Hypothesis to Explain Childhood Cancer near Nuclear Power Plants

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As reported in this journal in 2009, the 2008 KiKK study in Germany found a 60% increase in all cancers and a 120% increase in leukemias among children living within 5 km of all German nuclear power stations. The KiKK study has triggered debates as to the cause(s) of these increased cancers. This article discusses the available evidence of leukemias near nuclear installations around the world. Over 60 epidemiological studies exist, the large majority of which indicate increases in leukemia incidence. The article also outlines a possible biological mechanism to explain the increased cancers. This suggests that doses from environmental nuclear power plant emissions to embryos/ fetuses in pregnant women near the plants may be larger than suspected, and that hemopoietic tissues may be considerably more radiosensitive in embryos/ fetuses than in newborn babies. The article concludes with recommendations for further research. Key words: cancer; leukemia; radioactivity; radiation; nuclear power stations; relative risk; radionuclides; tritium; carbon-14; emissions; discharges; embryo; fetus; pregnancy outcomes; KiKK study; Germany.

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INTRODUCTION

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 that the cause(s) remained unknown but was (were) unlikely to involve radiation exposures.^{1–4} This was mainly because official estimates for radiation doses from these facilities were too low by two to three orders of magnitude to explain the increased leukemias.

As reported previously in this journal by Nussbaum,⁵ the 2008 KiKK study (Kinderkrebs in der Umgebung von KernKraftwerken [Childhood Cancer in the Vicin-

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ity of Nuclear Power Plants])^{6,7} rekindled the childhood leukemia debate. The KiKK study found a 120% increase in leukemias risk and a 60% increase in all cancers among children under five years old living within 5km of all German nuclear power plants (NPPs). The web publication⁸ of the KiKK study resulted in a public outcry and media debate in Germany but not elsewhere. It is now officially accepted in Germany that children living near nuclear power plants develop cancer and leukemia more frequently than those living further away. The German government has stated:

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.⁹

The US Environmental Protection Agency (US EPA) and US Nuclear Regulatory Commission (US NRC) have remained silent on these remarkable findings to date.

Other Studies of Childhood Leukemias near Nuclear Power Plants

It has been known at least since the late 1950s¹⁰ that radiation exposures can result in increased leukemias and that environmental exposures to radiation are a risk factor for leukemia.^{11–13} In addition, several ecological and case-control studies^{14–16} in the past have suggested or indicated an association between nuclear power plants and childhood leukemia among those living nearby.

In a little-noticed 1999 study,¹⁷ Laurier and Bard examined the literature on childhood leukemias near NPPs worldwide. They listed a startling total of 50 studies (29 ecological, seven case-control, and 14 multisite

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TABLE 1 Leukemia Mortality Risks ³⁰		
Age Group (years)	Proximity to Nuclear Facility	Leukemia Mortality
0 to 9	All distances Under 16 km	1.05 1.24
0 to 25	All distances Under 16 km	1.02 1.18

studies). The large majority revealed small increases in childhood leukemia near NPPs although the results in most of the ecological studies were not statistically significant. The policy implications of this study were apparently not discussed by official radiation protection agencies worldwide.

Then followed two studies^{18,19} indicating raised leukemia incidences in France and Germany, but official studies concluded the opposite. The 10th and 11th reports of the UK Government's COMARE^{20,21} and two studies in France^{22,23} stated there was no evidence of leukemia increases near NPPs.

After the KiKK study was published in 2008, two more government-sponsored studies found small leukemia increases near NPPs. The Bithell et al.²⁴ study found an increase in child leukemias within 0 to 5km at 13 out of of 14 UK NPPs studied, and Laurier et al.²⁵ found an increase within 0 to10km near French NPPs. In both cases, the numbers were low and therefore not considered statistically significant (that is, there was a greater than 5% possibility that the observations could have occurred by chance, or put another way, p-values were > 0.05).

However, instead of reporting these increases, the latter two studies concluded that there was "no suggestion" or "no evidence" of leukemia increases near UK and French nuclear reactors, respectively, simply because their data lacked statistical significance. These conclusions are incorrect because lack of statistical significance only means that chance was not excluded as an explanation, assuming no bias and assuming there was no real effect. The authors should have reported that small leukemia increases were found, but that there was a > 5% probability they could have occurred by chance. A p-value-that is, the probability that observed effects may be due to chance-is affected by both the magnitude of the effect as well as the size of the study.²⁶ This means statistical tests must be used with caution since the use of a given cut-off for statistical significance (usually p = 0.05) can lead to incorrectly accepting the null hypothesis: that there is no effect. This could dismiss a result merely because it is not statistically significant.²⁷ In statistics, this is termed a type II error. This can occur in small studies due to their small sample sizes rather than lack of effect.²⁸ This is the case for both the Bithell et al. and Laurier et al. studies, which have results which are statistically not significant simply because they are too small.

