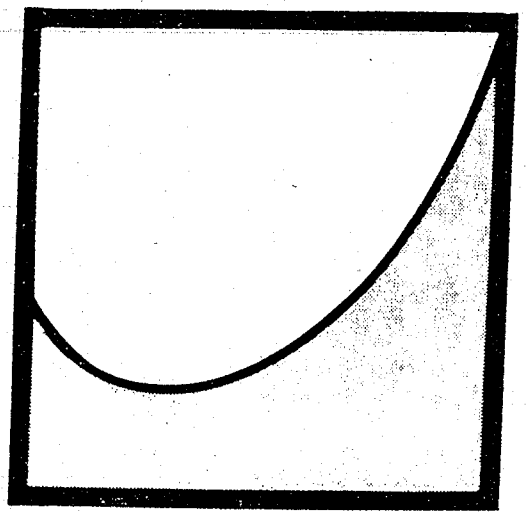

Conference On Radiation Hormesis

Oakland Airport Hilton Hotel

Oakland, California

August 14-16, 1985

PROGRAM AND ABSTRACTS

SPONSORS:

ELECTRIC POWER RESEARCH INSTITUTE
AMERICAN NUCLEAR SOCIETY - NORTHERN CALIFORNIA SECTION
HEALTH PHYSICS SOCIETY - NORTHERN CALIFORNIA SECTION
U.S. DEPARTMENT OF ENERGY
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SCHEDULE OF EVENTS

Tuesday, August 13, 1985

5:00p - 8:00p	Registration	California Room Foyer
5:30p - 8:30p	"No Host" Cocktail Mixer	California Room

Wednesday, August 14, 1985

8:00a - 12:00n	Registration	Ballroom Foyer
8:30a - 12:00n	Technical Session	Ballroom
1:30p - 5:30p	Technical Session	Ballroom
6:00p - 7:00p	"No Host" Cocktails	Ballroom
7:00p	Conference Banquet	Ballroom

Thursday, August 15, 1985

8:00a - 12:00n	Registration	Ballroom Foyer
8:30a - 12:00n	Technical Sessions	Ballroom
1:30p - 5:30p	Technical Sessions	Ballroom

Friday, August 16, 1985

8:00a - 1:00p	Technical Session	Ballroom

GUEST PROGRAM

Wednesday, August 14, 1985

8:30a - 10:00a	Coffee Mixer (complimentary)	Pacific Room

(A representative of the Oakland Convention and Visitors Bureau will discuss attractions and worthwhile activities for visitors to the Bay Area)

7:00p	Conference Banquet	Ballroom

Thursday, August 15, 1985

8:30a - 10:00a	Coffee Mixer (complimentary)	Pacific Room

Address correspondence to: Conference on Radiation Hormesis
816 Abbie Street
Pleasanton, CA 94566
phone (415) 846-4966, (415) 462-5300

CONFERENCE ON RADIATION HORMESIS
TECHNICAL PROGRAM

Wednesday, August 14, 1985

8:30a **WELCOME** - Jerry J. Cohen, Conference Chairman

8:45a to 12:00n **INTRODUCTION AND OVERVIEW** - Session Chair: Leonard A. Sagan, Electric Power Research Institute (EPRI) , Palo Alto, CA

What is Hormesis and Why Haven't We Heard About This Before?, Leonard A. Sagan, EPRI, Palo Alto, CA

Hormetic Effects in Pharmacology, Arthur Furst, Institute of Chemical Biology, University of San Francisco, San Francisco, CA

The Occurrence of Chemically-Induced Hormesis, Edward J. Calabrese, Margaret E. McCarthy, Elaina Kenyon, Div. of Public Health, Univ. of Massachusetts, Amherst, MA

Growth Hormesis - A Biproduct of Control, Anthony R.D. Stebbing, Institute for Marine Environmental Research, Plymouth, United Kingdom

The Physiology of the Hormetic Effect, John R. Totter, Oak Ridge Associated Universities, Institute for Energy Analysis, Oak Ridge, TN

→Radiation Hormesis May be Nurture by Ionizing Radiation, T.D. Luckey, Prof. Emeritus, University of Missouri, Loveland, CO

Subsidy-Stress Theory and the Response of Biological Systems to Environmental Perturbations, I. Lehr Brisbin, Jr. and Michael H. Smith, Savannah River Ecology Laboratory, Aiken, SC

1:30p to 5:30p **CELLULAR AND TISSUE LEVEL STUDIES** - Session Chair: Sheldon Wolff, Laboratory of Radiobiology and Environmental Health, Univ. of California, San Francisco, CA

