eisenberg [2009](#)).

She said:-

- Growth means a high rate of cell division in all organ systems. Cell division is the risky phase for radiation damage; an embryo grows at an almost explosive rate. Its cells are constantly dividing, which is why even tiny amounts of radiation are extremely hazardous.
- The repair mechanisms that our organism uses to identify and eliminate mutated cells are not yet effective in children, especially in unborn children.
- Children have a positive substance balance – in order to thrive they have to consume more than they excrete, in contrast to adults who merely have to maintain their fully grown bodies. The positive balance in children leads to a prolonged biological half life in incorporated radioactive isotopes.
- Malignancies have a long latency period; in pathologies caused by radioactivity, decades may lie between exposure and detectable onset of illness. Children have their lives ahead of them; in contrast to older people, they may have the misfortune of experiencing the end of the latency period.

There is no fixed agreement on the method of cancer causation or affected part of the body as a result of ionising radiation. Atom bombs, older strength medical X-rays and radiotherapy are established causes of leukaemia and other cancers. Only thyroid cancers have significantly increased after the Chernobyl accident, according to official sources, and links between cancer and residential or parental occupational exposure to nuclear facilities has produced mixed results. Lane ([2010](#)) asks for the development of credible radiological/nuclear event scenarios that will assist in identifying probable sources of radioactivity and pathways of exposure for children, to develop appropriate protection strategies. For instance, many cases of thyroid cancers were prevented after the Three Mile Island accident by giving high levels of iodine supplement which meant cells were saturated enough not to take in further contaminated iodine from the environment. This was not done at Chernobyl.

Information about the effect of ionising radiation on leukaemia rates comes primarily from atomic bomb survivors; *in utero* irradiation of the foetus by obstetric X-rays; occupational exposure to radiation in, and residential proximity to, nuclear facilities; nuclear fallout from power station accidents, such as Chernobyl and Fukushima; bomb testing; and natural sources of ionising radiation, such as radon.

Natural radiation

There have been a number of studies that show an association between radon, a naturally occurring gas, and childhood leukaemia (Henshaw & Allen 2002, Evrard [2006](#)), even if the association is a weak one (Raaschou-Nielsen [2008](#)). It is similar to the radiation risk estimates in another study by Evrard ([2005](#)) at 10 mSv, which is comparable with the natural background radiation in areas of Cornwall where there is a high level of exposure to radon. Due to the relatively ubiquitous exposure to background natural radiation, any childhood leukaemia excess would be undetectable in a case-control study. A report by Kaletsch ([1999](#)) found a link between residential radon exposure and CNS tumours, though the number of children affected was small, and radon levels vary from area to area and country to country.

In a complex multi-factorial illness such as childhood cancer, more than one factor may have to occur at the same or similar time, or sequentially. This may have some bearing on the inconsistency found in studies. Brauner ([2010](#)) found that air pollution from traffic may enhance the effect of radon on the risk of childhood leukaemia.

All journeys by air expose plane travellers to cosmic ionising radiation which is less shielded by the atmosphere at high altitude.

It is estimated that background ionising radiation is implicated in around 34% of cases of childhood leukaemia, particularly AML, with exposure during preconception, *in utero* and in the postnatal period being important (COMARE 4th Report, Doll & Wakeford 1997). Red bone marrow, the tissue in which leukaemia is considered to originate, can be affected by natural radiation. Doses *in utero* include contributions resulting from the ingestion of radionuclides by the mother and placental transfer to the foetus. Postnatal doses include those from radionuclides in breast-milk and those ingested in other food (Kendall [2009](#)).

In the UK, the percentage of cases of childhood leukaemia attributable to natural background radiation is suggested to be about 20% (Wakeford [2009](#)), though this has been revised downwards to 15-20% by Little ([2009](#)). The magnitude of the risk depends on the dose of radiation, the duration of exposure, and the age and susceptibility of the individual at the time of exposure.

Ionising radiation is relatively ineffective at inducing mutations in DNA, but is effective at inducing DNA strand breaks. Most single stranded breaks are rapidly repaired, but double-stranded breaks can result in chromosome re-arrangements. Such aberrations, if they are not lethal, or if they are mis-repaired, can lead to cancer.

The explosion of research into radiation-induced genomic instability (both direct and transgenerational (Vorobtsova [2008](#)) and the bystander effect has brought into sharp debate the risks of exposure to radiation at low doses.