The Bithell and Laurier conclusions are regrettable as they could 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. Axelson pointed out²⁹ that many negative and non-positive epidemiology studies (like the Bithell and Laurier studies) are of questionable validity because they may obscure existing risks. The stronger evidence from the KiKK study suggests there may well be such increases near nuclear power stations. This conclusion is supported by two meta-analyses that combine the results of various national multisite studies in order to achieve statistical significance. The first, by Baker and Hoel,³⁰ assessed data from 17 research studies covering 136 nuclear sites in the UK, Canada, France, the US, Germany, Japan, and Spain (Table 1). In children up to nine 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 would have given considerable support to the KiKK findings, but the study was not cited in the KiKK, Laurier, and Bithell studies. The second, more recent, meta-analyses³¹ covered NPPs in Germany, France, and the UK. This study also found a statistically significant increased risk of child leukemias and relative risk of leukemia deaths near NPPs (RR= 1.33; one-tailed pvalue = 0.0246).

Finally, in 2008 Laurier et al.³² reviewed epidemiological studies on childhood leukemia in 198 nuclear sites in 10 countries, including 25 major multisite studies. They found that increased risks of childhood leukemia near nuclear installations were a recurrent issue. The authors, employees of the French government's Institut de Radioprotection et Sûreté Nucléaire (IRSN), confirmed that clusters of childhood leukemia cases existed locally, but refused to generalize their findings.

The 2008 Laurier et al. study, taken together with Laurier and Bard's 1999 study, indicate that there have been more than 60 studies worldwide on childhood cancer near nuclear facilities, with the large majority finding cancer increases. These findings are discussed further by Körblein and Fairlie.³³

This consistent pattern of association of childhood leukemias worldwide with NPPs provides very strong support for the KiKK study. Indeed, in view of the above evidence, there is little scientific dispute about the association of childhood leukemia incidence with proximity to nuclear reactors: this association has been clearly established, at least among scientists independent of nuclear policies. Our remaining arguments focus on its causation and public policy ramifications.

NEED TO RELY ON BEST AVAILABLE SCIENTIFIC EVIDENCE

Policy makers need to be guided by the best available scientific evidence. It is preferable to rely on the larger KiKK study than the Bithell and Laurier studies for a number of reasons. First, the KiKK study found statistically significant cancer increases. The one-tailed p-values in the KiKK study were 0.0034 for all cancers and 0.0044 for leukemias, both of which are well below the usually applied 0.05 value for statistical significance. Second, the KiKK findings have been supported in two meta-analyses and many other studies as mentioned above. Third, KiKK was a case-control study (that is, it examined 593 with leukemia children under five years of age together with 1766 controls, that is, children under five years old who did not have leukemia. This means its findings take precedence over the Bithell and Laurier, which were ecological studies and thus considered less reliable. Finally, the KIKK study used very accurate distance measures. It estimated distances between the homes of cancer cases and NPPs to within 25 meters. This was the first time in Europe that a study measured how far each cancer case was from the nearest nuclear reactor. In contrast, the Bithell and Laurier studies measured the distances between NPPs and the population centroids of irregularly shaped electoral wards and other administrative areas. In other words, their findings are much less reliable than the KiKK study.

Our conclusion is that the Bithell and Laurier studies, despite what their authors seem to imply, simply have not invalidated the findings of the much more sophisticated KiKK study.

DISCUSSION

What are the Cause(s) of Increased Cancers near NPPs?

Since the first leukemia cluster was discovered in 1984 near the Sellafield nuclear reprocessing plant in the UK, many scientists have pondered the cause(s) for the cancer increases; however, we are not much closer to ascertaining them than we were in the 1980s. Many suggestions have been put forward, including: coincidence; a postulated virus from population-mixing (the Kinlen hypothesis); an unusual response to infectious diseases in children (the Greaves hypothesis); parental preconception irradiation; genetic predisposition to cancer; or a combination of these factors. Some of these suggestions are farfetched and are unsupported by the findings of the KiKK study. None of them addressed the central finding of the KiKK study-that increased cancers are directly associated with proximity to NPPs. Indeed, most the above suggestions appear designed to do the opposite, that is, to draw attention away from NPPs.