The Tritiated-Thymidine-Induced Adaptive Response of Human Lymphocytes to Subsequent Doses of X-Rays, Sheldon Wolff, Laboratory of Radiobiology and Environmental Health, University of California, San Francisco, CA

Adaptation of Cell Renewal Systems Under Continuous Irradiation, Jacob I. Fabrikant, Donner Laboratory, University of California, Berkeley, CA

Evidence that Cell Proliferation is Influenced by Background Radiation or Exposure to Very Low Gamma Chronic Radiations, Hubert Planel, Jean-Pierre Soleilhavoup, Renè Tixador, Gèrard Richoilley, and C. Caratero, Laboratoire de Biologie Cellulaire, Faculté de Mèdecine, Toulouse, France

Wednesday, August 14, 1985 (continued)

Radiation Hormesis - Its Expression in the Immune System, Shu-Zheng Liu, X.H. Liu, X.Y. Li, G.Z. Xu, Norman Bethune University of Medical Sciences, Changchun, Jilin, PR China

Delayed Effects of Low Dose Radiation on Measurements of Cellular Immunity in Atomic Bomb Survivors Residing in the United States, E.T. Bloom[1], E.L. Korn[2], and T. Makinodan[1], [1]VA Medical Center, UCLA Dept. of Med., Los Angeles, CA, [2]Dept. of Biomath., UCLA-Jonsson Cancer Center, Los Angeles, CA

Ionizing Radiation for Optimal Microbic Growth Rates, T.D. Luckey, Prof. Emeritus, University of Missouri, Loveland, CO

7:00p **BANQUET** - Radiation Risks: Politics and Morality, Margaret-N. Maxey, Professor of Bioethics, University of Texas, Austin, TX

Thursday, August 15, 1985

8:30a to 12:00n **PLANT AND ANIMAL EFFECTS** - Session Chair: Marvin Goldman, Univ. of California, Davis, CA

Life Shortening Effects of Chronic High and Low LET Radiation in Beagles, M. Goldman, University of California, Davis, CA

Increased Fertility Observed in Male Mice Exposed to Low Doses of Ionizing Radiation in a Region of High Natural Radioactivity, A. Léonard[1,2] M. Delpoux[3], R. Meyer[1], G. Decat[1], and E.D. Léonard[2], [1]Laboratory of Mammalian Genetics, Department of Radiobiology, MOL, Belgium; [2]Catholic University of Louvain, Belgium; [3]Paul Sabatier University, Toulouse, France

A Review of Certain Low Level Ionizing Radiation Studies in Mice from the Standpoints of Lifespan and Tumor Development, C.C. Congdon, Department of Medical Biology, University of Tennessee College of Medicine, Knoxville, TN

Radiation-Induced Stimulation Effects in Living Organisms, J. Simon, Scientific Director, Qualitas, Budapest, Hungary

Pre-Sowing Stimulation of Crop Seed, Stanton T. Friedman, Ionizing Energy Co. of Canada Ltd., Fredericton, NB, Canada

Factors Controlling the Hormesis Response from Irradiated Seed, S. C. Sheppard and W.G. Evenden, Environmental Research Branch, Whiteshell Nuclear Research Establishment, AECL, Pinawa, Manitoba, Canada

Thursday, August 15, 1985 (continued)

Observations of Plant and Animal Stimulation Resulting from Nuclear Detonations, Roderick G. Morrison, Sunburst Energy Systems, San Marcos, CA

Radiation Hormesis in Plants, Morton W. Miller and W. Marcus Miller, University of Rochester, Rochester, NY

1:00p to 2:30p **ALPHA PARTICLE EXPOSURES** - Session Chair: Jacob I. Fabrikant, University of California, Berkeley, CA

Cancer Incidence vs. Alpha Particle Dose, Charles W. Mays, Radiobiology Division, University of Utah, Salt Lake City, UT

Effects of Exposure to Plutonium and Low-Level External Radiation on Lung Cancer Rates, Gary Tietjen, Los Alamos National Laboratory, Los Alamos, NM

Lung Cancer Induction by Environmental Radon and Its Potential for Demonstrating Hormesis, Bernard L. Cohen, Univ. of Pittsburgh, Pittsburgh, PA

Hormesis of Alpha Radiation and Its Role in Cancer and Aging, Edward A. Martell, National Center for Atmospheric Research, Boulder, CO

