Infant leukaemia after the Chernobyl accident

In their Letter to *Nature*[1], Petridou *et al.* attributed an increased incidence of infant leukaemia in Greece to increased *in utero* exposure to ionizing radiation arising from the Chernobyl accident, which occurred on 26 April 1986. We see a similar increase in infant leukaemia in western Germany in children born after the Chernobyl accident. However, more detailed analyses of different contamination levels and dose rates show no relationship between exposure and incidence. We therefore conclude that the observed effect was not due to ionizing radiation from the Chernobyl accident.

Measurements of radioactive fallout and calculation of effective doses for the population show that large parts of Germany, especially in the south, experienced contamination comparable to that of Greece. The United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) estimated an effective dose-equivalent of 0.49 mSv attributable to the Chernobyl accident (over the following year) for the population in southern Germany and of 0.33 mSv for most of Greece[2].

There was a wide variation in levels of exposure in Germany, with UNSCEAR's first-year dose estimate for northern regions being 0.07 mSv, so it is possible to study potential dose–response patterns. Local fallout patterns and estimates of resulting average external and internal radiation doses are available for the 328 *Landkreise* of the former Federal Republic of Germany. Despite widespread long-distance transport of even fresh agricultural products in Germany, it has been shown that the variation in total dose closely follows ground-deposition patterns[3], which thus can be used as a surrogate for dose. We chose levels above 10 kBq m^{-2} ^{137}Cs to represent areas of high exposure and below 6 kBq m^{-2} for low exposure[4]. Taking shielding but not iodine contribution (which adds little to blood stem-cell dose) into account, this translates into average *in utero* doses (total for nine months) of 75 and 55 μSv respectively, for the exposure levels defined above.

Since 1980, a population-based childhood cancer registry has existed, which receives reports of more than 90% of malignancies occurring in children up to 15 years of age, for the former Federal Republic of Germany[5]. Therefore, unlike the Greek study, we did not have to ascertain the number of cases of leukaemia retrospectively. Using the definitions of Petridou *et al.* for *in utero* exposure (children born between 1 July 1986 and 31 December 1987) there were 928,649 'exposed' children in the FRG (cohort B). Among these, 120,440 lived in the areas of high exposure. Cohorts A and C, defined as 'unexposed' groups, consisted of 3,601,176 children born between 1 January 1980 and 31 December 1985 (cohort A) and 2,029,613 children born between 1 January 1988 and 31 December 1990 (cohort C). The incidence of infant leukaemia in the 'exposed' cohort B is higher than in cohorts A and C (Table 1). The incidence rate did increase from cohort A (23.0 per million) to cohort C (29.6 per million), possibly due to some under-reporting in the initial phase of the German childhood cancer registry.

Looking at regions defined by radioactive ground deposition, the increase in leukaemia rate is highest in the regions with the lowest contamination by radioactive fallout. We believe that it is highly unlikely that this observation is due to misclassification, as there was a clear geographical distinction between the areas of high and low exposure.

In addition, because there were many short-lived radionuclides, and as surface contaminations in the human environment and on food were quickly washed out, radiation exposures from Chernobyl showed quite steep gradients with time. The dose rate in the first days after fallout were 23 times higher than in the last month of 1987. Any potential excess of infant leukaemia caused by intra-uterine radiation exposure should thus be most apparent in the older children of cohort B. If we divide B into two subcohorts (birth date July 1986 to March 1987 and April to December 1987) the rate ratio is 1.29 for the older subcohort and 1.67 for the younger subcohort (data for all areas, comparison with the combined cohorts A and C). These results again are not in accordance with the radiation hypothesis.

Analysing the incidence of all leukaemias that occurred in children up to 5 years old shows that the relative increase in infant leukaemia seems to be compensated for in subsequent years, as the corresponding rate ratio of 'exposed' to 'unexposed' cohorts is 1.02 for the whole area (95% confidence interval, CI, 0.91–1.15). A decreased incidence in the second year of life was observed for the 'exposed' cohort (rate ratio, 0.84; 95% CI, 0.61–1.85).

Although our initial analysis is consistent with the observation of Petridou *et al.*, detailed trend analyses for contamination levels and critical time periods fail to correlate exposure levels with increased leukaemia rates. Thus we conclude that the observed increase of infant leukaemia is not caused by an increased *in utero* exposure to ionizing radiation from the Chernobyl accident.

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Table 1 Cases of infant leukaemia

Region	'Exposed' birth cohort (B) Cohort size	Number	Incidence rate	'Unexposed' birth cohorts (A+C) Cohort size	Number	Incidence rate	Rate ratio	95% CI
Former FRG	928,649	35	37.7	5,630,789	143	25.4	1.48	1.02–2.15
Ground deposition (kBq m^{-2} ^{137}Cs)								
<6	696,402	29	41.6	4,230,847	96	22.7	1.84	1.21–2.78
6–10	111,807	1	8.9	684,113	24	35.1	0.25	0.03–1.89
>10	120,440	5	41.5	715,829	23	32.1	1.29	0.49–3.40

Incidence, rates and rate ratios of children with acute leukaemia in the first year of life for the 'exposed' (B) and 'unexposed' (A+C) birth cohorts in the former Federal Republic of Germany and in regions with different levels of contamination. Incidence rate per 10^6 children.

Petridou et al. *reply* — The increase in incidence of leukaemia among infants exposed *in utero* to radiation from the Chernobyl accident in Germany is strikingly similar to that noted in Greece. No explanation other than an *in utero* effect of ionizing radiation or a highly improbable chance manifestation can be seriously considered. In particular, no confounding influence with the required time-dependent properties can be invoked.

The lack of response to exposure in several subgroup analyses in Germany is hardly surprising, given the unavoidable non-differential exposure misclassification, the questionable correspondence between environmental measurements and personal exposures, and the sparse data. The apparent within-country response to exposure in Greece could be explained by the different cut-off points used in that study, the agro-economic practices in Greece that favour smaller-scale production–consumption systems or, conceivably, more benevolent chance.

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