Aspects of the Normal Operation of NPPs

What aspects of the normal operation of NPPs might result in increased risks? We suggest that the following should be considered:

- direct radiation "shine" by gamma radiation and neutrons from reactor cores;
- "skyshine" from core neutrons reflected back to earth by nitrogen (N), carbon (C), and oxygen (O) atoms in the air;
- electromagnetic radiation from power lines near NPPs;
- water vapor emissions from cooling towers at about half of the German NPPs;
- parental preconception irradiation of nuclear workers;
- radioactive contamination of nuclear workers' homes (for example, by workers' clothing);
- chemical releases to the environment; and
- radioactive releases to the environment.

The increased cancers could also be due 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 which could act to increase cancer risks.^{34,35} Unfortunately, none of the above aspects was explored by the KiKK study (nor in depth by any other study known to the author) but the estimated risks from most of them individually are considered to be small or non-existent, with the major exception of NPPs releases-which are examined below. The KiKK study clearly had these releases in mind when it was set up. 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 Plants

Radioactive releases from NPPs occur through emissions to air and discharges to rivers in Germany (and to the sea in other countries). Air emissions are more important, as they cause most of the radiation dose to humans, including in the case of German reactors. For whatever reason, radiation risks from NPP nuclide releases are rarely discussed in the literature. A rare exception is the 2006 study by Evrard A-S et al., which concluded there was no association. However, this study suffered from the same type of weaknesses noted in the studies considered above, as well as from its reliance on "dose" estimates, which may contain significant uncertainties.³⁶

The largest emissions from German nuclear power stations are

- radioactive noble gases, including Krypton (Kr), Argon (Ar), and Xenon (Xe) isotopes;
- H-3 (tritium) as radioactive water vapor; and
- C-14 as radioactive carbon dioxide gas.

These emissions result in elevated nuclide concentrations in vegetation and foodstuffs near NPPs, as



FIGURE 1—Tritium concentrations in vegetation/food moisture near Canadian NPPs. Reproduced with permission from Ranasara Consultants and Richard Osborne³⁷ using data from Health Canada.³⁸

shown in Figure 1, which shows tritium concentrations in vegetation and food moisture near Canadian NPPs. This graph is log-log scale and indicates that (at least for distances under 20 km) the risk-proximity relationship is proportional to $1/r^2$ as the slope of the line is about minus 2. This tritium concentration/distance relationship is very similar to the risk/distance relationship revealed by the data of the KiKK study.

Although tritium emissions from Canadian heavy water nuclear reactors are much 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.

Uncertainties in Dose Estimates

Nuclear power plant releases are often discounted as a possible cause for elevated cancer prevalence because current official estimates of their resulting radiation doses are too low, typically by three or more orders of magnitude, to result in the cancer risks observed by the KiKK study. But how reliable are these dose estimates? Unfortunately this question is rarely examined: it was not examined for example by any of the various German, UK, and French studies on KiKK, nor was it considered in the KiKK study itself.

Published radiation doses from exposures to NPP releases are invariably very low $(10^{-2} \text{ to } 10^{-4} \text{ mSv per year})$. However, these are estimates not measurements. 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 meteorological models;
- human metabolism models which estimate nuclide uptake, retention, and excretion; and
- dose models which estimate radiation doses from internally retained nuclides.

Each model derives a range of probabilistic results lognormally distributed (such as in Figure 2); that is, they are skewed to the right. This means that, although the real value could be larger or smaller than the median value, some very high values could result. However, only the median value is used in official dose estimations.

The problem is that the "correct" value from each model may not be the median value: in scientific terms, the "correct" value is uncertain. Furthermore, the dose uncertainties from each model have to be combined to gain an idea of the overall uncertainty in the final dose estimate.³⁹ More uncertainties are introduced by radiation weighting factors and tissue weighting factors in official dosimetry models.⁴⁰ The result is that the cumulative uncertainty in official dose estimates could be very significant or in other words, official dose estimates may be unreliable. This was the main conclusion of the report of the UK government's Committee Examining the Radiation Risks of Internal Emitters (CERRIE)⁴¹ on the risks of internal radiation in 2004.

