RADIATION HORMESIS: AN EVOLUTIONARY EXPECTATION INVALIDATING THE LINEAR NO-THRESHOLD (LNT) PREMISE.

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ABSTRACT

Organisms survive best, or show high fitness, in the habitats in which they most commonly occur, a phenomenon referred to as hormesis in the literature of toxicology. Examples of hormesis accumulate rapidly in the literature. However, a lack of underlying models has led many to doubt its existence, especially for ionizing radiation. The evolutionary model developed here indicates that all potentially stressful environmental agents should show hormesis, so that the linear-no-threshold (LNT) premise should be invalid for all environmental agents including ionizing radiation. Furthermore, this evolutionary model incorporates aging towards environmental extremes.

Contributions from 1989 include:

(1.) Acetaldehyde utilization in Drosophila : an example of hormesis. Biol. J. Linnean Soc. **37:** 183-189, 1989.

Acetaldehyde is an essential metabolite at low concentrations and becomes a stress at high concentrations; this hormetic relationship is illustrated by fitness measured by longevity. Organic metabolites such as acetaldehyde and organisms such as Drosophila provide models for genetical and molecular studies of hormesis. This approach assists in our understanding of suggestions over many years of enhanced fitness at natural background levels of ionizing radiation.

(2.) Radiation hormesis: an evolutionary expectation and the evidence. Appl. Radiat. Isot. **41:** 857-860, 1990.

Since there is a tendency for organisms to become progressively adapted to those environments to which they are most frequently exposed, radiation hormesis is an evolutionary expectation.

(3.) Evolutionary adaptation and stress: the fitness gradient. Evolutionary Biology **26:** 191-223, 1992.

Impacts of environmental stresses are discussed in terms of fitness-stress continua which are necessarily non-linear. The evolutionary expectation of radiation hormesis is thereby put into an ecological context.

(4.) Radiation hormesis: an evolutionary expectation based upon exposure to background radiation. BELLE Newsletter 3: 9-11, 1994.

The material in (2) above is covered briefly with some emphasis on humans.

(5.) Are low levels of radiation phantom risks? In “Nuclear Science and Engineering in Australia”, Australian Nuclear Association Inc. 57-60, 1995.

Various mechanisms that underlie deviations from the LNT model such as DNA repair are considered. Small radiation doses at around background levels are phantom risks.

(6.) Low level exposure to ionizing radiation: do ecological and evolutionary considerations imply phantom risks? Perspectives in Biology and Medicine **43:** 57-68, 1999.

Here I develop arguments from the field of evolutionary biology, taking into account the stressful habitats in which organisms occur, in order to challenge the validity of the LNT model on evolutionary grounds.

(7.) Hormesis: an adaptive expectation with emphasis on ionizing radiation. J. Appl. Toxicol. 20: 103-112, 2000.

The model of radiation hormesis developed in (6.) is explained in more detail. Based upon the universality of stressful environments, radiation hormesis is postulated to have two components. The smaller component is background radiation hormesis from the direct adaptation of organisms to their habitats, and the larger is stress-derived radiation hormesis which derives from metabolic reserves that evolve from and are maintained as an adaptation to the totality of the diverse environmental agents to which organisms are exposed through evolutionary time

(8.) Caloric restriction, metabolic efficiency and hormesis. Human and Experimental Toxicology 19: 345-347.

Hormesis is selection for metabolic efficiency in response to any environmentsl variable including caloric stress and ionizing radiation

(9.) Radiation hormesis: an ecological and energetic perspective. Medical Hypotheses **57:** 277-279: 2001.

All environmental agents including radiation can be incorporated into a model of non-linear fitness gradients, assuming that the adaptation of organisms to their habitats depends upon high fitness manifested by high metabolic and energetic efficiency. In these terms, radiation hormesis can be interpreted in energetic terms as a second order effect deriving from the consequences of the array of stresses in natural populations. The invalidity of the LNT premise is a central theme

(10.) The hormetic zone: an ecological and evolutionary perspective based upon habitat characteristics and fitness selection. The Quarterly Review of Biology **76:** 459-467, 2001.

Hormesis is discussed for environmental agents generally but emphasizing ethanol and its metabolites especially acetaldehyde, and ionizing radiation.

(11.) Radiation hormesis: challenging LNT theory via ecological and evolutionary considerations. Health Physics **82:** 513-516, 2002.

The model of radiation hormesis in (6) – (8) is updated and additional evidence is incorporated. In the Conclusion section I write “Here I present a model of hormesis based upon the adaptation of organisms to stressful environments through evolutionary time, which can be tested empirically”. The “health benefits” claimed for hormetic zones derive from deviations from the LNT premise which are maximal in relatively benign environments.

