

Commentary: Childhood Cancer Near Nuclear Power Stations

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ABSTRACT

In 2008, the KiKK study in Germany reported a 1.6-fold increase in all cancers and a 2.2-fold increase in leukemias, among children living within 5 km of all German nuclear power stations. The study has triggered debates as to the cause(s) of these increased cancers. This article reports on the findings of the KiKK study; discusses past and more recent epidemiological studies of leukemias near nuclear installations around the world, and outlines a possible biological mechanism to explain the increased cancers. This suggests that the observed high rates of infant leukemias may be a teratogenic effect from incorporated radionuclides. Doses from environmental emissions from nuclear reactors to embryos/fetuses in pregnant women near nuclear power stations may be larger than suspected and hematopoietic tissues may be considerably more radiosensitive in embryos/fetuses than in newborn babies. The commentary concludes with recommendations for further research.

Background

Increased incidences of childhood leukemias were first reported near UK nuclear facilities in the late 1980s. Various explanations were offered for these increases; however the UK Government concluded in a series of reports^{1 2 3 4} that the cause(s) remained unknown but was (were) unlikely to involve radiation exposures. This was mainly because radiation doses from these facilities were estimated to be too low, by two to three orders of magnitude, to explain the increased leukemias.

Recently, the KiKK (**K**inderkrebs in der Umgebung von **K**ern**K**raftwerken = Childhood Cancer in the Vicinity of Nuclear Power Plants) study^{5 6} has rekindled the childhood leukemia debate. It reported a 2.2-fold increase in leukemias and a 1.6-fold increase in solid cancers among children living within 5 km of all German nuclear power stations. The web publication⁷ of the study in December 2007 resulted in a public outcry and media debate in Germany which has received little attention elsewhere.

The KiKK case–control study commands attention for a number of reasons. The first is its large size: it examined all cancers at all 16 nuclear reactor locations in Germany between 1980 and 2003, including 1,592 under-fives with cancer and 4,735 controls, with 593 under-fives with leukemia and 1,766 controls. This means that the study is statistically strong and its findings statistically significant. Small numbers and weak statistical significance often limit the usefulness of many smaller epidemiological studies.

Second is its authority: it was commissioned in 2003 by the German Government's Bundesamt für Strahlenschutz (BfS, the German Federal Office for Radiation Protection, approximately equivalent to the EPA's Office of Air and Radiation) after requests by

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German citizen groups. The study was carried out by epidemiology teams from the University of Mainz which could not be accused of being opposed to nuclear power.

Third is the validity of its results, as vouchsafed for by the German Government's Bundesamt für Strahlenschutz. It officially accepted that children living near nuclear power plants develop cancer and leukemia more frequently than those living further away. The BfS stated⁸

"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 nuclear power stations during normal operation is the cause. This study cannot conclusively clarify whether confounders, selection or randomness play a role in the distance trend observed."

Other studies on childhood leukemias near nuclear power stations

It has been known at least since the late 1950s⁹ that radiation exposures can result in increased leukemias and that environmental exposures to radiation are a risk factor for leukemia^{10 11 12}. In addition, several ecological and case control studies^{13 14 15} in the past have suggested or indicated an association between nuclear power plants and childhood leukemia among those living nearby.

In a little-noticed study¹⁶ in 1999, Laurier and Bard (1999) examined the literature on childhood leukemias near nuclear power stations world-wide. They listed a startling total of 50 studies (29 ecological; 7 case-control; and 14 national multi-site studies). The large majority revealed small increases in childhood leukemia near nuclear power stations although most of the ecological studies were not statistically significant. The policy implications of this study do not appear to have been widely discussed.

There then followed two studies^{17 18} indicating raised leukemia incidences in France and Germany, but several official studies indicated the opposite. For example, official reports in the UK^{19 20} and studies in France^{21 22} concluded there was no evidence of leukemia increases near their respective nuclear power stations.

After the KiKK study was published in early 2008, the same pattern continued with two officially-sponsored studies suggesting small leukemia increases near nuclear power stations, albeit without statistical significance. Bithell et al²³ found a small within 0 to 5 km near 13 of the 14 UK nuclear power stations, and Laurier et al²⁴ found a small increase within 0 to 10 km near French nuclear power stations. In both studies, the numbers were small and therefore considered not statistically significant (ie there was a greater than 5% possibility that the observations could have occurred by chance).

These studies incorrectly concluded that there was "no suggestion" or "no evidence" of leukemia increases near UK and French nuclear reactors respectively. These conclusions are regrettable because low statistical significance (ie a p-value greater than 0.05) should not be interpreted as measuring the probability of effect²⁵. The word "significance" refers to a statistical test and not the effect being examined^{26 27 28}.

In addition, weak studies which are not strong enough to pick up health effects should not conclude there are no effects: that is, absence of evidence should not be construed to mean evidence of absence²⁹.

These are widespread misconceptions, unfortunately. The conclusions in the Laurier et al and Bithell et al studies may mislead members of the public into thinking there are no increased leukemias near French or UK nuclear power stations when in fact the question remains open. The stronger evidence from the KiKK study suggests there may well be such increases – regardless of the country in which nuclear reactors are located.

This conclusion is supported by two meta-analyses: these combine the results of various multi-site studies in order to have a large enough data base to achieve statistical significance. The first is the Baker and Hoel meta-analysis³⁰ which assessed data from 17 research papers covering 136 nuclear sites in the UK, Canada, France, United States, Germany, Japan and Spain - see table 1. In children up to 9 years old, leukemia death rates were from 5 to 24% higher, and leukemia incidence rates were 14 to 21% higher. These findings were statistically significant and lent considerable support to the KiKK findings, but the study was not cited in the KiKK, Laurier and Bithell studies.