This does not mean that official dose estimates are always incorrect. But it does mean they contain unquantified uncertainties which could be large and which render them unreliable where evidence exists to the contrary. In other words, when we try to ascertain the reasons for the wide gulf between small estimated doses and large observed risks, we should not dismiss radiation exposures as a possible cause just because official dose estimates are very 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 used to estimate the likely level of cancers, but large uncertainties could exist in this model as well. For example, current official risks derive mainly from the Japanese survivors of the atomic bomb blasts in 1945. However, many scientists have worried that these risk estimates (from a sudden external blast of high-energy neutrons and gamma rays) are not really applicable to the risks that arise from environmental releases resulting in chronic, slow, internal exposures 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 (excluding babies and infants), 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.

The central question is whether the above uncertainties in official dose estimates taken together with the uncertainties in official radiation risk models are sufficiently large to explain the 10³ to 10⁴ discrepancy between estimated KiKK doses and observed KiKK risks? Interestingly, a recent article by Richardson⁴² went part way in explaining the discrepancy. Richardson pointed out that the "hazard" (the product of dose times risk) from internal radiation exposures increased considerably the younger a person was. In particular, hazards to neonates were greater than to infants (less than one year old) and greater in infants than in children (one to 15 year old) and adults (more than 15 years old).

Richardson indicated that, for a number of metabolic reasons, radionuclide dose coefficients for infants were approximately 10 times greater than those for adults. For example, official International Commission on Radiological Protection (ICRP) dose models inexplicably did not account for human growth. Richardson added, mainly from the evidence of the Japanese bomb survivors, that radiation risks were also about 10 times greater for infants than for adults. This meant that radiation hazards in infants were about 100 times greater than in adults. Richardson's helpful discussion went some of the way to providing an explanation for the discrepancy between the official estimated doses and observed risks in the KiKK study, but we still need to explain an additional factor of 100 or so to fully account for the discrepancy between estimated and observed risks. In my view, this may be provided by the added radiosensitivity of embryos and fetuses which the Richardson paper did not specifically address.

Hypothesis: In utero Exposures from Environmental Releases

We hypothesize that "spikes" in NPP releases may result in the contamination of embryos and fetuses of pregnant women living nearby in high concentration areas. These concentrations could be long-lived and could result in large exposures to radiosensitive tissues and subsequent cancers. This suggestion was first made by the late Professor Edward Radford, the former chairman of the Committee on the Biological Effects of Ionizing Radiation (BEIR) in the US. Radford made the suggestion 30 years ago during testimony to the Ontario Select Committee on Hydro Matters⁴³ which then was examining the possible health effects of tritium discharges from nuclear facilities near Toronto in Canada.

Spikes in the emissions of radioactive carbon and hydrogen (as carbon dioxide and water vapor) occur at NPPs when they are opened (approximately once a year) to replace nuclear fuel. Figure 3 indicates ¹⁴C air concentrations resulting from nuclide releases from a



Figure 2—Log-normal distribution with x axis = probability of occurrence (arbitrary units) and Y axis = dose value (arbitrary units).

German PWR nuclear power station in recent years. Tritium and noble gases were released at the same time as ¹⁴C. It can be seen that air concentrations (gaseous releases) were episodic, with spikes occurring about once per year on average.

In order to assess our hypothesis, we discuss below a number of further considerations, including:

- the nature of the emissions from NPPs, including carbon (¹⁴C) and hydrogen (³H);
- the bio-accumulation of ³H and ¹⁴C in embryos and fetuses;
- the increased radiosensitivity of embryos and fetuses; and
- the increased radiosensitivity of prenatal hematopoietic cells.

Major Emissions: Carbon $({}^{14}C)$ and Hydrogen $({}^{3}H)$

As stated above, the largest nuclide emissions from NPPs are radioactive carbon (14 C), hydrogen (3 H), and a number of noble gases. 3 H and 14 C exist in the forms of water, water vapor, and carbon dioxide. These isotopes rapidly exchange with stable hydrogen and carbon and recycle in all biota. Figure 1 indicates the relationship between tritium concentrations in food / vegetation and distance from NPPs. A similar relationship is expected for 14 C.