(12.) Metabolic efficiency in response to environmental agents predicts hormesis and invalidates linear no-threshold theory: ionizing radiation as a case study. Critical Reviews in Toxicology **33** : 443-449, 2003.

This article was requested for a special issue on hormesis.

(13.) Energy, stress and the invalid linear no-threshold premise: a generalization illustrated by ionizing radiation. Biogerontology **4:** 227-231, 2003.

This article provides a generalized approach in terms of energetic efficiency, which can be equated to fitness when considering responses to environmental agents, including ionizing radiation. Underlying mechanisms include stimulation of DNA repair, heat-shock proteins and immune responses, and the metabolic scavengers that remove damaging reactive forms of oxygen. However, published longevity and survival data, being measures of fitness or energetic efficiency, indicate that non-linearity and hence radiation hormesis extend to exposures substantially in excess of background radiation. Energetic and metabolic interactions among multiple environmental stresses provide an explanation.

(14.) Radiation phobia and phantom risks. Quadrant Dec. 2004:62-63
Radiation and the no-risk society. Quadrant July - Aug. 2005 : 60-62

These two articles appeared in Quadrant an Australian "intellectual magazine".

When scientific evidence replaces emotion, the "phantom" risks from the peaceful uses of ionizing radiation disappear. This conclusion follows from the valid assumption of hormesis for all environmental agents including radiation. The consequential inputs into debates on power generation are important today.

(15.) Environments and evolution: interactions between stress, resource inadequacy and energetic efficiency. Biol. Rev. **80**: 589-610, 2005.

An energetic ecological approach to evolution is presented, which automatically includes hormesis.

(16.) Radiation, ecology and the invalid LNT model: the evolutionary imperative. Dose Response **4**: 191-200, 2006.

An elaboration of the general model developed in (13) shows that non-linearity is the primary model for assessing risks from low-dose radiation, and becomes the evolutionary imperative for risk assessments.

(17.) The ecological stress theory of aging and hormesis: an energetic evolutionary model. Biogerontology 8: 233-242 2007.

An elaboration of (15) showing that hormesis and aging can be considered under the same evolutionary model, based upon energetic consequences of environmental variability.

CONCLUSION

Hormesis derives from high energetic efficiency and hence high fitness that evolve in response to single and multiple environmental agents in low to moderate stress habitats. Consequently, non-linear fitness continua are an evolutionary expectation for all environmental agents, which invalidates the LNT premise. For ionizing radiation, hormesis is interpreted to be adaptation to background radiation exposures, combined with adaptation to higher radiation exposures dependent upon metabolic protection from the array of other abiotic stresses in the environment. The model is compatible with a modification of exposure levels for radiation protection towards higher doses than are presently permissible, a deduction with substantial economic benefits. Thus background radiation is around 2mSv (milliSieverts) y^{-1} at sea level and substantially higher elsewhere including some geological outliers to beyond 200 $mSvy^{-1}$; the hormetic zone appears to incorporate this range.

RELEVANT CAREER ACTIVITIES

President, Australian Institute of Nuclear Science of Engineering 1975-76, Council 1970-87, Honorary Fellow 1991 –

Member, Australian Ionising Radiation Advisory Council 1987 – 93.

Editorial Board, Biological Journal of the Linnean Society of London, 1984 –

Editorial Board, Nonlinearity in Biology, Toxicology and Medicine 2001 – 2007

AM (mainly radiation biology) 2006

Recent addition

(18.) Survival across the fitness-stress continuum under the ecological stress theory of ageing: coloric restriction and ionizing radiation. Dose Response 8: 4 – 9. 2010

Illustrative case studies.

Radiation hormesis and evolution: incorporating recent cellular observations.

Scientists at the Lawrence Berkeley National Laboratory, USA, reported in PNAS* in January, 2012 that cellular DNA repair mechanisms work best at low radiation doses so providing an overdue link of cellular and population approaches to radiation hormesis (my comments here are based upon the enclosed Weekly Digest of the World Nuclear Association).

These experimental observations are in accord with evolutionary predictions developed in my publications from 1990 whereby risk from ionizing radiation is not linearly related to exposure. My predictions on non-linearity are based upon ecological stresses in habitats promoting selection for fitness assessed by metabolic efficiency (summarized in the enclosed reprint in Dose Response). The Berkeley work is clearly a pivotal step into molecular mechanisms underlying radiation hormesis with the potential for substantial future research activities. Implications for radiation exposure standards applicable for example to Chernobyl and the recent Japanese nuclear event are evident.

PS I anticipated that my Scientific Obit dated December 2011 distributed last month was final, but the enclosed indicates a necessary modification.

Peter A. Parsons

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* Neumaier, Teresa .....and Costes, Sylvain V. (2012) Evidence for formation of DNA repair centers and dose-response nonlinearity in human cells. PNAS 109: 44448.