Table 1. Leukemia mortality risks (Baker and Hoel, 2007)

Age group	Proximity to nuclear facility	leukemia mortality
0–9	All distances	1.05
	Under 16 km	1.24
0–25	All distances	1.02
	Under 16 km	1.18

The second is a recent meta-analysis³¹ covering leukemias near nuclear power stations in Germany, France and the UK. This also found a statistically significant increased risk of child leukemias near their nuclear power stations with a relative risk = 1.33 (p=0.0246 one-tailed).

Need for powerful epidemiological studies

The nub of the matter is that childhood leukemia is a rare disease. This means that statistically powerful, ie numerically large, studies are required to obtain statistically significant results. This was achieved by the powerful KiKK study and the above meta-analyses. The Bithell and Laurier studies were simply not large enough to achieve statistically significant results.

It is a truism that we should be guided by the best available scientific evidence. It is preferable to rely on the larger KiKK study for a number of reasons. First, the KiKK study found statistically significant cancer increases. The p-values in the KiKK study were 0.0034 for all cancers and 0.0044 for leukemias (both one-tailed), ie well below the common 0.05 figure for statistical significance. Second, the KiKK findings were supported by two meta-analyses, as mentioned above. Third, the KiKK study is a case-control study (examining 593 under 5 year olds with leukemia together with 1,766 controls) which means its findings should take precedence over the Bithell and Laurier studies which were less reliable ecological studies. Finally, the KiKK study used accurate distance measures. It estimated distances between the homes of cancer cases and the chimneys of nuclear power stations to within 25 metres, unlike the imprecise areas of the Bithell and Laurier studies. These were irregularly shaped as they were defined by ward or electoral

boundaries. The latter studies simply cannot invalidate the findings of the more sophisticated KiKK study, as their conclusions would seem to imply.

KiKK study findings

The KiKK study showed an increased risk of cancer in children under 5 years living near all nuclear power plants in Germany. The inner 5-km zone showed an increased risk (odds ratio 1.47; lower one-sided 95% confidence limit 1.16). For all leukemias combined, the study showed a statistically significant trend for proximity to nuclear power stations with a positive regression coefficient of 1.75 [lower 95%-confidence limit (CL): 0.65]. That is, the leukaemic children lived closer to nuclear power plants than randomly selected controls. A categorical analysis showed a statistically significant odds ratio of 2.19 (lower 95%-CL: 1.51) for residential proximity within 5 km compared to residence outside this area. The main findings of the KiKK study are set out in Table 2.

Table 2. KiKK odds ratios[†] for all cancers in children less than 5 years old

Distance from nearest nuclear power reactor	All cancers	leukemias
Within 5 km	1.61	2.19

KiKK estimates from its categorical regression model (Kaatsch et al, 2008).

These increased risks are statistically significant and are larger than the cancer increases observed near nuclear facilities in many other countries. In addition, regression analyses carried out on the results by the authors indicate that the increased risks may extend as far as 50 km from the reactors. The risk estimates for distances greater than 5 km are not statistically significant. However, as pointed out above, this does not necessarily mean that there are no increased risks beyond 5 km.

The most significant finding was the association between increased cancers and proximity to nuclear installations. Many previous reports (as discussed above) have studied increased cancer risks near nuclear facilities, but the KiKK report for the first time in Europe measured how far each cancer case was from the nearest nuclear reactor. This allowed the study to examine the distance/risk relationship. The proximity–risk relationship was pronounced for leukemias– see table 3.

Table 3. KiKK odds ratios for leukemias in children less than 5 years old

Distance from reactor km	Mean distance km	Odds ratio
>5	3	1.76
5 to <10	8	1.26
10 to <30	18	1.10
30 to <50	37	1.05
50 to <70	57	1.03
>70	74	1.02

KiKK estimates from its continuous regression model (Kaatsch et al, 2008)

The odds in table 3 were calculated by the KiKK authors using a linear relationship between distance and relative risk ($RR \sim e^{1/r}$). This is uncertain as we don't know the true

[†] The odds ratio (OR) is a measure of increased risk. Here it is the ratio of the odds (ie, chance) of a cancer occurring in nearby residents to the odds of a cancer occurring in the control group. An OR of 1 would mean the odds (chances) were the same.

relationship, and a quadratic relationship, [ie, the risk depending on $1/r^2$ ($RR \sim e^{1/r^2}$)] also fits the data as shown in figures 1 and 2. Further tests, [ie the sum of squared residuals and goodness of fit] indicate that a quadratic relationship actually fits the data better. All calculations are based on data from the KiKK study.