Organically bound tritium (OBT) and organically bound carbon (OBC) are formed by embryos and fetuses taking up radioactive hydrogen and carbon atoms during new cell production. The result is that embryos and fetuses near NPPs may be contaminated at the levels of ambient (environmental) ³H and ¹⁴C concentrations. This means that mothers living near NPPs may give birth to babies with enhanced concentrations of these nuclides

Bioaccumulation of ³H and ¹⁴C in Embryos and Fetuses

Stather et al.⁴⁵ estimated that, following tritium intakes by a mother during pregnancy, tritium concentrations



Figure 3—Quarterly ¹⁴C air concentrations near the Neckarwestheim 2 nuclear power plant in Germany. (Reproduced with permission from Bundesamt für Strahlenschutz).⁴⁴

in her fetus were 60% higher than in herself. As a result, the UK government's Health Protection Agency (formerly NRPB) now estimates ⁴⁶ 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 vapor. 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 epidemiologist, Alice Stewart, from the 1950s to 1980s.⁴⁷ Recently, Wakeford ⁴⁸ 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. Wakeford and Little⁴⁹ estimated from OSCC and other data that the relative risk (RR) of leukemia in children aged under 15 was 52 per Gy (95%CI, 28-76) from abdominal exposures to x-rays.

If we apply this risk estimate to the KiKK situation, we need to make three corrections. First, the leukemia risk

in children under five years old (as in KiKK) is greater than in those under 15 years old because the peak years for leukemia diagnoses are in children aged two to three years. This would result in the average RR being greater by a factor of perhaps ~1.5. Also, most (>90%) OSCC exposures were in the last trimester, and it has been estimated⁵⁰ that risks from exposures in the first trimester are perhaps five times greater than those from exposures in the last trimester. The OSCC risks arose from external x-rays, whereas the KiKK risks are hypothesised to arise from internal exposures to radionuclides. While there are few estimates of the risks arising from internal in utero exposures, Fucic et al.⁵¹ have recently suggested that in utero risks from internal nuclides were four to five times greater than from in utero x-rays. Summing these factors, we postulated that the RR of child leukemia in 0 to 5 year olds from internal nuclides in the first trimester near NPPs would be as follows:

RR = 52 per Gy (OSCC) × 1.5 (0 to 5 yr-olds) × 5 (1st trimester) × 5 (internal exposure vs x-ray exposure) = ~2 per mGy

This suggests that human embryos and fetuses are much more radiosensitive than currently acknowledged. It also seems to suggest that background radiation of about 1 mGy per year (excluding radon doses) could be a major cause of naturally-occurring childhood leukemia, a suggestion which has already been proposed.⁵²

If we were to apply the relative risk of 2.2 found by the KiKK study for childhood leukemia, it would suggest in utero doses to embryos in pregnant women near German NPPs of about 1 mGy. It is not possible to compare this with official estimates of exposures to embryos near German NPPs as these were not carried out, although that should be done. Nevertheless, such doses, although very low, are still about 1000 times higher than the official estimated annual doses of a few μ Gy to adults from NPP emissions.

Increased Radiosensitivity of Prenatal Hematopoietic Cells

Finally, we need to consider the different radiosensitivities of various embryonic tissues. Since we are primarily concerned with leukemia, our attention is focussed on the hematopoietic system, that is, on the blood-forming cells in bone marrow and lymphatic tissues. These tissues contain stem cells (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 (that is, in increased leukemia risks).

Bone marrow contains a high proportion of stem cells compared to other organs and it is likely to be among the most radiosensitive of embryonic / fetal tissues. This radiosensitivity has been hinted at previously on at least three occasions. In 1990, after the Gardner team⁵³ had published their hypothesis that paternal preconception irradiation caused the observed leukaemia increase, the British Medical Journal published letters questioning aspects of the hypothesis. One letter⁵⁴ by J. A. Morris stated that, assuming radiation-caused mutations were the cause of the observed 10-fold increase in leukemia incidence observed by Gardner's team, a 100to 1000-fold increase in the radiation-induced mutation rate would be required if the radiation were acting on the germ cell; a 10-fold increase would be required if the radiation were acting on lymphocytes during early extrauterine life; but only a 1.8-fold increase would be required if the radiation were acting on lymphocytes throughout intrauterine life. He added the latter seemed the most plausible mechanism even though the exposure pathways were unclear.55

In 1992, Lord et al.⁵⁶ suggested the same when they stated that embryonic hematopoietic cells could be up to 1000 times more radiosensitive than postnatal hematopoietic cells. They added that different mechanisms of inducing this damage operated at different embryonic/fetal stages.

