RESPONSE TO "URGENT CHANGE NEEDED TO RADIATION PROTECTION POLICY"

Dear Editors:

In a Forum titled "Urgent change needed to radiation protection policy," Jerry M. Cuttler argued in favor of a hormesis paradigm (Cuttler 2016), where ionizing radiation is assumed to be beneficial below some threshold, which was not specified. To defend this multi-parameter formulation, he began with a listing of the conspiracy theories that Edward J. Calabrese has put forward (Calabrese 2015) about the origins of the linear no-threshold theory (LNT). Before anyone gives the Calabrese theories credence, they should read the detailed rebuttals that have appeared (Cicerone and Crowley 2014; Crowley et al. 2015), including the most detailed one (Beyea 2016). These responses refute the charge that successive groups of scientists who served on panels of the U.S. National Academy of Sciences (NAS) were duped into supporting an LNT model by the opinions expressed in the genetic panel section of the 1956 "BEAR I" report (NAS 1956). I have served on many panels of the NAS; it is very unlikely that any panel would sheepishly follow its predecessors. In fact, successor NAS reports had their own views of the LNT model, relying on mouse and human data, not the fruit fly data on which the 1956 panel heavily relied. The most recent NAS panel (NAS 2006), after undertaking a comprehensive review of the biology data, concluded that, "The risk would continue in a linear fashion at lower doses without a threshold and that the smallest dose has the potential to cause a small increase in risk to humans."

The 1956 report was not biased and corrupted. Its conclusions matched concurrent reports from the UK (MRC 1956) and opinions expressed at a workshop organized by the World Health Organization (WHO 1957). Most of the 1956 report's numerical estimates of genetic damage remain consistent with current views (Beyea 2016). Although the BEAR I report was influential in reducing worker doses, it had minimal influence on the adoption of the LNT. The LNT had already been implicitly accepted in the U.S. by the National Council on Radiation Protection (report No. 17) for radiation protection purposes in the 1950s, followed by a similar proposal by the British in 1955 (Kathren 1996). Fruit fly data down to a 500-mSv dose definitely influenced views on linearity of genetic effects, with linearity for somatic effects assumed for protection purposes. Subsequent linearity in fruit fly data was found down to approximately 80 mSv by Japanese researchers (Shiomi et al. 1963) and then down to approximately 10 mSv by an Austrian researcher (Schweizer 1995). There have always been some fruit fly data indicative of non-linearity (Sankaranarayanan and Sobels 1976), most recently in studies carried out by the research center of the Japanese electricity industry, which reported non-linearity at 200 mSv for most endpoints presented, but not all (Koana et al. 2012). As a 1972 NAS report put it, "Some Drosophila [fruit fly] data suggest a threshold, but there is good evidence that at least some of the effect has linear relationship to dose" (NAS 1972).

The idea that in the 1940s and 1950s researchers like Curt Stern (see Neel 1983 for an appreciation) deliberately misled the scientific community is an astounding claim. Supporters of unconventional theories like hormesis have an important role to play in challenging prevailing scientific views, but not by unleashing character attacks on those with whom they disagree.

Today, there is a great deal of epidemiologic data involving 100,000 or more persons exposed both to single and protracted doses. These data can be compared to predictions of linearity, supralinearity (Morgan and Sowa 2009), or sublinearity. Below 100 mSv, however, it is difficult to get consensus on dose response; proponents of individual theories require very strong evidence to change their views. When the number of excess cancer cases compared to background cases is small, which occurs at low doses, random fluctuations can make dose-response patterns vary greatly. As a result, at low doses, the shape can appear to fall below linearity in one A-bomb survivor study (Preston et al. 2007, Fig. 3) and yet appear to rise above linearity in another (Ozasa et al. 2012, Figs. 4 and 5). Not surprisingly, supporters of particular dose response models will focus on those studies that support their views or modify them until they do so (Doss 2012), rather than try to average over the dose response curves that have been fitted or graphed in the various epidemiologic studies.