Figure 1. Relative risk as a function of distance from nuclear power reactor and its regression estimated using a linear relationship

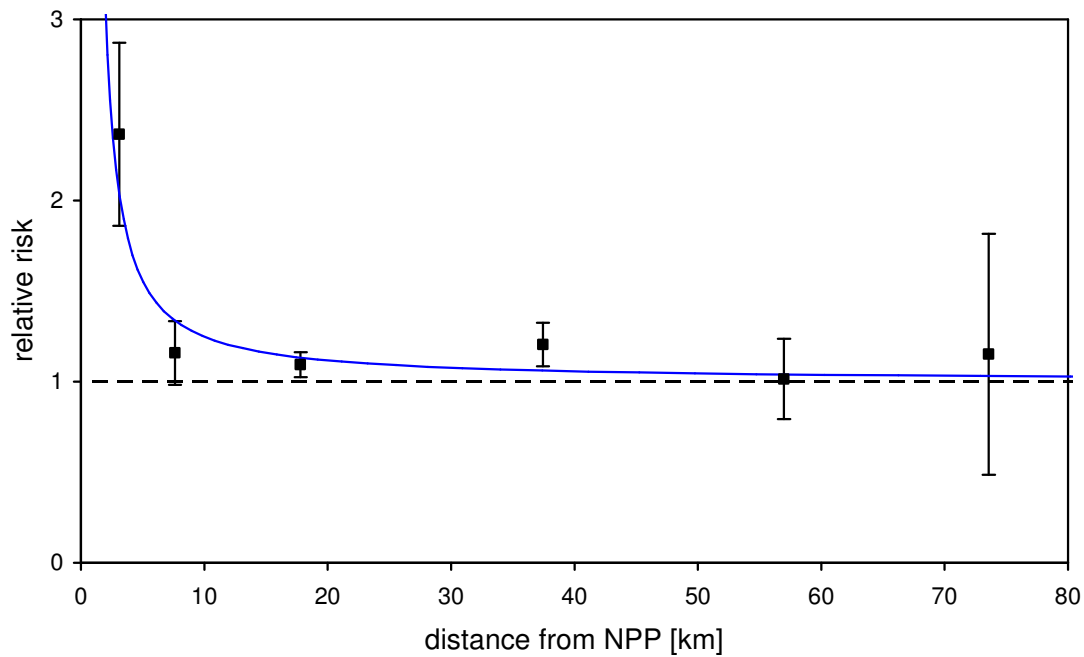
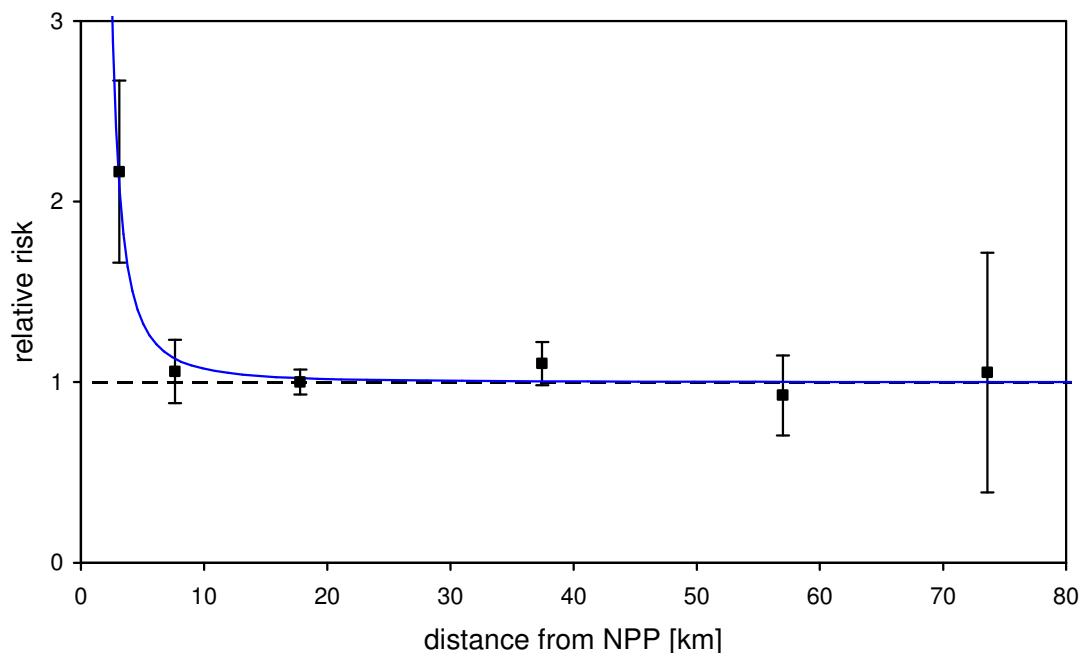


Figure 2: Relative risk as a function of distance from nuclear power reactor and its regression estimated using a quadratic relationship



Confounders

The study further tested the proximity–risk relationship by examining whether other risk factors (ie confounders) could have had an appreciable effect on the result. This proved not to be the case: No confounder had an appreciable influence on the distance trend. In other words, nearness of residence to the nuclear power plant remained the most likely explanation. The study rejected coincidence as an explanation for the results. The study also concluded that the cancer increases were not due to population mixing – often mooted as an explanation for increased cancers near nuclear power stations. However it should be added that this part of the study was underpowered, statistically speaking.

The KiKK authors also removed each nuclear power station in turn from their analyses to see if the results were dependent on the findings near one nuclear power station alone, and the answer was no. (Unfortunately, the KiKK authors have refused to release the data for each of the 16 nuclear power stations for further analyses.)

Possible explanations for increased cancer incidences near NPPs

Various hypotheses have been put forward to explain these cancer increases near nuclear installations including coincidence; a postulated virus from population-mixing (the Kinlen hypothesis); the response to the lack of childhood immunity to infectious diseases (the Greaves hypothesis³²); parental preconception irradiation (the Gardner hypothesis³³); genetic predisposition to cancer; synergistic effects between radiation and unnamed chemicals; or combinations of these factors. Some remain little more than suggestions: others have not been supported by the KiKK study. Although some hypotheses are vigorously promoted by some individuals, none commands widespread support.

