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Response to Invited Commentary

Yamada et al. Respond to "Radiation and Reproductive Health"

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We thank Dr. Lie (1) for his interest in our study (2) and appreciate his comments and recognition that the primary data were collected 7 decades ago. We respond to his main points as follows.

Lie points out that a prevalence of less than 1% for all major malformations together seems to be too low, raising the possibility that many cases in important categories were missed (1). In our study, all major malformations were diagnosed at birth, and thus we might have missed malformations (such as congenital heart disease) that may not be detected at birth (2). The frequencies of malformations in children at the Tokyo Red Cross Maternity Hospital during 1922–1940 (0.92%) and in children of nonirradiated parents included in this study were quite comparable (3). Checking the findings of the Atomic Bomb Casualty Commission against observations in the 2 largest hospitals in Nagasaki also showed no evidence that substantial proportions of major defects diagnosable at birth were missed (3).

Regarding radiation exposures, Lie questions whether, given the persistent radioactive contamination of the 2 Japanese cities after the blasts, exposures were sustained by the reference group (1). Turning to radiation exposure from the blasts, the characteristics of radiation exposures from the atomic bombs are different from those sustained by Chernobyl liquidators and those in regions contaminated by the Chernobyl accident (4). There were 2 types of exposures related to the atomic bombs: One was exposure to "initial radiation" released at the time of detonation of the bombs, and the other was subsequent exposure to "residual radiation" (5). The parental radiation doses used in our paper were based on the initial (acute, external) radiation from the bombings (2). Estimates of residual radiation doses are much lower than the initial radiation doses for nearly all atomic bomb survivors, even though the estimates have wide confidence intervals. Even if residual radiation exposures were considered, we do not expect that radiation risk estimates would change materially (5).

Lie suggested that women in the highest exposure categories had fewer children during the study period, based on the parity distribution shown in our Table 2 (2). His intuition might be correct, but other plausible explanations include the possibility that stigma and discrimination related to possible genetic effects led to a later age of marriage and avoidance of pregnancy (6).

We expect that a comprehensive genomewide study will add information on possible mechanisms for transgenerational effects, as Lie mentioned in the "Opportunities for Genetic Studies" section of his commentary (1). We appreciate his article title, indicating the fact that "old cohorts still deserve attention." Hopefully, the unfortunate experience of this cohort will never be repeated. The original investigators—Drs. James V. Neel, William J. Schull, and others (3)—did recognize the unique opportunity afforded by the children of survivors to advance knowledge for the world on potentially adverse consequences of radiation exposure for pregnancy outcomes. We are grateful for their foresight.

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