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GUEST EDITORIAL

Revisiting radiation realities

During the recent COP28 summit, numerous nations reached a consensus on the crucial role of nuclear power in advancing energy security and transitioning away from fossil fuels. This agreement is influenced, in part, by the acknowledged technological challenges confronting renewable energy sources such as solar and wind, which struggle to meet baseload power requirements in the absence of sufficiently advanced battery storage technologies. Despite widespread recognition of the advantages of nuclear power by energy researchers, policy analysts, environmentalists, and governments, its global contribution to electricity generation remains below 11%. Criticisms, including high investment costs, the potential severity of nuclear accidents, challenges in managing nuclear waste, and general radiation concerns, have hindered its broader adoption. If nuclear power is to triple by 2050, a re-evaluation of the realities of radiation becomes essential.

The realities of radiation can be categorized as positive, negative, and problematic, all stemming from the Linear No Threshold (LNT) model, which proposes that any dose of radiation carries a proportional cancer risk, with no safe threshold. First, let's explore the problematic – the flawed science behind the LNT. The foundational principles of LNT include: (i) claiming that even a single radiation-induced DNA mutation can result in fatal cancer, despite the fact that cancer typically necessitates multiple mutations; (ii) asserting there is no repair of radiation damage, contrary to substantial evidence supporting the existence of DNA repair mechanisms; (iii) suggesting that the impact of radiation is consistent whether delivered slowly or all at once, whereas in reality, gradual delivery allows for more effective functioning of repair mechanisms; and (iv) asserting that processes at low radiation doses are identical to those at high doses, overlooking the potential for different mechanisms to operate.

This controversial model initially surfaced as an attempt to comprehend the effects of ionizing radiation on evolution, spearheaded by Herman J. Muller and other geneticists in the early 1900s. However, Muller later repurposed this model to explain the health risks linked to ionizing radiation, especially in the aftermath of atomic bombings. Criticisms, notably presented by Professor E. J. Calabrese, reveal the model's flawed origins, rooted in a competitive race and flawed study designs (Calabrese, E. J., 2018, 10.1186/s13010-018-0066-z). Despite relying on high-dose data and lacking validation at lower doses (Muller, H. J., 1927, 10.1126/science.66.1699.84), Muller's LNT model gained traction, supported by influential endorsements and institutional backing, including from the oil industry-backed Rockefeller Foundation. Despite initial doubts about its scientific merit, it was integrated into radiation risk assessment by the International Commission on Radiological Protection (ICRP) in 1966. To address its limitations at low doses (generally understood to be <100 mSv), the ICRP later introduced the Dose and Dose Rate Effectiveness Factor. Presently, the global acceptance of the LNT model, especially at low doses, has ramifications evident in conservative radiation regulations and a prevailing fear of ionizing radiation.

Now turning to the negative aspect – the conservative regulations and radiophobia stemming from the widespread acceptance of the LNT model. Radiation regulations generally strive to maintain radiation exposure as low as reasonably achievable (ALARA) in all occupational and accidental exposure scenarios, requiring significant investments in safety systems and shielding. While undoubtedly essential in mitigating the health risks associated with high doses, applying the same precautions to doses below 100 mSv appears excessively cautious. These rigorous measures, particularly at low doses, result in increased costs, complicate designs, and necessitate additional manpower allocation. This places a considerable strain on nuclear reactor operators during the licensing of their designs and constrains their operational capabilities. Moreover, this conservatism at low doses also impacts related sectors such as crop/seed/food irradiation practices in agriculture and patient therapy in nuclear medicine, particularly burdening healthcare systems in densely populated countries like India.