Factors connected with proximity to nuclear power stations

Any possible explanation must be guided by the KiKK study's main finding - that the increased risks were directly linked with proximity to NPPs. Therefore we need to examine those aspects of the normal operation of NPPs which might result in increased exposures and risks. These include -

- direct radiation, ie gamma rays and neutrons, from reactor cores;
- “skyshine” from reactor neutrons being reflected back to earth by N, C and O atoms;
- electro-magnetic radiation from power lines near NPPs;
- water vapour emissions from cooling towers at about half the 16 German NPPs, and
- radioactive releases to the environment.

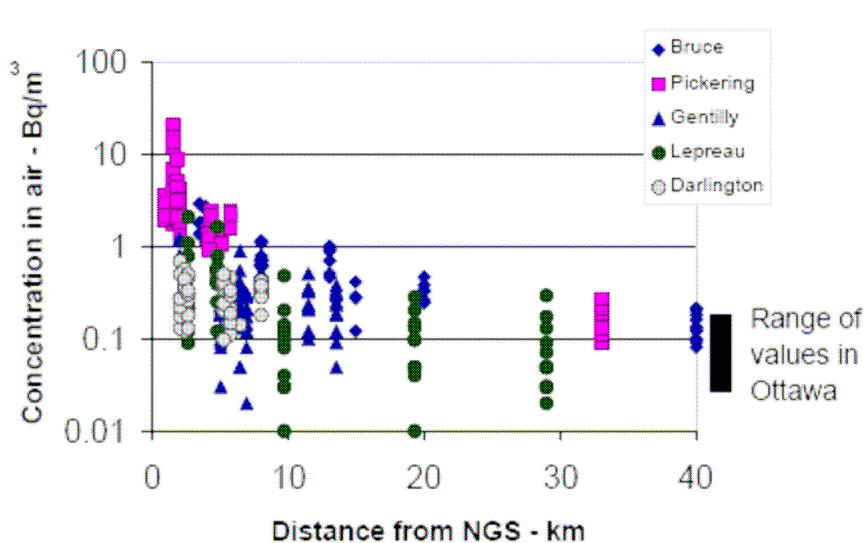
It could also be a combination of the above factors, as there may well be interactions between environmental exposures we are yet to understand. For example, synergistic effects may exist between radiation and chemicals may act to increase cancer risks^{34 35}. Nevertheless, this is considered unlikely as synergistic effects would not exist in combination with radiation exposures from NPPs alone and not from exposures to the Chernobyl plume in 1986, natural radiation and medical radiation. These latter exposures would differ for persons living at approximately the same place.

None of these aspects was explored by the KiKK study, but the estimated risks from most of them are considered to be small or non-existent. The major exception is nuclide releases from nuclear power stations which are examined next. It is noted that the KiKK study clearly had these releases in mind when it was established. All distances to cancer cases were measured from the station chimneys, and the geographical areas monitored specifically included areas downwind from the stations.

Radioactive releases from nuclear power stations

Radioactive releases from nuclear power stations occur by emissions to air and liquid discharges to rivers in Germany (or to the sea in other countries). Air emissions³⁶ are more important, as they cause most of the radiation dose to humans. The relationship between air releases and proximity to nuclear power stations is complicated by variable weather patterns. To say there is no relationship between releases from nuclear power stations and proximity to them would be incorrect. Figure 3 clearly shows the proximity /concentration relationship (note the y-axis is logarithmic). Of course, tritium air concentrations near German NPPs will be lower than those near Canadian Candu reactors (which emit higher levels of tritium) but the proximity /concentration relationship is likely to be similar.

Figure 3 Annual averages of tritium concentrations in air measured at distances from nuclear power stations in Canada, 1985–1999.



sources: *Tritium in the Canadian Environment: Levels and Health Effects*. Report RSP-0153-1. Prepared for the Canadian Nuclear Safety Commission under CNSC contract no. 87055-01-0184 by Ranasara Consultants and Richard Osborne³⁷. Data from Health Canada (2001)³⁸.

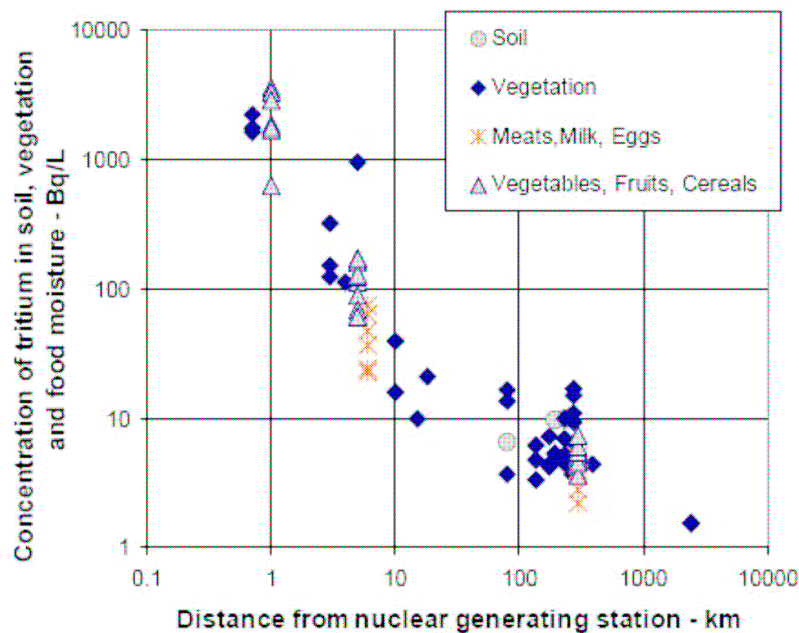
When there is no wind, a simple diffusion relationship would exist in all directions from the NPP chimney. When winds occur then a relationship would exist but only in the predominant downwind direction. What should have been created by KiKK is a computer model to investigate the air releases/proximity relationship for each NPP in Germany. This would incorporate annual major nuclide releases, Pasquill weather categories, wind speeds, wind directions, and average them over a number of years, in order to estimate likely nuclide concentrations in air at the homes of cancer cases near all NPPs, and the resulting possible inhalation/ingestion doses.

