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Hormesis hypothesis may be acknowledged by US regulatory action

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When environmental toxicologist Edward Calabrese in the School of Public Health and Health Sciences at the University of Massachusetts Amherst heard recently that the U.S. National Regulatory Commission has opened a new docket on proposed rule changes and standards for radiation protection, he felt it as "a vindication of my 30-year career, in many ways."

In its late June announcement, the NRC states that three petitioners, a radiation-health organization, a health physicist and a professor of radiation oncology at the University of California, Los Angeles, ask that it amend its radiation protection standards to change the basis of those regulations from the linear no-threshold (LNT) model to the hormesis model. The NRC explains, "The radiation hormesis model provides that exposure of the human body to low levels of ionizing radiation is beneficial and protects the human body against deleterious effects of high levels of radiation."

The regulatory agency will be accepting comments on the matter until Sept. 6.

Calabrese has long argued that for a variety of reasons, the LNT model has never been properly validated and current federal and international rules on human exposure to chemicals, drugs and low-dose radiation based on it were adopted without rigorous testing. He says that in "substantial validation tests, only the hormetic (biphasic) dose-response made consistently accurate predictions." He is pleased to see that the

regulatory agency may finally acknowledge this.

It was in 1985 that Calabrese presented a paper at the first hormesis conference, reporting a hormetic response before that word was in wide use, documenting the occurrence of chemically-induced hormesis. Hormesis is a non-linear, biphasic approach to dose-response and risk assessment for ionizing radiation and toxic chemicals.

Based on what he calls considerable research over the past three decades, the UMass Amherst toxicologist has argued that a reappraisal of cancer risk assessment methods is needed because the LNT model was adopted into U.S. regulatory policy based on faulty assumptions and even unethical manipulations of the scientific literature. The LNT model was recommended by the U.S. National Academy of Sciences in 1956, and soon accepted by national and international advisory committees for risk assessment and human exposure guidelines.

The LNT model was later generalized to chemical carcinogens and is now used by public health and regulatory agencies worldwide, Calabrese notes. He recalls the open hostility and deep skepticism that greeted the alternative hormesis concept more than 30 years ago. "In my first research experience with it, I consistently observed hormesis. Thus, I had seen my own version of the phenomenon repeatedly. Therefore, my beliefs are based on much personal experience."

By May 1990, he had hosted his first hormesis meeting at UMass Amherst, where, he says, "the idea was reborn and refocused." He and others formed a group, Biological Effects of Low Level Exposure (BELLE), which evolved into the Dose-Response Society and has an annual meeting on campus.

He recalls, "At UMass, we have done a lot in terms of scientific leadership, publishing nearly 200 papers on the topic and encouraging

others to test their own hypotheses. The field has really matured. In the whole decade of the 1980s, there were about 10 citations on hormesis per year. In 2014 alone, there were 6,500, on many different topics including microbiology, arthritis, mitigating heart attacks, stroke, cancer therapies, preparing for organ transplantation, enhancing stem cell function and enhancing plant productivity. It's very exciting how diverse the research has become."

Calabrese adds, "Hormesis is much deeper and more rich than just a tool for regulatory agencies such as the Nuclear Regulatory Commission or the EPA, though that is very important. As a basic biological principle it holds very real promise to help improve medicine and public health in the future. Coming from being totally marginalized to now an exciting and potentially transforming concept, it makes the possible NRC rule change more special. If something like this can happen on the radiation side with the NRC, there is possibly a whole revolution coming on the chemical side with EPA."

He points out, "This isn't an academic debate, it's practical, because all of our rules about chemicals and low-level radiation are based on unvalidated assumptions and scientific panel decisions made without sound evidence. Somebody had to break through the prejudice and attempt to convince the skeptics. It took 30 years to challenge old paradigms, and for people to notice that substantial data support the hormesis model."

He says technical advances in chemical analysis have revolutionized the field, so toxicologists and biomedical scientists can now investigate low doses and conduct a full examination of hormesis even at detailed levels of molecular mechanisms.

Another reflection is more personal, the toxicologist says. He is extremely grateful for the academic tenure system that allowed him to

take a risk and even offer encouragement to continue this line of study. "We need to leave room for ourselves to be surprised in science," he notes. "It's important, even when it doesn't seem plausible, to keep an open mind and pursue the facts. Without this academic freedom I would not have been able to keep going forward. I'm very glad to have seen the day when others, many others, are now taking hormesis seriously and applying it to help people and the environment."

Provided by University of Massachusetts Amherst

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