Response to Busby

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I thank Dr. Busby for his interesting comments (above) on my *Perspectives* article (Jordan 2016), in which he details why, in his opinion, the studies led by the Radiation Effects Research Foundation (RERF) on atomic bomb survivors in Hiroshima and Nagasaki underestimate the deleterious effects of low doses of ionizing radiation. I'd like to mention at this point that I have also been approached by advocates of the "radiation hormonesis" theory (Sanders 2010) who argue that my presentation badly overestimates these effects because of the existence (according to them) of a threshold level below which radiation effects are nonexistent.

Dr. Busby criticizes the choice of the control population for the RERF studies (all in-city individuals with doses <5 mGy), on the grounds that these may have been exposed to radioactive contamination, with possible deleterious effects, thus providing an elevated baseline. However it is clear from the set of data (see *e.g.*, figure 1 in Cologne and Preston (2000) that the apparent excess mortality within this group (separated according to distance from the explosion site) is somewhat variable and actually higher for the more distant individuals (7–10 km from the hypocenter), which points to "some unobserved selection factor." As also seen in this figure, among those who were not in the cities at the time of the explosion, "early entrants" have lower mortality than "late entrants" (those who came back to the cities after 1 month), while the reverse would be expected if contamination was a significant factor. It is true that the contribution of radioactive contamination is largely unknown due to lack of measurements and secrecy; the issue would be quite different in Hiroshima (uranium bomb) and Nagasaki (plutonium bomb). A study published in 2008 (Wanatabe 2008) and quoted by Busby recomputes the mortality ratios taking as a control either the population of the whole Hiroshima prefecture or of the neighboring Okayama prefecture. It concludes that there is a significant excess mortality at very low doses (below 5 mGy); however, in a number of cases, the risk is lower for medium (5–100 mGy) doses than for very low ones, also the intervals in the radiation levels are very large (<5 mGy, 5–100 mGy, and >100 mGy) and the statistics are often inadequate because of low sample sizes. In summary, while acknowledging that the definition of the control group is critical and that this affects the precision of the conclusions for very low doses, I believe the statements made in my article still stand.

Regarding the relationship between radiation dose and biological effect, there seems to be majority agreement on a linear relationship with no threshold (Leuraud 2015). The RERF results are remarkably consistent in that all detected effects increase with radiation dose, which gives confidence in extrapolation to very low levels for which measurement is difficult as discussed above. In contrast, Busby argues for a biphasic dose response, in which the effect would be high at very low doses, then decrease and increase "gently" at high doses. If this concerns the effect per milligray, it seems unlikely but conceivable; if it is the absolute effect, it does not make sense: How could a 50-mGy exposure be less damaging than 5 mGy? As mentioned, another minority opinion argues for a threshold below which no effect is observed. A linear relationship seems to be the best estimate at this time, as generally agreed.

The lack of detection of genetic effects is an important facet of my article (Jordan 2016), especially since many in the general public believe that even small amounts of radiation are highly mutagenic. Busby briefly discusses RERF results on sex ratios, which I didn't mention in this paper. I presented instead data on malformations at birth (broken down according to paternal and maternal exposure) and on attempts to detect mutations by various means including microsatellite analysis. The conclusion is that so far no genetic effects have been detected; this has been strengthened by publication of a cohort study on risk of death among

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these offspring (Grant 2015) that shows "no deleterious health effects after 62 years." Obviously, there must be some effect, at least at the higher doses, and extensive sequencing studies should be done to assess its magnitude—but it will be quite small.

In summary, while there are some shortcomings in the RERF studies, most notably the absence of information on the extent of radioactive contamination, this remains a very complete and consistent set of studies with good statistics and long follow-up that puts solid limits on the somatic and genetic effects of exposure to ionizing radiation. While these results are reassuring and moderate widely held and alarmist beliefs, they should of course not lead to complacency about the effects of nuclear war, which would involve immensely greater levels of radiation and fallout and have devastating effects.

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