The largest emissions from all PWR and BWR nuclear power stations are, in order of magnitude

- H-3 (tritium) as radioactive water vapour
- C-14 as radioactive carbon dioxide, and
- radioactive noble gases including Kr, Ar and Xe isotopes.

These emissions result in elevated nuclide concentrations in vegetation and foodstuffs near nuclear power stations as shown in figure 4 which indicates tritium concentrations in vegetation and food moisture near Canadian nuclear power stations. This graph is log-log scale and indicates that (at least for distances under 20 km) the risk-proximity relationship varies approximately with $1/r^2$ as the slope of the line is about minus 2. In other words, the tritium concentration/distance relationship resembles the risk/distance relationship observed in the KiKK study. Although tritium emissions from Canadian heavy water nuclear reactors are larger than from German PWR and BWR reactors, the same pattern of raised concentrations in vegetation and food is expected to occur near German reactors.

Figure 4. Tritium concentrations in vegetation / food moisture near Canadian nuclear power stations



Source: Reproduced with permission of the CNSC from *Tritium in the Canadian Environment: Levels and Health Effects*. Report RSP-0153-1. Prepared for the Canadian Nuclear Safety Commission under CNSC contract no. 87055-01-0184 by Ranasara Consultants and Richard Osborne. Data from Health Canada (2001) Environmental Radioactivity in Canada. Radiological Monitoring Report. Ottawa, Government of Canada.

The most obvious explanation - releases from nuclear reactors- is often discounted because current official estimates of the radiation doses from reactor emissions are too low, typically by about 3 orders of magnitude, to result in the cancer risks observed by the KiKK study. But how reliable are these dose estimates and risk estimates? Unfortunately this question was not examined by the above German, UK and French studies, nor by KiKK study itself.

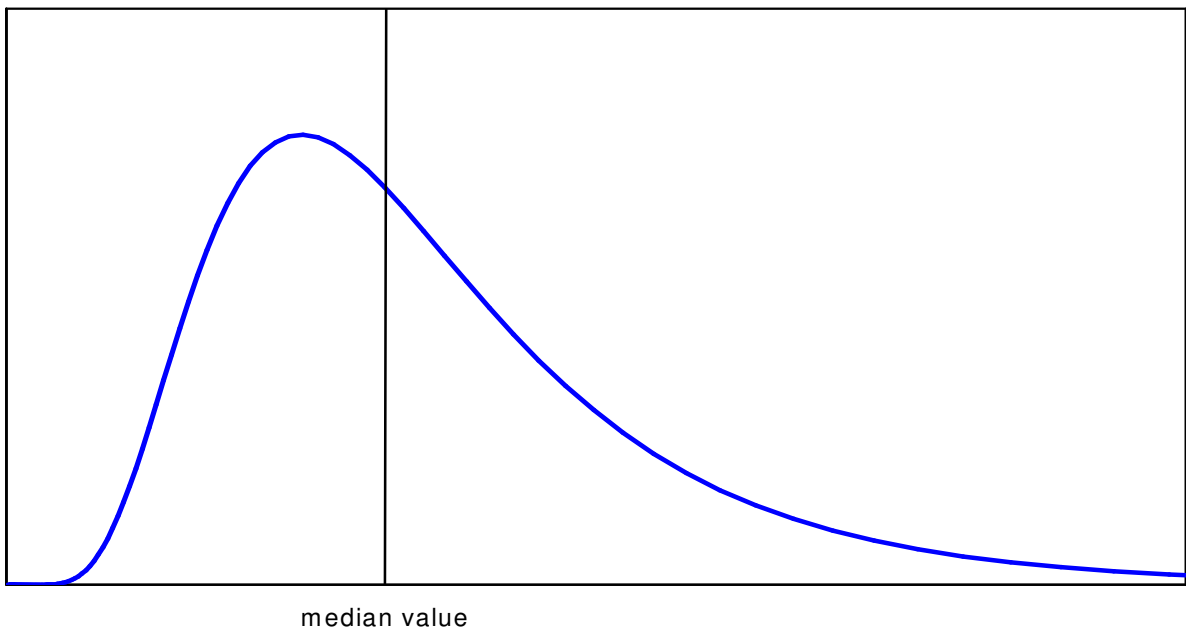
Uncertainties in dose estimates

Estimated radiation doses to adults near nuclear power stations are invariably very low (10^{-2} to 10^{-4} mSv per year). How these estimates are derived is not widely understood by scientists, and not at all by members of the public. In fact, the methodology is quite complicated, as they are derived using at least four computer models in sequence

- models for the generation of fission/activation products in reactor cores; these generate the emission data published by utilities for most nuclides
- environmental transport models for radionuclides, including weather models
- human metabolism models which estimate nuclide uptake, retention and excretion
- dose models which estimate radiation doses from internally retained nuclides

Each model derives a range of results log-normally distributed (such as in figure 5 below) from which only the median value is normally used. Each of these probability distributions would be log-normal rather than normal distributions; that is, they would be skewed to the right as in figure 4 below. This means that, although the real value could be larger or smaller than the median value, in practice some very high values could result.