Medical diagnosis and treatment

X-rays, CT scans & ultrasound

Sir Richard Doll produced a paper (Doll & Wakeford [1997](#)) showing a 40% increase in risk to the child as a result of a radiographic examination. Excess cancer deaths decreased suddenly for births in and after 1958, largely as a result of campaigning for change by Dr Alice Stewart. Concerted action was initiated in 1956 to reduce radiation exposure of foetal gonads for fear of genetic hazards. In 1957 and early 1958 obstetric radiography began to be used much less

frequently, and the use of pelvic X-rays was virtually abandoned. In the 1970s the rate of X-raying increased again and so did cancer risk but not significantly.

Other studies found that obstetric X-rays of the foetus produce an increased risk of leukaemia later in childhood (Boice & Miller [1999](#), Shu [1994](#), [2002](#)). Wakeford ([2008](#)) found an increase in risk of leukaemia for prenatal X-ray exposure, but not postnatal, however, he expressed uncertainty about the safety of paediatric CT scans. Hammer ([2009](#), [2010](#), Meinert [1999](#), Naumberg [2001](#)) found no increase in cancer, or in some studies specifically leukaemia, risk for children from very low doses of diagnostic ionising radiation (X-rays). Different types of leukaemias may be more likely to result from X ray exposure. Hammer ([2011](#)) found a positive dose-response relation in 5 patients with endocrine or metabolic disease who underwent diagnostic X-rays. Shu ([2002](#)) noted a significantly increased risk for children with pre-B cell ALL, especially if they had 3 or more X-rays, and they were more than 5 years old. Bartley ([2010](#)) found an association between post-natal diagnostic X-rays and B-cell ALL, but not AML or T-cell ALL. It may be that, in some cases, the medical reasons that women receive prenatal X-rays might be responsible for the increased leukaemia risk and not the X-ray exposures themselves. One study (Schmitz-Feuerhake & Pflugbeil [2011](#)) recommended a reduction in diagnostic exposures as a measure for preventing several cancers, including childhood leukaemia.

In a review of 25 studies published between 1990 and 2006, there was no association found between pre- and postnatal X-rays and brain tumours (Schulze-Rath [2008](#)). Khan ([2010](#)) found no association between head injury and exposure to diagnostic head X-rays and medulloblastoma or PNET.

Patton ([2004](#)) found no association between neuroblastoma risk and maternal exposure to radiation, and only a slight one with paternal radiation exposure. No consistent pattern of association between Wilms tumour (nephroblastoma) and maternal radiation exposure during pre-pregnancy or pregnancy was found in a study by Goel ([2009](#)).

Bunin ([2011](#)) found that both paternal and maternal exposure to medical radiation of the gonads increased the risk of their child's developing retinoblastoma by more than 3 times or 7 times respectively.

Due to the pioneering work of Alice Stewart, X-rays as a matter of course during pregnancy were discontinued and they are rarely done now. The risk associated with X-ray exposure has decreased over time as once the damage from ionising radiation was acknowledged, the diagnostic and therapeutic levels were reduced to the minimum necessary for its purpose.

X-rays have been superseded in most cases by ultrasound scans, which have not been associated with the same level of risk. Ultrasound exposure has not been found to be a risk for brain tumours (Stålberg [2008](#)), or cancer generally (Rajaraman [2011](#)) but there are other concerns about ultrasound exposure leading to neurological changes, including autism, which suggest that they should only be used where there are concerns about the child's wellbeing, rather than an automatic procedure.

Diagnostic X-rays are the largest man-made source of radiation exposure to the general population, contributing about 14% of the total annual exposure worldwide from all sources. It is accepted that about 0.6 per cent of UK cancers in general are due to medical X-ray procedures (Berrington de González & Darby [2004](#)), rising to a figure as high as 3% in Japan.

CT scans are increasingly used to diagnose medical problems. A single CT scan exposes the patient, on average, to a 7 times higher dose than a normal X-ray. A chest CT scan is the equivalent dose of 60 normal chest X-rays. Although the risk from a single CT scan to an individual is small, there are concerns about the build-up of risk over time, especially for

children, who are more susceptible to radiation. Wakeford (2010) and Rajaraman (2011) recommended caution when considering administering paediatric and pregnancy CT scans, because of the small, extra risk of developing leukaemia attached to each one. Obese people require more radiation to get the same amount of physiological information. Many CT centres are set up for adults, and are therefore not suitable for children, who need adjustments to limit dose and radiation risk, without making appropriate changes in exposure.