3:00p to 5:00p **HUMAN STUDIES** - Session Chair: Genevieve Matanoski, Johns Hopkins University, Baltimore, MD

Is There a Protective Effect from Radiation in Radiologists?, Genevieve M. Matanoski, Elizabeth A. Elliott, and Alice Sternberg, Johns Hopkins Univ., School of Hygiene and Public Health, Baltimore, MD

A Dose Response Among A-Bomb Survivors Exposed to Low Level Radiation, Hiroo Kato[1], William J. Schull[2], Akio Awa[1], Mitoshi Akiyama[1], and Masanori Otake[1], [1]Rad. Effects Research Foundation, Hiroshima, Japan; [2]Center for Demographic & Population Genetics, University of Texas, Houston, TX

Association of Nuclear Fallout with Thyroid Cancer in the United States, Victor E. Archer, University of Utah, Salt Lake City, UT

Possible Human Health Benefits of Radiation Hormesis, Richard J. Hickey[1], Richard C. Clelland[1], Evelyn J. Bowers[2], and Babette S. Zemel[2], [1]Dept. of Statistics, The Wharton School, University of Pennsylvania, Philadelphia, PA; [2]W.M. Krogman Ctr. for Research in Child Growth & Development, Univ. of Pennsylvania, PA

Friday, August 16, 1985

8:30a to 11:00a **MECHANISMS** - Session Chair: Victor P. Bond, Brookhaven National Laboratory Upton, NY

Hormesis; Mutagenesis and Carcinogenesis, V.P. Bond, L.E. Feinendegen, and C.A. Sondhaus, Brookhaven National Lab, Upton, NY, and Institute for Medicine, Nuclear Research Center, Julich, FRG

Low Dose, Low LET-Irradiation Simulates Intracellular Biochemical Control Mechanisms, L.E. Feinendegen, H. Muhlensiepen, and V.P. Bond, institute for Medicine, Nuclear Research Center, Julich, FRG, and Brookhaven National Lab, Upton, NY

Theoretical Physiological Basis for Radiation Hormesis, Joseph W. Moon, Rutgers University, Department of Radiation Science, Piscataway, NJ

Critical Values of LET, Dose Rates and Doses for Radiation Hormesis, K. Okamoto, Tokyo Gakugei University, Tokyo, Japan

Epistomological Problems in Assessments of Cancer Risks at Low Radiation Doses, Gunnar Walinder, Unit of Radiological Oncology, Univ. of Stockholm, Sundbyberg, Sweden

Biochemical Mechanisms Involved in the Stimulating Effect Induced by Very Low Doses of Gamma Radiations on Cell Proliferation, Annie Conter, Francoise Croute, and Hubert Planel, Univ. Paul Sabatier, Toulouse, France

11:00a **REPORT OF RAPPORTEURS**

ABSTRACTS

ASSOCIATION OF NUCLEAR FALLOUT WITH THYROID CANCER IN THE UNITED STATES

Victor E. Archer (University of Utah, Salt Lake City, UT 84112)

Much of the United States population has been exposed to low levels of fresh nuclear fallout which contained short half-life radioiodines. Past data has been equivocal as to whether or not this exposure was associated with increased thyroid cancers. Using death data published by the National Cancer Institute, four different epidemiological approaches were used to investigate this subject on a national level. All four exhibited an association. For children under 5 years of age in the United States during the period of maximum exposure (1952-55), the risk of fatal thyroid cancer was at least doubled during the subsequent 20 years. Since the incidence of thyroid cancer is about 40 times greater than the mortality in this age group, this finding suggests that stable iodine and radiation control of milk be used as preventive measures whenever populations are exposed to appreciable amounts of fresh nuclear fission products.

DELAYED EFFECTS OF LOW DOSE RADIATION ON MEASUREMENTS OF CELLULAR IMMUNITY IN ATOMIC BOMB SURVIVORS RESIDING IN THE UNITED STATES.