The ethical dilemma surrounding the adoption of a no-threshold safety paradigm at lower radiation doses primarily stems from uncertainties related to cancer risk. While a cautious approach assumes potential harm with every dose, evidence challenging the LNT model raises questions about the necessity of stringent regulations. For instance, individuals residing in high-background radiation areas receive doses of up to 260 mSv/year without experiencing elevated cancer rates. Medical procedures and activities involving potential radiation exposure lack clear evidence of excess cancers. Incidents such as Fukushima and Chernobyl, where doses reached hundreds of mSv, did not exhibit particularly high cancer incidence, and astronauts in high-dose environments have not shown any apparent elevated cancer risk. These real-world examples underscore the disparities between regulatory limits and observed evidence, especially at low doses.

Despite advancements in reactor designs, safety regulations, and the minimal impact of nuclear reactor operations on the environment (Kumar, A. V. *et al.*, 2023, 10.1016/j.scitotenv.2024.169936), public apprehension towards nuclear technologies persists due to the entrenched mindset of the LNT model. Addressing this issue involves considering the implications of an alternative perspective, which includes recognizing a specific dose range as posing no health risks and acknowledging the existence of a potential dose threshold. This alternative could lead to significant relaxation in radiation safety considerations and this shift may result in reduced capital and operating costs for nuclear power plants and allied industries such as nuclear medicine, along with easing concerns related to low radiation levels. However, establishing a dose threshold requires rigorous scientific evidence to ensure its validity and reliability.

This leads us to the positive aspect – the potential presence of hormesis or a threshold model at low doses. A growing body of epidemiological and radiobiological evidence indicates that low-dose radiation can instigate adaptive biological responses, triggering intrinsic stress responses in cells and bolstering their ability to endure higher doses (Chaurasia *et al.*, 2024, 10.1016/j.scitotenv.2024.170178). This involves activating the DNA damage response, increasing antioxidant production, antiapoptotic function, and regulating the cell cycle, challenging the tenets of the LNT model. Experimental evidence suggests that low-dose radiation may impede tumorigenesis, enhance immune response, and boost antioxidative capacity. These findings propose the potential existence not only of a dose threshold range but also of potential beneficial or hormetic effects at low doses.

Collectively, these non-linear biological processes in the low-dose regime (<100 mSv) are widely believed to play a significant role in mitigating the adverse effects of low-dose exposures. This perspective is further supported by the absence of statistically significant excess cancers observed in various cohorts across diverse geographical regions, industries, and accidental scenarios. All these observations prompt a re-evaluation of the dose limits driven by the LNT model, particularly for public exposures. Considering that external natural background radiation induces DNA mutations approximately a million times less than the intrinsic metabolically driven DNA mutations, an additional 1 mSv is unlikely to significantly impact this substantial difference. In fact, even an additional 100 mSv would not substantially alter this balance. Given this understanding and the accepted institutional definition of low dose, we propose that the occupational/public dose limit be increased to at least 100 mSv per year.

Unfortunately, the evidences supporting the above argument regarding adaptive responses face similar limitations to those encountered by studies endorsing LNT principles – namely, inadequate cohort sizes leading to heightened uncertainty in epidemiological studies, and a focus on lower biological organisms in radiobiological studies. Considering these challenges, we propose the potential of quantum biology to provide a framework for comprehending these adaptive responses (Chandra, A., 2023, 10.1007/s12647-023-00710-5). Quantum mechanisms, such as the radical pair mechanism, offer an explanation for the control of reactive oxygen species (ROS) and could further elucidate how low levels of ionizing radiation impact ROS activity. Another promising avenue is exploring the role of quantum tunnelling in DNA mutations and the modulation of repair machinery. Quantum coherence and tunnelling may also contribute to non-targeted effects, such as the bystander effect, challenging traditional radiation risk models.

Hence, dedicated efforts in quantum biology hold the promise of revealing unexpected insights at low doses. Consequently, this could strengthen the scientific evidence supporting the hormetic or threshold radiation paradigm. The imperative shift from fear-based approaches to evidence-driven policies, rooted in a precise scientific understanding, is vital for fostering public trust in the utilization of nuclear power and applications involving ionizing radiation.

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