Perseverating on Epidemiology and Linearity: A Journey into the Minds of LNT Model Advocates

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Linear no-threshold (LNT) model advocates maintain that large sums of money should fund ever larger epidemiologic studies to uncover low-dose cancer risk to validate the model. This advocacy is flawed in many ways. LNT model advocacy groups, such as the National Council on Radiation Protection and Measurements (NCRP) and the International Commission on Radiological Protection, mutually support and reinforce these efforts (in part because they share the same members). They ignore or dismiss the growing body of peer-reviewed experimental and observational (epidemiologic) literature providing evidence of a threshold below which biologic responses from cells, tissues, and organisms repair/remove radiogenically damaged cells, thereby preserving and even improving the organism's health. This literature soundly refutes the LNT model (*1–9*).

Consider that a recent article from Boice et al. (*10*) (academic authors including a past and current president of the NCRP, with strong ties to international radiation protection bodies that advocate for the LNT model) still assumes that which has been repeatedly shown to be false. They asserted that:

> Large and high quality epidemiologic studies in the U.S. and elsewhere, such as the study of One Million U.S. Radiation Workers and Veterans (the Million Person Study), coupled with the best of the new radiation biology, could be merged and produce biologically based risk models that significantly improve the estimation of *risk at lower doses and dose rates* than possible today [emphasis added].

The authors' evidence-impervious conclusion is that future improvements in risk assessment for radiation protection may come from "increasingly informative epidemiologic studies, melded with mechanistic radiobiologic understanding of *adverse outcome* pathways, with both incorporated into biologically based models" [emphasis added]. The authors thus indicate their faith (not confidence, which requires an evidentiary foundation) that there is a needle in the haystack yet to be discovered, indicating their belief that by increasing the statistical power through ever-larger studies the needle will suddenly sparkle in the sunlight.

The authors go on to state that the challenge for epidemiology is that the signal to be detected (excess numbers of cancers associated with low-dose radiation exposure) is so very small that "it cannot be seen against the very high natural occurrence of cancer in the population." They posit a signal "so very small" but never doubt its unproven existence.

How can researchers identify a needle when a mountain of contrary evidence eludes their vision? They note "assuming that extrapolating risks observed at high doses to lower doses has validity, then an acute exposure to about 10 mGy might theoretically increase the probability (chance) of developing cancer in a lifetime by about 0.1% or roughly from about 38% to 38.1%." Their assumed validity of extrapolation has no evidential basis and wrongly puts the conclusion before the proposed investigation, something that scientists should never do. Even more important, science demands that a hypothesis be testable and falsifiable. Yet the authors release the LNT model from these requirements by shielding epidemiology from such scrutiny, saying "Epidemiology cannot detect such increases because of issues of statistical power and the inability to control confounding factors such as cigarette smoking and other major influences of cancer risk."

With this, Boice et al. have effectively conferred the label of pseudoscience on their proposed validation of the LNT model. To these authors and fellow linearity advocates undetectability does not suggest even the possibility of falsity. Nor do they propose a method that could validate the LNT model, let alone falsify it. Yet beyond their vision the LNT model has indeed been falsified through repeated confirmations of the net beneficial response to low exposures of ionizing radiation (*11-13*).

Life forms are not pebbles; our bodies have passed through the filters of natural selection and respond defensively to radiation or any other toxin. And they respond differently to high and low doses and to changing dose rates. Continually mounting evidence indicates that at low doses/dose rates our bodies not only repair or remove initial damage but do so in excess of immediate need. Thus, the induced protective response to external toxins also helps protect against the far greater (and continual) internal onslaught of reactive oxygen species (ROS) ejected out of mitochondria in the course of normal metabolism. Indeed, most of the damage from episodic low-dose, low–linear energy transfer ionizing radiation also occurs via the increased levels of ROS produced when photons collide with the body's abundant water molecules.

This conclusion is both testable and falsifiable, and the results of said testing repeatedly confirm the presence of a threshold between high-dose harm and low-dose net benefit. The unshakeable assumption that because high-dose risk

exists it can be reliably extrapolated down to low doses may be appealingly simple, but it is scientifically indefensible. No matter how large, epidemiologic studies will never demonstrate the validity of low-dose cancer risk—not because the risk is too low but because it is nonexistent. Continued advocacy for the LNT model endorses pseudoscience, and investment in this effort entails a scandalous waste of resources, effort, and time.

Despite the absence of valid evidence of imaging-related cancer risk, the extraordinary contributions of CT imaging to life-and-limb preservation have been falsely brought under suspicion by LNT model advocates. A number of studies purport to demonstrate such risk, but they have been shown to entail circular reasoning or to conflate cause with effect and end up assuming that which they hope to prove. Fortunately, despite significant LNT-fostered fear, CT has replaced exploratory surgeries—procedures that risk immediate death—and facilitates treatments that prolong life, in contrast to the LNT model's falsely projected cancers decades in the future.

There is nothing new about nonlinearity in biology or in the body's differential response to different dose ranges for any agent. In the 500-year-old words of Paracelsus "Poison is in everything, and no thing is without poison. The dosage makes it either a poison or a remedy." Although Paracelsus presented this fact as though it were solely a property of the agent, we now know that it is primarily the evolved capabilities of the body that provide a beneficial response—unless high doses of the agent overwhelm that capability. Well-known examples abound. Ingesting 100 aspirin tablets at a time is known to kill, whereas 1 per day is thought to confer benefit. Two bottles of wine per day may cause cirrhosis and death, but a glass or 2 with dinner is believed to confer benefit. Excessive exertion can cause injury or death, whereas regular exercise is widely known to confer benefit. High doses of a pathogen produce illness, but the low doses in vaccines prime the immune response. Thus, even if high doses are toxic, low doses may provoke a detoxifying bodily response that ends up providing benefit.

What is needed is an accurate 2-sided radiobiologic assessment to ascertain under what conditions risk is incurred and under what conditions benefit is conferred, not simplistic 1-sided epidemiologic studies that mis-assign the role of the null to an undetectable hypothesis. In agreement with our work, Cynthia Jones, PhD, Senior Technical Advisor for Nuclear Safety and Analysis, U.S. Nuclear Regulatory Commission, recently asserted (*14*): "To advance radiation protection in practice, there is a need to improve realism, not conservatism [the frequently offered, but misplaced, defense of the LNT model], in the assessment of health effects."

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