E.T. Bloom (GRECC, VA Med. Ctr. West LA, CA 90073, and UCLA Dept. of Med., LA, CA 90024), E.L. Korn (Dept. of Biomath., and UCLA-Jonsson Cancer Center, LA, CA 90024), and T. Makinodan (GRECC, VA Med. Ctr. West LA, CA 90073, and UCLA Dept. of Med., LA, CA 90024)

Survivors of the atomic bombs exploded in 1945 in Japan and presently residing in the United States were recruited for this study. They were given medical examinations and blood was collected for immunological tests. The survivors in this study were exposed to various low doses of radiation (T65D) at the time of the bomb (ATB). More than half of the subjects received "0" rads (n=102, S_0 group). Of those exposed to >0 rads (n=66, S_+ group), 89% received <50 rads ATB. Lymphocytes were isolated from the blood samples and four parameters of cellular immunity were measured. These included: a) mitogenic response to phytohemagglutin, b) mitogenic response to allogeneic lymphocytes, c) natural killer cell (NK) activity, and d) interferon production. In every case the response of the S_+ group was greater than that of the S_0 group, although only the difference for NK activity was statistically significant ($p=0.03$). The trend was supported by studies on serological parameters (Bloom et al., Rad. Res. 96:399, 1983). Studies are presently being performed on a larger sample population of survivors residing in Japan and exposed to a wider range of radiation doses ATB to determine a) whether these results might be influenced by factors affecting migration to the US, and b) what the delayed effects of larger doses of radiation (e.g., >100 rads) are. (Supported by contracts EY-76-S-03-0034 and DE-AT03-83ER60169 from the US Department of Energy.)

HORMESIS; MUTAGENESIS AND CARCINOGENESIS

V.P.Bond, L.E.Feinendegen, C.A.Sondhaus; Brookhaven National Laboratory, Upton N.Y. 11973/USA and Institute for Medicine, Nuclear Research Center Jülich, D-5170 Jülich

With radiation, unlike chemicals, a small absorbed organ dose can deliver amounts of energy to macromolecular cell targets so large that even the best efforts of any repair processes probably cannot prevent cell transformation. Data are shown for both mutagenesis and carcinogenesis, indicating that, in this respect, the smallest average organ absorbed dose can be effective, particularly for high LET radiation. However, protective processes enhanced by hormesis may render ineffective amounts of energy deposition just above threshold 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. The usefulness of the radiation hormesis concept may well be decided on the carcinogenesis - mutagenesis question 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.

SUBSIDY-STRESS THEORY AND THE RESPONSE OF BIOLOGICAL SYSTEMS TO ENVIRONMENTAL PERTURBATIONS.

I.Lehr Brisbin, Jr. and Michael H. Smith. (Savannah River Ecology Laboratory, P.O. Drawer E, Aiken, SC 29801)

Although the concept of hormesis has been studied almost exclusively at the level of the individual organism and below (ie. cellular and mollecular), its interpretation and relevance must also be considered at higher levels of biological organization (ie. the population, community and ecosystem). Understanding of hormesis at these more complex levels of biological organization is best achieved thru the application of so-called "subsidy-stress" theory of modern ecology. As compared to considerations of hormesis at the cellular, mollecular and individual levels, subsidy-stress theory, applied at the higher levels of biological organization, raises questions concerning hormesis that are related to: (1) perception of the phenomenon, (2) interpretation of observed responses, and (3) definition and delineation of the biological scale or scope over which the phenomenon is observed. Examples of these issues are provided from published studies describing hormetic-like responses in the ecological literature and through reinterpretations and reanalyses of studies of the responses of growth to a variety of environmental stressors, using a reparmeterized Richards sigmoid model.

THE OCCURRENCE OF CHEMICALLY-INDUCED HORMESIS

Edward J. Calabrese, Margaret E. McCarthy, Elaina Kenyon, Division of Public Health, University of Massachusetts, Amherst, MA 01001

The presentation will provide an overview concerning the potential generalizability of chemical hormesis. Evidence will be presented on the occurrence of chemical hormesis by chemical classes studied (e.g., heavy metals, polycyclic aromatic hydrocarbons, etc.), by affected biological and toxic end points (e.g., growth enzyme activities, DNA-repair capacity, lifespan, tumor incidence) and by biological/taxonomic systems. Several specific examples of possible hormetic effects with respect to agents of environmental concern such as chloroform will be presented along with a discussion of future research directions.

LUNG CANCER INDUCTION BY ENVIRONMENTAL RADON AND ITS POTENTIAL FOR DEMONSTRATING HORMESIS

Bernard L. Cohen (Univ. of Pittsburgh, Pittsburgh, PA 15260)

Studies of health impacts of low level radiation require very large numbers of subjects, which suggests the use of natural radiation. External natural radiation is hopeless in this regard as it is expected to cause only 0.5% of all cancers, whereas unknown factors are well known to cause fluctuations of 25% or more from state to state. The situation is orders of magnitude more favorable for environmental radon which, according to conventional wisdom, is expected to cause 15%-100% of all lung cancers in non-smokers. All females prior to 1970 are a reasonable surrogate for non-smokers.

