correlation between pyrene collected on filter and pyrene collected on XAD (2). On average, we found 1.6 \mu g/m^2 pyrene on filter and 1.9 \mu g/m^3 on XAD; i.e., 46\% on filter and 54\% on XAD. This is in good agreement with Ny et al. (3). The correlation between pyrene on filter and the sum of pyrene on filter and pyrene on XAD was 0.69. Since this is less than 1, it is likely that a better correlation between pyrene in air and urinary 1-hydroxypyrene would have been the result of using an XAD backup in our study.

The timing of urinary sampling is an important issue. However, it is impossible to select a perfect sampling time for biological monitoring. Even if you sample for 8 hr and start at a time point equal to the half-life of 1-hydroxypyrene after the start of work, some of the collected urine will contain 1-hydroxypyrene from the previous day’s exposure, and day-to-day variation may be significant. Jongeneelen (4) has studied samples collected after and before shift and found a correlation between pyrene in the air and urinary 1-hydroxypyrene both when collected after shift and before the shift the next day. The American Conference of Industrial Hygienists (ACGIH) has established biological exposure indices (BEI) for several organic compounds (but not pyrene) and suggested sampling times. The ACGIH suggested end of shift and prior to next shift as the time when sampling time is critical (5). Compromises have to be made in practical biomonitoring, but for validation of methods, 24-hr sampling of urine may be important.

We agree that 1-hydroxypyrene is the main metabolite and that other metabolites are important, but urinary 1-hydroxypyrene is a marker for PAH exposure and does not represent the total exposure. A large proportion of PAHs are excreted in feces. In a recent study of voluntary ingestion and dermal application of pyrene, less than 4.5\% (ingestion) and 0.2\% (dermal) of the dose was recovered in a 48-hr collection period (6). The study of the influence of genetic factors and lifestyle factors is important in validating biomarkers like urinary 1-hydroxypyrene. We are currently conducting such studies. But PAH uptake is also influenced by particle size of the PAH. The new filter cassettes called IOM (7) show that construction of cassette orifice can have a great impact on the fraction samples and may be more important than AD backup, which mostly gives a constant loss that can be corrected for.

There is still need for more validation studies of the biomarker 1-hydroxypyrene. To sum up, we would like to cite from implementation of the BEI (5): “Biological monitoring should be considered complementary to air monitoring. It should be conducted when it offers an advantage over the use of air monitoring alone.”

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Radiation and Childhood Cancer

Ostensibly, the impetus for Wakeford’s review of reported associations of childhood cancers with radiation exposures (EHP 103:1018–1025) was to refute our judgment that cancer risk coefficients for low-dose exposures of populations, as officially adopted by national and international radiation commissions, have been substantially underestimated (EHP 102:656–667). We based our judgment on documented inconsistencies and omissions in the literature, as well as on discrepancies between official predictions and observed health effects among various groups, including nuclear workers and residents of radioactively contaminated areas. We reviewed a wide range of studies under low-dose exposure conditions, especially those that found radiogenic cancer risk coefficients inconsistent with official estimates for protracted low-dose exposures. These significant discrepancies between observed and expected values contradict the model assumptions made when low-dose, low-rate risks were extrapolated from primarily one-shot, high-dose effects (1,2).

Wakeford ignores these inconsistencies by neither refuting nor discussing them. His substantive criticism of our contribution is limited to just two of our reported findings, which we can accept. Yet, this in no way affects our stated conclusions:

1) We had overlooked a downward revision of the prenatal exposure risk of 20 fatal childhood cancers per 10^4 person-cGy (3) to 12.7 cancer deaths (and 17 nonfatal cancers) per 10^4 person-cGy, as derived from the Oxford Survey of Childhood Cancers (OSCC) (4), generally recognized as the most extensive database on childhood cancers. The main body of Wakeford’s paper, however, is a presentation of alternative radiogenic risk estimates, emphasizing those that are closer to the generally accepted norm; i.e., those derived from the A-bomb survivor data. This brief communication is not the appropriate place for a detailed evaluation of Wakeford’s selection of data. Yet, a crucial omission from his review is the evidence we referenced in our paper showing that, as a consequence of significant selection effects among A-bomb survivors, prenatal exposure risks as derived from A-bomb data are intrinsically incompatible with those based on X-ray exposures of general populations (such as the OSCC). Recently released data on early radiation injuries among the LSS survivor cohort by the Radiation Effects Research Foundation, Hiroshima, strongly confirm Stewart’s earlier conclusions about the effects of selection (5). From now on, evaluations of risk from prenatal exposures to X-rays, low-dose gamma rays, or internal radioisotopes will have to stand on their own reliability in methodology, since agreement or disagreement with the A-bomb data appears to have become irrelevant.