Figure 5. Log-normal distribution



The problem is that each model's central result is inherently uncertain (the real result lying within the shown distribution). The uncertainties from each model have to be multiplied together to gain an idea of the overall uncertainty in the final dose estimate³⁹. Further uncertainties are introduced by unconservative radiation weighting factors and tissue weighting factors in official models⁴⁰. The cumulative uncertainty in dose estimates could be very large as recognised by the report of the UK Government's CERRIE Committee⁴¹.

This does not mean that official dose estimates from nuclear power plant releases are always incorrect. But it does mean they contain unquantified uncertainties which could be large and which render them unreliable where evidence exists that they may be incorrect. In other words, when we try to ascertain the reasons for the wide gulf between estimated risks and risks observed by KiKK, we should not dismiss radiation exposures as a possible cause just because official dose estimates are too low.

Uncertainties in risk estimates

In addition, there are uncertainties with estimated **risks** as well as estimated **doses**. This is because a risk model has to be applied to doses to estimate the likely level of cancers, but large uncertainties could exist in this model as well. For example, current official risks are derived mainly from the Japanese survivors of the atomic bombs. However many scientists worry that these risk estimates (from a sudden external blast of high energy

neutrons and gamma rays) are not really applicable to environmental releases which result in chronic, slow, internal exposures usually to low-range beta radiation. Uncertainties in official risk model also derive from the application of risks from a Japanese to a European population, from its application to adults only, from its application of age and gender-averaged risks, and from the practice of arbitrarily halving risks to take account of cell studies suggesting lower risks from low doses and low dose rates. However it is difficult to quantify these uncertainties and to give a figure which may indicate how much the current risk estimate for adults (5% per Sv effective dose) may be an underestimate.

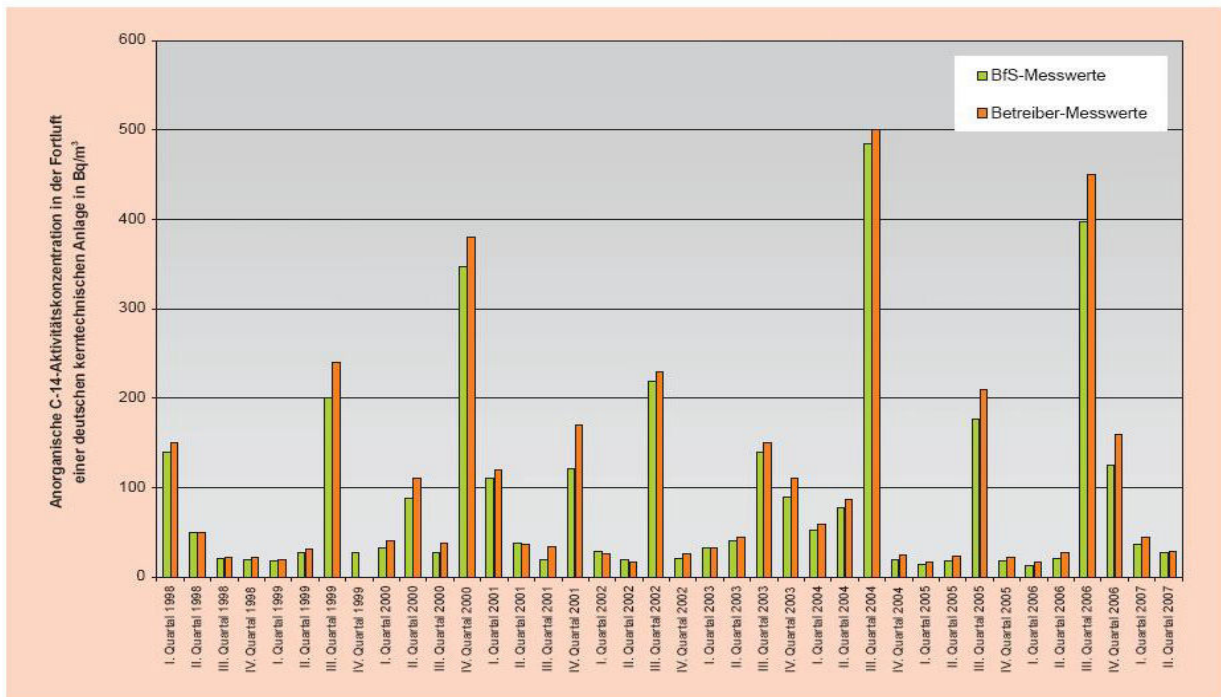
Hypothesis: *In utero* exposures from environmental releases

The KiKK findings have prompted much debate among scientists throughout Europe as to the cause(s) of the increased leukemia cases near German nuclear power stations. Indeed, it is a primary task of science to attempt to explain observed phenomena which are apparently at odds with received wisdom or, in this case, with the current understandings of radiation risks. It is for this reason that the following hypothesis is suggested to explain the risks shown by the KiKK study.

