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Hormesis Revisited by T.D. Luckey

Hormesis is the stimulation of an organism by low doses of any agent. Large doses generally inhibit or damage. The term was first used in 1943 to describe the effect of a toxic extract of cedar bark upon beetles. A remarkable number of workers 'discovered' the stimulating effect of low doses without knowing the results of others who preceded them. Diverse names for stimulation by low doses (Table I on back) are presented. In spite of the mass of papers and large numbers of reviews of this subject, few investigators knew and applied the principles of hormesis in their work. More recent names are: the J-curve in cancer, the reverse effect in nutrition and metabolism, U-shaped functions in neurotoxicity, and adaptive survival response (ASR) in cell culture. The "no observed adverse effects level" (NOAEL) applies to chemical toxicants. Stimulation by low doses of an agent is a general rule in biology.

Radiation hormesis conforms to and extends the general concept. Radium and uranium were the main sources of ionizing radiation used at the beginning of this century. In the 1950's, neutrons and beta ray sources (3H,32P,35S,45Ca, and 65 Zn) came into use. By 1960, filtered radiation from cobalt and radium allowed exploration with gamma and x rays, respectively. "Hormesis with ionizing radiation" included 55 reviews listed in its 1,200 references. "Radiation Hormesis" cited 1,000 references; mostly concerned with experimental animals. Late reviews concentrate on decreased total cancer mortality rates in humans following whole body exposures. Radiobiologists generally accept the evidence and the concept but unfortunately, governmental agencies do not. Benefits from increased background levels of ionizing radiation are found consistently in experimental animals and, where there is pertinent data, in humans.

Radiation hormesis is less often found in cells in culture; these laboratory artifacts lack many homeostatic responses and have incomplete physiologic activities. Death is their usual response to adverse conditions. Hormesis involves responses from naturally occurring, independent organisms. Examples of benefits from low-dose irradiation are listed in Table 2. Conclusions are:

1. Ionizing radiation is essential for life;
2. We live in a partial **deficiency** of ionizing radiation; **and**
3. Safe supplementation with lowdose irradiation would provide a new plateau of health.

Regulatory agencies must begin to use health, rather than risk and presumed harm, as their major guide in establishing protection guidelines. The human and national damage done by adherence to the "linear nothreshold" (LNT) concept is devastating. The entrenched membership of advisory committees with a lifetime commitment to LNT must change. An open forum should present evidence of hormesis in radiation and toxicology with the objective of revealing the lack of scientific evidence supporting LNT and current recommendations and regulations, which use LNT as their basis. The concept of horrnesis should become accepted in national affairs as it is in science.

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Table 1. Concepts of low-dose stimulation

YEAR	DISCIPLINE	AUTHOR	CONCEPT
1500 BC	Medicine	Hatshepsu	Poisons stimulate
1000 BC	Immunization	Chou	Smallpox vaccination
700 BC	Medicine	Sargon II	"Dual" belladonna
400 BC	Therapy	Hippocrates	Give no fatal dose
1540	Pharmacy	Paracelsus	The dose is everything
1780	Medicine	Withering	Potential toxicants
1878	Botany	Bernard	Stress builds strength
1897	Botany	Townsend	Trauma increases plant growth
1888	Fermentation	Schulz	The Arndt-Schulz law
1906	Bacteriology	Richet	Oligodynamic effect of metals
1908	Psychology	Yerkes	The invented U-curve
1919	Radiation	Davey	Homeostatic doses
1922	Medicine	Hahnemann	Minute dose heal
1930	Toxicology	Maximov	Toxicants increase plant growth
1930	Therapy	Merck	Theuraputic index
1936	Radiation	Gager	Radiation increases plant growth General
1936	Physiology	Seyle	adaptive syndrome (GAS) Hormesis
1943	Entomology	Southam	Antibiotics stimulate growth
1946	Nutrition	Moore	Psuedo growth effect
1950	Radiation	Lorenz	Dietary promotant
1950	Nutrition	Briggs	Radiation enhances immunity
1951	Immunology	Taliaferro	Hormoligosis
1959	Toxicology	Luckey	The beta curve
1960	Pharmacology	Townsend	Adaptive enzyme induction
1961	Bacteriology	Jacob	Probiotics
1974	Nutrition	Parker	Biopositive effects
1974	Agronomy	Zelles	Paradoxic reversal
1976	Radiation	Sacher	Perculiar curve
1976	Radiation	Friedberg	T-cell activation
1979	Immunity	Hellstrom	Radiogenic metabolism
1980	Radiation	Luckey	Di-phasic action
1980	Radiation	Luckey	The J- or Hockey Stick Curve
1985	Cancer	Hickey	The reverse effect
1988	Metabolism	Heiby	The U-shaped functions
1990	Neurotoxicity	Davis	Adaptive survival response (ASR)
1996	Cell culture	Salone	Cytodynamic 2-stage (CD2)
1997	Cancer	Bogen	The dose is everything
1997	Chemistry	Calabrese	

Table 2. Benefits of low-dose irradiation

Fecundity	Increased numbers of young	*Healing*	Wounds heal faster
Reproduction	More young survive to weaning	*Immunity*	Enhanced cellular and chemical immune systems
Sterility	Human sterility is decreased	*Cancer*	Decreased cancer death rate
Growth	Faster growth rate in animals	*Resistance*	Survival following lethal irradiation
Development	Early neuromuscular activities	*Lifespan*	Decreased total mortality rate
Mental acuity	Improved learning and memory	*Life*	Viability in sub-radiation environments*

*In non-vertebrates; vertebrate research is needed.