2) Regarding the “Gardner hypothesis” (postulating a genetic component for leukemia in young people through preconceptual parental exposure), we reviewed several findings, supportive and unsupportive. In view of the unknown contribution of internal radioisotopes to the health hazards in some of the conflicting findings, as well as confounding clustering effects of leukemia with infectious epidemics in rural areas (6), we consider the discussion as undecided at this time. In contrast to this more cautious approach, Wakeford, without presenting a plausible counter-hypothesis for either the
Sellafield or some other reported leukemia clusters, leaves little room for doubt by concluding that "a causal interpretation of the association between childhood leukemia and paternal preconception irradiation reported by Gardner et al. cannot be sustained." 2

Taken as a whole, while contributing to the ongoing discussion on intrauterine and preconception exposure risks for childhood cancers, Wakeford's paper in no way invalidates the major conclusions from our review of the literature on health hazards from low-dose exposures.

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Response
In their wide-ranging, critical review of the current estimates of the risks of adverse health effects after exposure to low doses of ionizing radiation (EHP 102:656-667), Nussbaum and Kohnlein claim that "official" risk estimates derived by scientific bodies such as the Committee on the Biological Effects of Ionizing Radiation (BEIR V) (1) "substantially underestimate real risks. Two pieces of evidence used by Nussbaum and Kohnlein in support of this contention concern the risk of childhood cancer after exposure in utero and the risk of childhood leukemia after paternal exposure before conception. The stated purpose of my article (EHP 103:1018-1025) was to provide a timely review of the scientific literature associated with these risks and, from this, to determine how well the pertinent criticism of Nussbaum and Kohnlein stood up to close scrutiny.

Nussbaum and Kohnlein persist in referring to a single high point estimate of the risk of childhood cancer after intrauterine irradiation, using the database of the Oxford Survey of Childhood Cancers (OSCC). I noted in my article that this excess absolute risk coefficient for cancer incidence (not mortality) under 15 years of age of 13.6% (95% CI, 10.0–18.4%) per Gy has been derived by Muirhead and Kneale (2) using OSCC data. However, the fetal doses upon which this estimate was based were a personal communication from G.M. Ardran to Stewart and Kneale (3), which "may need to be revised in the light of further evidence." Stewart and Kneale later stated that "the accuracy of the Ardran estimates ... is an unknown quantity, though we have since learnt that another expert in the subject would have given us a different estimate of the time trend" (4). Muirhead and Kneale (2) also derived an equivalent risk coefficient of 6.4% (95% CI, 4.1–10.0%) per Gy from the OSCC data, but based on the fetal dose estimates of the 1972 report of the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) (5). However, the accuracy of these dose estimates is also unclear (6), although they are more compatible with the temporal variation of excess risk displayed by the OSCC data (7). Given the systematic and statistical uncertainties inherent in these risk estimates, it is questionable whether an inconsistency with the risk experienced by the Japanese atomic bomb survivors irradiated in utero can be claimed with any confidence, recognizing the uncertainties also associated with the risk estimate of 0.5% (95% CI, -0.2% to 2.4%) per Gy derived directly from this group. In any case, the estimate for the excess risk of cancer mortality under 10 years of age of 2.0–2.5% per Gy presented in the BEIR V report (1) is based on OSCC data.

As discussed in my article, the novel association between the dose of radiation measured by film badges worn by men employed at the Sellafield nuclear facility before the conception of their children and leukemia in these children has been found to be confined to those born in Seascale (this is so, even though more than 90% of the children of Sellafield workers were born outside this village). The Seascale association has not been confirmed by other studies using objective estimates of radiation dose. Interestingly, Kneale and Stewart, using OSCC data, concluded that "there is no support for the idea that exposure of parental gonads to diagnostic x-rays is conducive to cancer in the next generation" (8).

Further, as pointed out in my article, the Seascale association cannot be explained by paternal doses received from internally deposited radionuclides, and studies of other groups associated with such doses have found no association. It was Sir Richard Doll and his colleagues who concluded, in a comprehensive review, that "the hypothesis that irradiation of the testes causes any detectable risk of leukaemia in subsequent offspring cannot be sustained" (9).

Through a detailed review of the scientific literature concerning the risks of childhood cancer after intrauterine and preconception irradiation, I have demonstrated that the analysis of Nussbaum and Kohnlein regarding these particular risks does not withstand examination. Others will have to decide whether their remaining criticisms have scientific validity.

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