It is theorised that observed high rates of infant leukemias in KiKK may be a teratogenic effect from nuclides released by nuclear reactors being incorporated in embryos and fetuses in the womb. Spikes in releases from nuclear power stations may result in the labelling of the embryos and fetuses of pregnant women living nearby at high concentrations. These concentrations could be long-lived and could result in high doses to radiosensitive tissues and subsequent cancers. This suggestion was first made by the late Professor Edward Radford, the former Chairman of BEIR III Committee. He mooted it 30 years ago during testimony to the Ontario Select Committee on Hydro Matters⁴² which then was examining possible health effects of tritium discharges from nuclear facilities near Toronto, Canada.

Spikes in the emissions of radioactive carbon and hydrogen (as carbon dioxide and water vapour) occur at nuclear power stations when they are opened (approximately once a year) to replace nuclear fuel. Figure 6 indicates quarterly ¹⁴C releases from a German PWR nuclear power station in recent years. Tritium and noble gases will be released at the same time as ¹⁴C. It can be seen that gaseous releases are episodic with spikes occurring about once per year.

Figure 6: Quarterly ¹⁴C releases from the Neckarwestheim 2 nuclear power station in Germany



Vergleich der vom Betreiber und dem BFS ermittelten Kohlenstoff-14-Aktivitätskonzentrationen in der Fortluft am Beispiel eines süddeutschen Druckwasserreaktors (KKW Neckarwestheim 2)

source: Jahresbericht (Annual Yearbook) 2007, Bundesamt für Strahlenschutz, Berlin.

In order to assess this hypothesis, we discuss below a number of aspects which lend support to it, including

- the nature of the emissions from nuclear power stations ie mostly carbon (^{14}C) and hydrogen (^3H)
- the bio-accumulation of ^3H and ^{14}C in embryos and fetuses
- the increased radiosensitivity of embryos and fetuses, and
- the increased radiosensitivity of pre-natal hematopoietic cells

Major emissions: carbon (^{14}C) and hydrogen (^3H)

As stated above, the largest nuclide emissions from nuclear power stations are radioactive carbon (^{14}C), hydrogen (^3H) and noble gases. ^3H and ^{14}C exist in the forms of liquid water, water vapour and carbon dioxide gas. These isotopes rapidly exchange with stable H and C; and recycle in all biota. Figure 3 above indicates the relationship between tritium concentrations in food / vegetation and distance from nuclear power stations. A similar relationship is expected for carbon-14.

Organically Bound Tritium (OBT) and Organically Bound Carbon (OBC) are formed by embryos and fetuses taking up tritium and ^{14}C atoms during new cell production. The result is that embryos and fetuses near nuclear power stations may be labelled at the levels of ambient (environmental) ^3H and ^{14}C concentrations. This means that mothers living near nuclear power stations may give birth to babies with enhanced concentrations of these nuclides.

Bio-accumulation of ^3H and ^{14}C in embryos and fetuses

Stather et al⁴³ have estimated that, following tritium intakes by the mother during pregnancy, tritium concentrations in her fetus are 60% higher than in herself. As a result, the HPA now estimates⁴⁴ that doses in embryonic and fetal tissues are raised by factors of 1.5 to 2 compared to adult tissues following exposures to air releases of tritiated water vapour (HTO). Both studies showed similar increases for ¹⁴C.

The radiosensitivity of embryos and fetuses

The best data on the radiation risks of *in utero* exposures, that is, on the radiosensitivity of embryos and fetuses, are from the UK Oxford Survey of Childhood Cancer (OSCC) carried out by the pioneering radiation epidemiologist, Alice Stewart, in the 1950s to 1980s⁴⁵. Recently, Wakeford⁴⁶ comprehensively reviewed the OSCC and more than 30 similar studies worldwide. The latter studies confirmed the presence and size of the risks of *in utero* radiation initially found by Stewart. From OSCC and other data, Wakeford and Little⁴⁷ have estimated that the excess relative risk (ERR) of leukemia in children aged under 15 was 51 per Gy (95% CI: 28, 76) from abdominal exposures to X-rays.

If we apply this risk estimate to the KiKK situation, three corrections are needed. First, the leukemia risk in under 5 year-olds (as in KiKK) is greater than in under 15 year-olds because the peak years for leukemia diagnoses are in children aged 2 to 3 years. This would result in the average relative risk being greater by a factor of perhaps ~1.5. Also, most (>90%) OSCC exposures were in the last trimester, and it has been estimated⁴⁸ that risks from exposures in the first trimester are perhaps 5 times greater than those from exposures in the last trimester.

These risks arose from external X-rays, whereas the KiKK risks are hypothesised to arise from internal exposures to radionuclides. There are few estimates of the risks arising from internal *in utero* exposures. However, Fucic et al⁴⁹ have recently suggested that *in utero* risks from internal nuclides were 4 to 5 times greater than from *in utero* X-rays[‡]. Summing these factors, we postulate that the RR of child leukemia in 0-5 year olds from internal nuclides in the 1st trimester near nuclear power stations would be

$$\begin{aligned} \text{RR} &= 52 \text{ per Gy (OSCC)} \times 1.5 \text{ (0-5 yr-olds)} \times 5 \text{ (1}^{\text{st}} \text{ trimester)} \times 5 \text{ (internal vs X-rays)} \\ &= \sim 2 \text{ per mGy} \end{aligned}$$

This suggests that human embryos and fetuses may be considerably more radiosensitive than currently acknowledged. It also seems to suggest that background radiation of about 1 mSv per year (excluding radon doses) could be a major cause of naturally-occurring childhood leukemia: this has already been proposed⁵⁰.