According to Berrington de González (2009), 15% of cancers resulting from CT scans were due to scans at ages younger than 18 years, though the study did not make it clear what the latency period might be. Smith-Bindman found (2009) that *“within each type of CT study, effective dose varied significantly within and across institutions, with a mean 13-fold variation between the highest and lowest dose for each study type. The estimated number of CT scans that will lead to the development of a cancer varied widely depending on the specific type of CT examination and the patient's age and sex.”*

Pflugbeil (2011) suggested that there are 3 excess tumours (especially meningiomas) in the head out of every 1000 annual paediatric CT scans of the skull (cataracts were also a potential problem.), as well as an increased risk of childhood leukaemia as a result of CT scans of the bone marrow.

Nuclear facilities and accidents

There have been over 60 epidemiological studies on the incidence of leukaemia and other childhood cancers near nuclear power plants. Ghirga (2010), reviewed scientific articles and government documents on the incidence of childhood cancer near nuclear power plants and concluded that there may be increases, irrespective of the country concerned. Fairlie (2010) suggests that doses from environmental nuclear power plant emissions to embryos/foetuses in pregnant women near the plants may be larger than suspected, and Wakeford (2010) suggests that maybe the leukemogenic effect of radionuclides taken into the body has been seriously underestimated, which could explain the increased incidence of childhood leukaemia near some nuclear installations.

Many studies have investigated the possibility of paternal occupational exposure to ionising radiation being a potential risk factor in the development of leukaemia in their children.

Gardner (1991) found that the risk of leukaemia was higher in children born near Sellafield, and for children of fathers employed at the plant at their conception, and that the higher the dosage they were exposed to (particularly the testicles), the higher the risk (Roman 1999). Other studies did not find the increased risk in children whose fathers worked at Sellafield, but who lived further away from the installation (Doll 1994). It could be that there was a synergistic effect of paternal exposure and something else nearer the child's home before the leukaemia was initiated.

Dickinson & Parker (2002) included all children born to mothers who lived in Cumbria between 1950 and 1991. They found that the children of radiation workers had an increased risk of developing leukaemia and non-Hodgkin's lymphoma. Gathering data about occupational exposure is complicated by the fact that external radiation exposure does not necessarily correlate with potential internal contamination of workers, which was not measured.

Some studies looking at different types of parental occupational environments found increased risks of leukaemia with radiation (McKinney 1991) whilst other studies found no correlation (Watson 1991, Kinlen 1993, McLaughlin 1993). Maternal exposure was also included by Meinert (1999) who found that there was an association with radiation and some forms of childhood cancer and was also dependent on the age of the child.

Urquhart (1991) did not find a link to childhood leukaemia and parental occupational exposure, but they did find one for use of beaches within 25 kilometres of the Dounreay nuclear facility. It has been suggested that other nuclear power facilities (Sellafield, La Hague, etc.) have cancer clusters in the residential areas around them and that merely living nearby could increase the likelihood of a child developing cancer (Spix 2008). Some study authors have acknowledged that the number of children suffering from leukaemia in Cumbria (Draper 1993), Berkshire (Barton 2001), Hampshire (Roman 1993) and Germany (Hoffmann 2007, Kaatsch 2008, 2008, Nussbaum 2009) was higher than would be expected, but they were unsure of the cause. Nussbaum found a doubling in risk in children under 5 living within 5 km of plant exhaust stacks. Laurier (2008) found no such link in children below the age of 5 years with French nuclear power plants, neither did Heinävaara find an increase in childhood leukaemia near Finnish nuclear power plants (2010), though the study authors acknowledged that the small sample size limited the strength of the conclusions. Spycher (2011) found little evidence of an association between childhood cancer and nuclear power plants in Switzerland. We wonder whether governmental reliance on nuclear plants for electricity supplies may, in some way, influence the outcome of specific studies.

Dr Körblein commented on the leukaemia cancer clusters (2009) saying *“ecological studies are much less able to detect regional clusters than more elaborate case-control studies. When the authors refer to the results of a recent study from England that, in contrast with the German study, has not shown a leukaemia increase in the vicinity of nuclear power stations, it has to be borne in mind that this study, again, is an ecological study.”* Bithell (2008) commented *“this apparent discrepancy (in study findings) could be accounted for by a number of differences in approach, especially those relating to the distances from the power stations and the ages of the children studied.”* Laurier (2008) in a review of 198 nuclear sites in 10 countries concluded *“A large variability was noticed in the quality of the data as well as in the definition of the study population and in the methods of analysis”* although the review also confirmed that *“some clusters of childhood leukaemia cases exist locally.”*

A large meta analysis was carried out by Baker & Hoel (2007) on studies that included 136 nuclear facilities, and found that the majority of these found elevated levels of childhood leukaemia in nearby residents.

