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A hypothesis to explain childhood cancers near nuclear power plants

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ABSTRACT

Over 60 epidemiological studies world-wide have examined cancer incidences in children near nuclear power plants (NPPs): most of them indicate leukemia increases. These include the 2008 KiKK study commissioned by the German Government which found relative risks (RR) of 1.6 in total cancers and 2.2 in leukemias among infants living within 5 km of all German NPPs. The KiKK study has retriggered the debate as to the cause(s) of these increased cancers. A suggested hypothesis is that the increased cancers arise from radiation exposures to pregnant women near NPPs. However any theory has to account for the >10,000 fold discrepancy between official dose estimates from NPP emissions and observed increased risks. An explanation may be that doses from spikes in NPP radionuclide emissions are significantly larger than those estimated by official models which are diluted through the use of annual averages. In addition, risks to embryos/fetuses are greater than those to adults and haematopoietic tissues appear more radiosensitive in embryos/fetuses than in newborn babies. The product of possible increased doses and possible increased risks per dose may provide an explanation.

1. Introduction

In the early 1950s, Folley et al. (1952) observed an increased risk of leukemia among Japanese bomb survivors. In the late 1950s, Stewart et al. (1958) also observed that radiation exposures can result in increased incidences of leukemia. A number of studies since then (BEIR, 1990; Preston et al., 1994; IARC, 1999) have shown that ionising radiation including medical, occupational and environmental exposures, are a risk factor for leukemia. In addition, older ecological and case–control studies (Forman et al., 1987; Gardner, 1991; Pobel and Viel, 1997) revealed an association between nuclear power plants and childhood leukemia among those living nearby.

In the late 1980s and early 1990s, increased incidences of childhood leukemias were reported near several UK nuclear facilities. Various explanations were offered for these increases, however the UK Government's Committee on the Medical Aspects of Radiation in the Environment (COMARE) concluded in a series of reports (1986; 1988; 1989; 1996) that the cause remained unknown but was unlikely to involve radiation exposures. This was mainly because official estimates for radiation doses from these facilities were too low by orders of magnitude to explain the increased leukemias. Indeed, any theory will have to account for the >10,000 fold discrepancy between official dose estimates from NPP emissions and observed increased risks.

A pattern of epidemiological evidence world-wide now clearly indicates increased leukemia risks near nuclear power plants (NPPs). Laurier and Bard (1999) and Laurier et al. (2008) examined the literature on childhood leukemias near NPPs world-wide. These two studies identified a total of over 60 studies. An independent review of these studies (Fairlie and Körblein, 2010) indicated that the large majority of these studies revealed small increases in childhood leukemia although in many cases these were not statistically significant. Laurier and Bard and Laurier et al., mostly employees of the French Government's Institut de Radioprotection et Sûreté Nucléaire (IRSN), confirmed that clusters of childhood leukemia cases existed near most NPPs but refrained from drawing wider conclusions. Fairlie and Körblein (2010) in their review concluded that the copious evidence indicating increased leukemia rates near nuclear facilities, specifically in young children, was quite convincing.

This conclusion was supported by two meta-analyses of national multi-site studies. Baker and Hoel (2007) assessed data from 17 research studies covering 136 nuclear sites in the UK, Canada, France, the US, Germany, Japan, and Spain. In children up to nine years old, leukemia death rates were from 5 to 24% higher and leukemia incidence rates were 14–21% higher. However their analysis was criticised by Spix and Blettner (2009).

The second meta-analysis by Körblein (2009) covering NPPs in Germany, France, and the UK also found a statistically significant

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increased risk of child leukemias and relative risk of leukemia deaths near NPPs (RR = 1.33; one-tailed p value = 0.0246). Further studies (Guizard et al., 2001; Hoffman et al., 2007) indicated raised leukemia incidences in France and Germany. However COMARE (2005; 2006) declined to support these conclusions.

Later, Bithell et al. (2008) and Laurier et al. (2008) found increases in child leukemias near UK and French NPPs respectively. In both cases, the numbers were low and not statistically significant – i.e. there was a greater than 5% possibility that the observations could have occurred by chance. However instead of reporting these increases, the studies incorrectly concluded that there was "no evidence" (Bithell) and "no suggestion" (Laurier) of leukemia increases near UK and French nuclear reactors, merely because their data lacked statistical significance. These conclusions were incorrect: the authors should have reported the observed leukemia increases but added there was a >5% probability they could have occurred by chance.

In more detail, p values (that is, the probabilities that observed effects may be due to chance) are affected by both the magnitude of effect and the size of study (Whitley and Ball, 2002). This means statistical tests must be used with caution as the use of an arbitrary cut-off for statistical significance (usually p = 5%) can lead to incorrectly accepting the null hypothesis (ie nil effect) merely because it is not statistically significant (Sterne and Smith, 2001): a possible type II error. This often occurs in small studies due to their small sample sizes rather than lack of effect (Everett et al., 1998). Axelson (2004) has pointed out that many epidemiology studies with negative results – statistically speaking, are of questionable validity as they may obscure existing risks.