If we were to apply the KiKK relative risk for childhood leukemia of 2.2, it would suggest *in utero* doses to embryos in pregnant women near German nuclear power stations of about 1 mGy. Although this is very low, it is still about 1,000 times higher than the official estimated doses of a few μGy (albeit to adults) from emissions from nuclear power stations.

Increased radiosensitivity of pre-natal hematopoietic cells

Finally, we need to consider the different radiosensitivities of various embryonic tissues. Since we are primarily concerned with leukemia which affects white blood cells, our

[‡] the internal nuclides studied by Fucic et al were mainly ^{99m}Tc and ¹³¹I.

attention is focussed on the hematopoietic[§] system, ie bone marrow and lymphatic tissues. These tissues contain many stem cells, ie cells which are self-renewing. When they divide, some daughter cells remain stem cells, so the number of stem cells stays about the same. Radiation-caused mutations to stem cells would clearly be damaging to hematopoietic system and could result in increased malformation rates of white blood cells, ie in increased leukemia risks.

Bone marrow contains a very high proportion of these proliferating stem cells compared to other organs and it is likely to be among the most radiosensitive of embryonic/fetal tissues. This pronounced radiosensitivity has been mentioned previously. In 1990, after the Gardner team⁵¹ had published their paternal preconception irradiation hypothesis, the BMJ published letters questioning aspects of the hypothesis. One letter by Morris⁵² stated that, assuming mutations were the cause of the observed 10-fold increase in leukemia incidence observed by Gardner's team, it would require a 100 to 1,000-fold increase in the radiation-induced mutation rate if acting on the germ cell; a 10-fold increase if acting on lymphocytes during early extra-uterine life; but only a 1.8-fold increase if acting on lymphocytes throughout intrauterine life, ie a 1,000 fold increase in radiosensitivity *in utero*. He added the latter seemed the most plausible mechanism even though the exposure pathways were unclear⁵³.

In 1992, Lord et al⁵⁴ suggested the same when they stated that embryonic hematopoietic cells could be up to 1,000 times more radiosensitive than post-natal hematopoietic cells. They added that different mechanisms of inducing this damage operated at different embryonic/fetal stages. More recently, the suggestion that pre-natal hematopoietic cells were highly radiosensitive was supported by Ohtaki et al⁵⁵ in their study of chromosome translocation frequencies in the white blood cells of Japanese A-bomb survivors irradiated *in utero*. They found that precursor lymphocytes of the fetal hematopoietic system may be highly radiosensitive, perhaps 100 times more so than post-natal lymphocytes. From this study, Wakeford⁵⁶ surmised that radiosensitive primitive cells (whose mutation may result in childhood cancers) remain active throughout pregnancy, including during the third trimester but not after birth, although it is not known at present why this is the case.

It is concluded that the increased radiosensitivity of hematopoietic cells before birth might prove to be a major factor in explaining the discrepancy between official dose estimates and the observed level of risks in the KiKK study.

What about the increases in solid cancers?

The above may explain the leukemia increases, but what about the lower increase in solid cancers also observed by KiKK? Although the increased numbers of solid cancers in the KiKK study were not statistically significant, this does not mean that there are no such risks (see above). In addition, there are good theoretical grounds for expecting solid cancers. For example, the OSCC study¹⁴ found increased solid cancers from *in utero* exposures. The numerical difference between leukemia risks and solid cancer risks could be explained by the exceptional radiosensitivity of hemopoietic tissues *in utero* compared to other tissues *in utero*. This in turn could be explained by the higher concentrations of stem cells in hemopoietic tissues, as the majority of stem cells in adults are found in hemopoietic tissues, ie bone marrow and lymph glands.

Conclusion

[§] hematopoiesis - sometimes termed hemopoiesis - is the formation of blood cellular components.

The hypothesis proposed here is that observed high rates of infant leukemias in KiKK may be a teratogenic effect from incorporated radionuclides. These effects, eg congenital malformations, are often recognised at birth, but infant leukemia is not easily ascertained at birth. Such babies are born pre-leukemic with full-blown leukemias only being diagnosed years after birth, ie after their bone marrows have accumulated sufficient radioactive decays.

A possible biological mechanism to explain the KiKK observations is that emission spikes from nuclear reactors result in the radioactive labelling of embryonic and fetal tissues in pregnant women living nearby. Such concentrations, factored over a number of years (2-5 years) both before and after birth could result in the accumulation of relatively high doses in radiosensitive organs of embryos and fetuses, particularly their hematopoietic tissues. Cumulative radiation doses and risks to specific organs and tissues in embryos/fetuses from nuclide uptakes during pregnancy are not specifically considered in official publications.

Recommendations

Whatever the final explanation for the increases, the KiKK study and its implications raise many questions, including whether vulnerable people – in particular, pregnant women and women of child-bearing age – should be advised on possible risks of living near nuclear power stations. Another question is whether local residents should be advised about the risks of eating produce from their gardens or wild foods, as the food pathway is the largest contributor to local doses.

It is recommended that US regulatory agencies should estimate ^{14}C and ^3H intakes near US nuclear power stations and ^{14}C and ^3H intakes from other sources. They should also establish whether a significant relationship exists between proximity to nuclear power station and intakes of these nuclides. In particular, they should estimate doses and risks from episodic nuclide emissions from nuclear power stations; estimate bone marrow doses of developing embryos and the subsequent risks of leukemia and solid cancers in young children; assess the confidence intervals around their estimates; and publish its results. It is also recommended that US regulatory agencies should also establish a KiKK-style epidemiology study of cancer near all US nuclear power stations with precise distances being measured between cancer cases and nuclear reactors.

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