What to do about risk assessment, in light of the residual uncertainty and lack of consensus? If risk estimates are to be made at low doses, all views can be incorporated by taking a linear response as the centroid with uncertainty bands broadened to incorporate the theories of both

0017-9078/16/0
ISSN: 0017-9078

DOI: 10.1097/HP.0000000000000540

hormesis and supralinearity (Beyea 2012) to the extent they are consistent with the uncertainty in epidemiological data points and biologic theories of cancer.

Recent epidemiologic data have produced a consistency problem for hormesis models. The fact that protracted exposure accumulated by hundreds of thousands of workers gives essentially the same or greater dose-response slope as a single exposure (Jacob et al. 2009; Muirhead et al. 2009; Leuraud et al. 2015; Richardson et al. 2015) provides a strong argument for linearity. It is hard to justify a threshold, and even harder to justify a hormesis model, when a dose accumulated from a continuous exposure or a large number of small exposures has the same impact as a one-time exposure. If radiation damage were to reduce background cancer rates (the hormesis postulate), the benefits assumed to result from small doses should have accumulated. The slope of the response should have fallen well below the slope determined from the A-bomb survivor studies, which it generally did not. At the very least, hormesis models will need to be significantly moderated to be consistent with the similar dose response curves seen in epidemiologic studies of both single and protracted exposures. These data raise similar consistency questions for models of supralinearity.

Given the controversies, should risk assessments be made at all at low doses? It doesn't matter much for the individual which of the four theories is used to estimate individual risk for single doses well below 20 mSv, such as a 0.1 mSv chest x-ray, whether it be hormesis, threshold, LNT, or supralinearity. Predictions from all four models are low. (Based on Fig. 5 of Ozasa et al. 2012, I take a factor of 4 above the LNT as the most a supralinear model would exceed the LNT.) That low individual risk is the good news, which, to minimize public confusion and distress, should be highlighted, especially in the midst of fierce debates over the shape of the dose response curve. On the other hand, in situations where hundreds of thousands of people are irradiated, radiation risk is spread out over a huge population in a kind of reverse lottery, leading to potentially large absolute excesses in a much larger background population. The need to understand population effects (e.g., as part of a cost/benefit study) is a major reason why low-dose risk assessment matters. Especially in the internet age, recommendations to hide the population response issue from the public in the hope of reducing fear is likely to backfire by increasing suspicion of authorities and reducing trust in them.

Patients have been afraid of x rays to the consternation of radiologists for a long time, as a 1958 news article makes clear (SciNews 1958), although the use of x rays in medical diagnostics has increased greatly, despite continuing public unease. Two key contributing factors in ongoing, generic worries about radiation appear to be, first, loss of trust in information providers, and second, a lack of confidence that the true risks are known (Sjoberg 2001; Poortinga and Pidgeon 2004), a concern that has been exacerbated by the continuing controversy over health effects (Hacker 1992; Walker 1994). Perhaps, as has been suggested (McCollough 2016), a useful way to allay concerns of nervous patients would be to put more effort into quantifying, and making easily accessible, risk reduction gained from diagnostic medical procedures, examples of which have been estimated recently by Zanzonico and Stabin (2014). Earlier efforts can be found in work by Pochin et al. (1981). Such calculations can be subtle and are not always easy to do; a systematic approach will require allocation of significant resources to allow cost/benefit comparisons to be made for the full gamut of diagnostic exposures. Grant-making organizations should take note.

Choices that regulators make in risk models, the changes they make over time, and their communication strategies can affect trust and confidence (Slovic 1999; Poortinga and Pidgeon 2003; Tuler and Kasperson 2010; Tateno and Yokoyama 2013). For U.S. regulatory agencies to adopt a hormesis paradigm, when faced with opposition from the U.S. National Academies of Science and Medicine (as well as from the USEPA), would likely lead to increased distrust among the U.S. public. A new NAS study is in formation (http://dels.nas.edu/). Those who support the hormesis paradigm can try again by making a new presentation to the new Committee.

The author declares no conflicts of interest.

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Acknowledgments—No sources of funding were involved in the production of this response or any work by the author cited in it. In the past, the author has advised plaintiffs' attorneys on litigation involving overexposures from CT exams, high voltage radar tubes and releases of radioactivity from the weapons complex. No attorney has seen this submission, nor commented on it.

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