Whether parental preconceptual or *in utero* exposure to radiation increases the risk of infant leukaemia remains controversial. One report suggests that there might have been a transient increase in infant leukaemia in northern Greece in association with radioactive fallout from the Chernobyl accident (Petridou 1996). Busby (2009) looked at the records of over 15 million children born in the UK, Greece, and Germany between 1980 and 1990. He found an excess of infant leukaemia reported from 5 different countries; Scotland, Greece, Germany, Belarus and Wales and Scotland combined. The excess risks showed a biphasic response to exposure. Busby concludes *“Since the cohort is chosen specifically on the basis of exposure to internal radionuclides, the result can be expressed as evidence for a significant error in the conventional modelling for such internal foetal exposures.”* Fairlie (2009) looked at studies of leukaemia near nuclear installations and suggested that *“the observed high rates of infant leukaemias may be a teratogenic effect from incorporated radionuclides. Doses from environmental emissions from nuclear reactors to embryos and fetuses in pregnant women near nuclear power stations may be larger than suspected. Hematopoietic tissues appear to be considerably more radiosensitive in embryos / fetuses than in newborn babies.”*

However, the European Childhood Leukaemia-Lymphoma Incidence Study failed to show any increase in the incidence of childhood leukaemia as a consequence of this event (Parkin 1996). Likewise, in a subsequent study, German investigations were not able to correlate an increased incidence of infant leukaemia with ionizing radiation from the accident (Michaelis 1997).

Nuclear accidents

A review of research into the genetic damage done to children by accidental exposure to ionising radiation (Fucic [2008](#)) concluded that *“the evidence from the studies conducted following the Chernobyl accident, nuclear tests, environmental radiation pollution and indoor accidental contamination reveals consistently increased chromosome aberration and micronuclei frequency in exposed children.”* They suggested that further research should be carried out with regard to the combined effects of low doses of radiation and chemical agents from food, water and air. It is important that not just *in utero* exposure is considered, as Mangano, looking at the Three Mile Island as well as the Chernobyl accidents (Mangano [2006](#)) documents that there is a short latency of cancer onset in young children who are especially susceptible to adverse effects of radiation exposure, even at relatively low doses.

There have been various investigations into the after effects of the Chernobyl accident. Noshchenko ([2001](#)) found that *in utero* exposure caused the rates of ALL to be dramatically elevated for males and to a lesser extent for females. A study by Peterka ([2007](#)) found that a significantly decreased number of male babies were born in the areas most affected by Chernobyl fallout. This may reflect a greater susceptibility to radiation for males rather than females, especially prenatally. For both genders combined, the risk for ALL was more than three times greater in the exposed compared to the unexposed regions. Petridou ([1996](#)) found an increased risk for infant leukaemia, Hjalmar (1994) found an increase in cancer in children aged under 5, Steiner ([1998](#)) was ambivalent and Sali ([1996](#)) did not find significantly increased leukaemia risks, although the latter did not rule out the possibility of a small increased risk. The incidence of thyroid cancer in children and adolescents in the Russian Federation has been directly linked to the radiation pollution in the area of residence (Romanchishen [2010](#)).

It is difficult to compare many of the studies due to a) difficulties of getting information following the breakup of the Soviet Union into its constituent countries; b) differences in cancer registration systems; c) means of case ascertainment; and d) very real differences in Chernobyl-related exposures across regions within countries (Hjalmar [1994](#), Parkin [1996](#)). A study looking at the population exposed to fallout from Chernobyl (Maenhaut [2011](#)) concluded that *“Several lines of evidence suggest that the predisposition to developing cancer after radiation exposure is variable in the general population.”* 39% of children exposed to radioactive fallout from Chernobyl as children had changes to chromosome 7, that none of the unexposed children had (Hess [2011](#)). The authors concluded *“it is likely that different molecular subgroups and routes of radiation-induced carcinogenesis exist.”*

Atomic Bomb and fallout survivors

Yamamoto & Goodman ([2007](#)) investigated patterns of leukaemia incidence in the United States and reported that Asian-Pacific Islanders had the highest rates of AML. A possible explanation for this may be that DNA damage due to bomb testing was passed on to successive generations.

The Atomic Bomb survivors' risk factors for leukaemia were based on radiation doses of much higher levels (from 0.1 to 10 Sieverts (Sv) than the average UK natural background level of 2.2 millisieverts (mSv) per year). It is likely that using Atomic Bomb survivors as subjects for research could distort the effect of ionising radiation, as it is certain that those susceptible to varying (even small) amounts will have died as a result of their exposure, leaving a more resistant (i.e. not necessarily random) group of survivors.

The standardised mortality rate for Japanese boys exposed to low doses of radiation in 1945 were significantly higher for solid cancer (Goto [2011](#)).