More recently, the suggestion that prenatal hematopoietic cells are highly radiosensitive was supported by Ohtaki et al.5⁷ in their study of chromosome translocation frequencies in the white blood cells of Japanese atomic 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 postnatal lymphocytes. From this study, Wakeford⁴⁸ 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.

We conclude 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.

Why Were In Utero Exposures not Considered in the 1980s and 1990s?

In the 1980s and 1990s, the possible cause or causes of the increased leukemia incidence near the Windscale nuclear power plant in Sellafield, UK were much discussed. The explanation favoured by the Gardner team,⁵³ which reported that the increase was due to paternal preconception irradiation of the sperm cells of Windscale employees. Later this was discredited partly because the fathers studied resided throughout the region of Cumbria, but the leukemia excess was restricted to the village of Seascale, which is only about five kilometers from the Windscale complex.

It is difficult to recreate the situation prevailing more than 20 years ago, but we propose three possible reasons for discounting in utero exposures at the time. First, if in utero exposures were the cause of increased leukemia incidence, then we should expect to see other effects, such as increased congenital malformations, stillbirths, and neonatal deaths; however, various studies conducted at the time,⁵⁹ as well as later studies,⁶⁰ found few adverse pregnancy outcomes. Now it is realized that ascertaining these outcomes is fraught with difficulty due to the reluctance (or refusal) to report these effects, or due to the difficulty of distinguishing between spontaneous abortions, stillbirths, and heavy periods (see, for example, the 1993 discussion by Sara Downs⁶¹). Consequently, these epidemiological studies could have reported false negative results.

Second, although Stewart's findings¹⁰ of increased risks from low x-ray exposures in utero are currently widely accepted as valid, this was less the case in the 1980s and 1990s. At that time, in utero exposures were not widely considered to be unduly risky. Finally, but perhaps most importantly, there was little awareness then of the considerably increased radiosensitivity of hematopoietic tissues in embryos and fetuses. In particular, apparently little attention was given to Morris's letter on the increased radiosensitivity of lymphocytic cells in utero.

What about the Increases in Solid Cancers?

The previous discussion might explain leukemia increases, but what about the (smaller) increase in solid embryonal cancers also observed by KiKK? Although the increased numbers of solid cancers in the KiKK study were not statistically significant, there are good theoretical grounds for expecting increased solid cancers as well. For example, the OSCC study¹⁰ also 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 hematopoietic tissues 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 hematopoietic tissues such as bone marrow and lymph glands.

CONCLUSION

To summarize, a possible biological mechanism to explain the KiKK observations is that NPP emission spikes resulted in the radioactive labelling of embryos and fetal tissues in pregnant women living nearby. Such a concentration, factored over two to five years both before and after birth, could result in the accumulation of relatively high doses in radiosensitive organs of embryos and fetuses, particularly in hematopoietic tissues. Unfortunately, cumulative radiation doses and risks to specific organs and tissues in embryos / fetuses from nuclide uptakes during pregnancy are not specifically considered in the publications of the ICRP.

In sum, the observed high rates of infant leukemias in the KiKK study may be a teratogenic effect from incorporated radionuclides. Teratogenic effects arise from exposures of toxic substances to embryos and fetuses in the womb. These effects, such as congenital malformations, are often recognized at birth, but infant leukemia is not. Such babies are born preleukemic and full-blown leukemias are only diagnosed after birth, perhaps after their bone marrows have accumulated sufficient radioactive decays from incorporated nuclides.

Recommendations

Whatever the final explanation for the increases in childhood leukemia reported in the KiKK study, its findings continue to raise difficult questions, including whether vulnerable people—in particular, pregnant women and women of child-bearing age—should be advised not to reside near nuclear facilities. Another question is whether local residents should be advised as to the anticipated dates of reactor openings so they can move away on these days if they so wish. Finally, it should be asked whether local residents should be advised not to eat produce from their gardens or wild foods, as the food pathway is the largest contributor to local doses.

As a first step, we recommend that the following should be estimated for NPPs:

- the radiation exposures and risks from episodic NPP emissions ("spikes");
- the radiation doses to the bone marrow of developing embryos;
- the subsequent risks of leukemia to infants and young children; and
- confidence intervals associated with these dose and risk estimates.

It is also recommended that in the US, a national study of leukemias near NPPs be conducted using the same methodology as the KiKK study, in particular, using measurements of precise distances between cancer cases and NPP stacks. Finally, a data analysis comparing downwind and upwind cancer incidences based on meteorological data for each NPP would be useful.

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