All studies to date indicate a strong negative correlation between female lung cancer rates and radon exposure. Cumberland County, PA was found to have 9 times the average radon exposure, but it has well below average lung cancer rates. A similar situation is reported for a large area in Finland, and a comparison between two well-matched areas of China gives even stronger evidence. All large areas known to have high radon exposure have below average lung cancer rates (e.g. Eastern PA, Eastern North Dakota, Sweden, Finland) and in all high lung cancer rate areas where radon levels have been studied, they have been found to be below average (e.g. England, San Francisco area, New York City area).

Measurements are now in progress to determine radon levels in all U.S. counties in various population ranges with very high and very low lung cancer rates. If the latter are found to have consistently higher radon levels than the former, this would give strong evidence for hormesis.

A REVIEW OF CERTAIN LOW LEVEL IONIZING RADIATION STUDIES IN MICE FROM THE STANDPOINTS OF LIFESPAN AND TUMOR DEVELOPMENT.

C. C. Congdon (Department of Medical Biology, University of Tennessee College of Medicine, Knoxville, TN 37920)

Lorenz and his collaborators at the National Cancer Institute and the Argonne National Laboratory during the 1940's et seq. examined lifespan and other effects of low level chronic gamma ray exposures. Their rationale was to study the 0.1R per day permissible exposure level for man of that era. The experiments were performed on mice, guinea pigs, and rabbits. Primary results were published in 1950 and in 1954.

A most striking effect in male mice at exposures of .11R through 4.4R per 8 hour day was the body weight increase averaging 15 grams above control values. On a repeat experiment the increase was due to fat accumulation. Guinea pigs also showed the weight increase at the lower exposure levels. This body weight effect was greatest at 1.1R.

Enough data now exists to support the same type of conclusion by Luckey (Health Physics 43: 771-789, 1982) - "The results of many studies ... are consistent with the viewpoint that the increased average life span noted in lightly irradiated animals appears to be due to the prevention of premature mortality rather than to unusually old individuals". The details and intimate mechanisms of lessened premature mortality and therefore the issue for further study.

BIOCHEMICAL MECHANISMS INVOLVED IN THE STIMULATING EFFECT INDUCED BY VERY LOW DOSES OF GAMMA RADIATIONS ON CELL PROLIFERATION.

Annie CONTER, Françoise CROUTE and Hubert PLANEL. Laboratoire de Biologie Cellulaire, Faculté de Médecine, 37 allées Jules Guesde, 31 000 Toulouse (France).

In order to explain the mechanism of effect of very low doses on cell proliferation, we can assume that radiations can affect the pathways involved in detoxication of peroxides created by cell metabolisms. In Cyanobacteria, peroxides are generated under photooxidative circumstances and induce a higher activity of protective enzymes. In good agreement with this assumption, the most obvious stimulating effect appears in starting cultures with a high level of glutathione reductase and superoxide dismutase. Under irradiation, these enzymatic activities and the activity of glucose 6 phosphate-dehydrogenase increases leading to a stimulation of oxidative pentose pathway. Similar results were obtained in Aerobacter aerogenes and in human fibroblasts : in both cases, very low doses can stimulate cell proliferation and this effect appears only in cultures with a high level of glutathione reductase and G6DP. Furthermore, uptake of $2H^3$ deoxy-D-glucose by fibroblasts is enhanced under irradiation.

ADAPTATION OF CELL RENEWAL SYSTEMS UNDER CONTINUOUS IRRADIATION.

Jacob I. Fabrikant (Donner Laboratory, University of California, Berkeley, California, 94720)

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. Factors that determine the adaptation response involve cellular radiosensitivity, i.e., cell cycle effects, which determine the rate of cell sterilization and death, and compensatory cell proliferation and the capacity for regeneration, i.e., changes in the patterns of cell population kinetics, which determine the rate of cell birth. In rapidly dividing cell renewal systems, there is an effective elimination of damaged cells with almost complete repair of cellular nonlethal damage. In slowly dividing renewal systems, there is some repair or elimination of cellular radiation damage, and the pattern of cell proliferation during regeneration is relatively little disturbed by prior continuous irradiation. Experimental data on intestinal epithelium, hematopoietic tissues, seminiferous epithelium, and regenerating liver and kidney will be presented. Discussion includes differences in tolerance involving intracellular and extracellular control mechanisms of adaptation which regulate cellular proliferation and differentiation and, thereby, control cell population levels and physiological function. (Research support by USDOE No. DE AC03-76SF00098)

