Hormetic use of stress in gerontological interventions requires a cautious approach

Hormesis is a biphasic dose-response pattern in which the response at low doses is opposite to that at higher doses. According to the hormesis concept, a small dose of a potentially harmful agent can exert a beneficial action. Hormesis has been demonstrated experimentally for many factors. Theoretic basis of some hormetic mechanisms has been discussed within the scope of stress response pathways. Some kinds of stress represent an integral part of the environmental impact on living organisms, which have been adapted to it. Stress is a quite manifold and vaguely delineated phenomenon, so that hormetic responses should not be a priori assumed for all kinds of stress. Besides, it is sometimes unclear whether hormetic effects proven at the cellular level or in animals can be extrapolated to humans. If an agent is present in the natural environment, a hormetic effect due to adaptation of living organisms to the environmental level may be assumed. This can be illustrated by ionizing radiation, where the linear no-threshold theory (LNT) has provided theoretical basis for the safety norms. According to the LNT, the risks proven for higher doses can be extrapolated down to minimal doses. The LNT does not take into account that DNA damage and repair are permanent processes in dynamic equilibrium.

Living organisms are probably adapted to the natural radiation background as it is for light, UV, gravitation, products from radiolysis of water and many other substances normally present in the environment. Moreover, adaptation to a changing environmental factor would lag behind its current value and correspond to some average from the past, especially for such an ancient mechanism as the DNA repair. Life evolved with a radiation background that was higher than that existing today, which means that living organisms may retain some of the capability of repairing damage from higher radiation levels than exist at present. This is in accordance with experimental evidence in favor of radiation hormesis. Admittedly, some studies in humans reported cancer risk elevation after low-dose exposures. Possible mechanisms of cancer incidence increase unrelated to radiation (dose-related differences in medical surveillance and self-reporting etc.) were discussed as a possible explanation. It can be reasonably assumed that people with higher dose estimates would be on average more motivated to undergo medical examinations, being at the same time given more attention, hence more cancer cases revealed.

Along with the elevated cancer risk, an increased risk of non-neoplastic (cardiovascular, bronchopulmonary, gastrointestinal) diseases was observed in populations exposed to low-dose radiation. Although there may be some enhanced risk of cardiovascular disease after high dose and dose rate exposures, the present data are not sufficient to establish a causal relationship between radiation and cardiovascular diseases at low doses while plausible mechanisms are unknown. The increased risk of non-neoplastic diseases can be seen as circumstantial evidence in favor of dose-related differences in medical surveillance and self-reporting. With regard to radiation safety norms, the author shares the opinion by Professor Edward Calabrese that certain agencies and scientists push for doses that are progressively lower, although the risks at such doses have

not been proven. Finally, impacts of multiple stressing agents may produce combined effects larger than those expected from isolated impacts i.e. act synergistically. Adding the effect of a damaging stress to another damaging stress would possibly augment the damage; however, if two mild stresses have positive hormetic effects, their combination can have additive positive effects. The dangers inherent in using too high a dose of any hormetic agent are self-evident especially in senile age or a state close to decompensation when minor stimuli might be damaging. In conclusion, a hormetic use of stress in gerontological interventions requires a cautious approach.

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