First Conference on Radiation Hormesis Explores Nonhazardous Effects of Exposure

At the Conference on Radiation Hormesis, held last August in Oakland, CA, investigators from 12 countries exchanged scientific data on studies which may indicate that radiation exposure results in nonhazardous as well as hazardous biologic effects.

Although the word "hormesis" denotes beneficial results from a substance which is harmful at higher doses, "such value-laden terms are best avoided, and we should restrict ourselves to investigating and understanding the phenomena," said Leonard A. Sagan, MD, senior scientist in the energy analysis and environment division of the Electric Power Research Institute (EPRI) in Palo Alto, CA.

"The term 'hormesis' has not been widely used, at least in the radiation community. I believe that the term should be applied to any physiologic effect which occurs at low doses which cannot be anticipated by extrapolating from toxic effects observed at high doses," said Dr. Sagan, who chaired the introductory session at the conference.

The meeting covered plant, animal, and human studies, cellular- and tissue-level studies, alpha-particle exposures, and biochemical mechanisms. Unlike most scientific meetings, this conference was not held to update scientists on the latest developments in the field, noted Dr. Sagan.

"Rather than consider new information, we are going to consider the fundamental paradigm on which radiation science is based. We are going to examine existing data to study how well they are explained by the conventional radiation paradigm and to answer the question of whether the time has come to change or amend that paradigm, particularly as it applies to low doses," he explained.

The conference was sponsored by the EPRI, and the Northern California chapters of the American Nuclear Society and the Health Physics Society. According to Dr. Sagan, the conference papers are now undergoing peer review and will be published next year in *Health Physics*.

Radiation effects paradigm

Dr. Sagan described the radiation effects paradigm currently held by the scientific community as the belief that radiation exposure is harmful, and that effects at low doses can be extrapolated from the harmful effects at high doses.

(Thomas S. Kuhn, author of *The Structure of Scientific Revolutions*, defined paradigms as scientific theories of the operation of complex systems which channel scientific work in specified acceptable directions.)

"There has been little dissent from this view. Only the shape of the dose-response curve and the absolute levels of risk have been the center of scientific attention," commented Dr. Sagan.

Investigators design experiments to detect increases in biologic effects, such as mutations and cancers, while ignoring any decreases which may occur, said Dr. Sagan. "We are blind to them because they are not part of our paradigm," he added.

Citing a study which indicated a reduced rate of mortality and infertility, but an increased rate of malformation, among trout conceived following the irradiation of sperm, Dr. Sagan pointed out that both harmful and hormetic effects may occur with the same dose of radiation. "The debate about whether low doses are 'harmful' or 'beneficial' may be overly simplistic," he said.

Mutagenesis and carcinogenesis

Victor P. Bond, MD, PhD, of the Brookhaven National Laboratory in Upton, NY, said, "The usefulness of the radiation hormesis concept may well be decided on the carcinogenesis/mutagenesis questions because of the general awareness that even a moderate average life lengthening in the population would not eliminate marked shortening of useful life in the young with induced cancer or serious genetic defects."

Working with the Nuclear Research Center Juelich in Germany, Dr. Bond presented data on radiation mutagenesis and carcinogenesis indicating that "the smallest average organ absorbed dose" can affect macromolecular cell targets and result in cell transformation. The group found, however, that protective processes enhanced by hormesis may render amounts of energy deposition just above threshold ineffective for a given cell target.

"This could reduce the incidence of carcinogenesis and mutagenesis for radiations of any LET, and does not exclude the possibility of a threshold for at least the radiations of lowest LET," said Dr. Bond.

Biochemical control mechanisms

Prof. Dr. Ludwig E. Feinendegen, of the Nuclear Research Center Juelich, presented data indicating that low-dose, low-linear-energy-transfer (LET) irradiation simulates intracellular biochemical control mechanisms.

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In a study conducted with the Brookhaven National Laboratory, low-dose gamma irradiation of normal deoxyribonucleic acid (DNA)-synthesizing mouse cells caused an acute, temporary, and partial inhibition of thymidine kinase that was dose-dependent up to one rad, and a synchronous increase of free serum thymidine.

"These two effects were reproduced by a vitamin-E-deficient diet," said Prof. Dr. Feinendegen.

"The data imply that low-dose, low-LET radiation causes temporary subtle changes in metabolism within the normal range of metabolic reactions, within which adaptive controls may result in a threshold for detrimental effects on DNA," he concluded.

Cell renewal systems

Jacob I. Fabrikant, MD, PhD, of the Donner Laboratory at the University of California, Berkeley, discussed the adaptation of cell renewal systems under continuous irradiation.

"The experimental evidence suggests that there are adaptation changes in the proliferative characteristics of renewal tissues under the stress of continuous low-dose-rate irradiation, which indicate that cell and tissue kinetics will have a considerable effect on the radiation response," said Dr. Fabrikant.

Atomic bomb survivors

Dr. Hiroo Kato, of the Radiation Effects Research Foundation in Hiroshima, Japan, presented data from studies of the atomic bomb survivor population. About 38,000 survivors received doses ranging from one to 50 rads.

"In general, the dose responses for these indices varied among subgroups within the low-dose range, and failed to suggest the existence of radiation hormesis," said Dr. Kato.

In a study of atomic bomb survivors who had migrated to the United States, investigators at the Veterans Administration Medical Center in West Los Angeles and at the University of California, Los Angeles (UCLA) studied four parameters of cellular immunity in lymphocytes.

Survivors who had received 0–50 rads showed a greater response (although it was not statistically significant for three of the parameters) than subjects who had received "0" rads, and these studies are now being performed on the larger sample population in Japan.

Several papers discussed epidemiologic data, comparing cancer rates between populations living in geographic areas with significant differences in background radiation, or between populations exposed to radioactive fallout or occupational radiation and control groups. Some of these studies indicated reduced rates for some cancers among exposed populations, although other studies found increased rates for various cancers.

Epidemiology studies

Dr. Shu-Zheng Liu, of the Norman Bethune University of Medical Sciences in Changchun, China, presented data on one epidemiologic survey that included immunologic studies performed on the study population.

"The nature of health effects on low-level ionizing radiation has been a problem of considerable controversy. It is suggested from the present investigation that small doses of ionizing radiation in a certain range might have hormetic effects on some immunologic parameters which might be relevant in the explanation of some of the epidemiologic data," said Dr. Shu-Zheng Liu.

Many of the presentations involved the stimulatory effects of radiation on germination and growth of seeds and plants, probably the most commonly investigated hormetic effect within the scientific community.

Problem of defining "low dose"

According to Dr. Sagan, "This concept of hormesis will be more precisely defined when those effects, if any, are identified and their mechanisms understood." When the mechanisms become clear, he added, hormetic phenomena can be characterized in terms of those known mechanisms, "and the problem of defining low doses of radiation will disappear."

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