2. KiKK study

The KiKK study (**K**inderkrebs **i**n der Umgebung von **K**ern**K**raftwerken = Childhood Cancer in the Vicinity of Nuclear Power Plants) found a 120% increase in leukemia and a 60% increase in all cancers among infants and children under 5 years old living within 5 km of all German NPPs (Kaatsch et al., 2008b; Spix et al., 2008). The increase of risk with proximity to the NPP site, tested with a reciprocal distance trend, was significant for all cancers (p = 0.0034, one-sided), as well as for leukemias (p = 0.0044).

KiKK is a large well-conducted study; its findings are scientifically rigorous; its evidence is particularly strong; and the German Government's Bundesamt für Strahlenschutz, which commissioned the study, has confirmed its findings. A BfS-appointed expert group stated (BfS, 2008) "The present study confirms that in Germany there is a correlation between the distance of the home from the nearest NPP [nuclear power plant] at the time of diagnosis and the risk of developing cancer (particularly leukemia) before the 5th birthday. This study is not able to state which biological risk factors could explain this relationship. Exposure to ionising radiation was neither measured nor modelled. Although previous results could be reproduced by the current study, the present status of radiobiological and epidemiological knowledge does not allow the conclusion that the ionising radiation emitted by German NPPs during normal operation is the cause. This study cannot conclusively clarify whether confounders, selection or randomness play a role in the distance trend observed."

One potential problem is that the KiKK study considered residence at the time of leukemia diagnosis and not residence at the time of early pregnancy: if my hypothesis (see below) were correct this would add uncertainty to the findings. The best way to deal with this would be a new study which established residence at the time of early pregnancy.

Table 1
Studies of observed (O) and expected (E) leukemia cases within 5 km of NPPs.

Dataset	O	E	SIR = O/E	90%CI	p-value
Germany	34	24.1	1.41	1.04–1.88	0.0328
Great Britain	20	15.4	1.30	0.86–1.89	0.1464
Switzerland	11	7.9[a]	1.40	0.78–2.31	0.1711
France[b]	14	10.2	1.37	0.83–2.15	0.1506
Pooled data	79	57.5	1.37	1.13–1.66	0.0042

[a] derived from data in Spycher et al. (2011).
[b] acute leukemia cases.

3. Post-KiKK studies

KiKK reignited the childhood leukemia debate (Nussbaum, 2009) and resulted in studies being carried out in the UK (COMARE, 2011), France (Sermage-Faure et al., 2012) and Switzerland (Spycher et al., 2011). Together with a geographical study from Germany (Kaatsch et al., 2008a) using data from the KiKK study region, four datasets now exist of similar design and with the same endpoints, distance definitions and age categories. These four studies have similar findings. In particular, the leukemia increases in the 5 km zone observed in the four studies are very close as shown in Table 1.

Körblein and Fairlie (2012) pooled the data of acute leukemia in children under 5 within 5 km of NPPs from these four studies: the standardized incidence ratios (SIRs) within 5 km are shown in Table 1. Their analysis yielded an overall SIR of 1.37 in the 5 km zone (90% CI: 1.13–1.66, p = 0.0042, one-sided).

To study the shape of the distance dependency of leukemia risk, Körblein and Fairlie (2012) also carried out a joint Poisson regression of the four datasets using linear and linear-quadratic dependencies on reciprocal distance. The linear-quadratic model yielded a better fit to the data – see Fig. 1.

The best fit, judged by the Akaike information criterion, was obtained with a model estimating the excess rate in the 5 km zone relative to the rate in the >5 km zone. The authors found a SIR of 0.95 (0.90–1.00) at distances $r \geq 5$ km. From the ratio of the two SIRs, a relative risk of 1.37/0.95 = 1.44 (p = 0.0018) was obtained. With a one-sided test, the result was highly significant (p = 0.0009). This pooled analysis provides statistically strong evidence of leukemia increases near NPPs which contradicts statements by the above authors to the contrary.

In view of the preponderance of the above evidence, there is little dispute about the association of childhood leukemia incidence with proximity to nuclear facilities. The remaining arguments are about its causes and energy policy implications.

4. What are the causes of increased cancers near NPPs?

The KiKK authors stated "the reported findings were… not to be expected under radiation biological and epidemiological considerations" and that the increase in leukemias "remains unexplained". They added that "no risk factors of the necessary strength for this [KIKK] effect are known for childhood cancer and specifically childhood leukemia". (Kaatsch et al., 2008b).

Since the first leukemia cluster near nuclear facilities was discovered in 1984 near the Sellafield nuclear facility in the UK, there has been much discussion as to possible causes for these cancer increases. However we are little closer to ascertaining them than we were in the 1980s.

Various suggestions have been put forward, including a postulated virus from population-mixing (Kinlen, 2004); an unusual response to infectious diseases in children (Greaves, 2006); genetic predisposition to cancer; or a combination of factors. None of these addresses KiKK's central finding that the increased cancers were