LOW DOSE, LOW LET-IRRADIATION SIMULATES INTRACELLULAR BIOCHEMICAL CONTROL MECHANISMS

L.E. Feinendegen, H. Mühlensiepen, V.P. Bond; Institute for Medicine, Nuclear Research Center Jülich, D-5170 Jülich and Brookhaven National Laboratory, Upton, N.Y. 11973/USA

Low dose gamma-irradiation, in the range in which single absorption events hit gross critical volumes, such as cell nuclei, caused, in normal DNA-synthesizing cells in the mouse, an acute temporary and partial inhibition of thymidine kinase that was dose dependent up to 1 rad, and a synchronous increase of free serum thymidine. These two effects of 1 rad were reproduced by a vitamin-E deficient diet. The partial inhibition of thymidine kinase caused by irradiation with 1 rad or a vitamin-E deficiency were restored in mice immobilized in a magnetic field of 1.4 tesla for 30 minutes. 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.

PRE-SOWING STIMULATION OF CROP SEEDS

Stanton T. Friedman (Ionizing Energy Co. of Canada Ltd.,
P.O. Box 393, Sta. A., Fredericton, New Brunswick, Canada, E3B 4Z9)

Review of an enormous amount of information mostly from Eastern Europe clearly indicates that an appropriate low dose (100-1500 rad) of ionizing energy (gamma rays or x-rays) can provide a substantial improvement in crops. The optimum dose depends on the particular type of seed, the duration of time between radiation and planting, growing conditions, the dose rate and apparently a number of other variables. Much of the work supposedly showing no beneficial effects has been done without consideration of these variables or reference to the successful testing results. Typical benefits might include: 30% increase in yield of potatoes as noted in Canadian work in 1984, a 22% increase in yield of wheat, earlier germination of corn, increased number of ears per stalk, increased vitamin C in potatoes, vitamin A in carrots, sugar in sugar beets, oil from oil seeds. Considerable effort is being made to develop commercial mobile x-ray seed stimulation systems similar to those used in Hungary where more than 10,000 acres have been planted with radiation stimulated seed, as reported at the 1984 meeting of the Working Group on Stimulation of Biological Organisms with Radiation, of the European Society for Nuclear Methods in Agriculture.

HORMETIC EFFECTS IN PHARMACOLOGY

Arthur Furst (Institute of Chemical Biology, University of San Francisco, San Francisco, CA 94117-1080)

A biologic, physiologic or biochemical response to a drug at a low dose may be completely opposite to the response of that organism to a higher dose. This observation is as old as the use of medicinal preparations and alcoholic beverages. The term pharmacological inversions, can also be used to describe this phenomenom. Inversions can be of two types, one can be related to the time following the administration of the drug or compound; the other may be a function of an increased dose.

Examples of one or another of these two types will be discussed using the following agents as examples: alcoholic beverages, anesthetic gas phenobarbital, some tranqualizers, many vitamins, caffeine, nicotine, salicylates, and some toxic metals such as arsenic and cadmium.

LIFESHORTENING EFFECTS OF CHRONIC HIGH AND LOW LET RADIATION IN BEAGLES *

Marvin Goldman

University of California

Davis, CA 95616

In a lifespan study of some 848 Beagles given bone-seeking radionuclides, the relative toxicity of ingested strontium-90 (low LET) was compared to injected radium-226 (high LET). Strontium-90 did not cause significant lifeshortening at average cumulative skeletal doses of about 25 Gy, and at higher doses the response curve was curvilinear. Normal median survival of about 14.5 years was not altered by radium-226 exposures after cumulative skeletal doses of up to 3 Gy, and at higher doses exhibited a different response function than did strontium-90. No abscopal radiation effects have been observed and almost all lifeshortening now seems to be a function of cancer induction in the tissues in and around the skeleton, i.e. only in irradiated tissues. Cancer appearance times are inversely related to radiation dose, and each cancer type followed a distinctive temporal distribution pattern.

* Supported by U.S. Dept. of Energy

POSSIBLE HUMAN HEALTH BENEFITS OF RADIATION HORMESIS

Richard J. Hickey, Richard C. Clelland (Dept. of Statistics, The Wharton School, University of Pennsylvania, Philadelphia, PA 19104); Evelyn J. Bowers, Babette S. Zemel (W.M. Krogman Center for Research in Child Growth and Development, Univ. of Pennsylvania, Philadelphia, PA 19104).

Human epidemiological data for USA and China have shown mortality rates for several cancer classifications other than leukemia to be significantly lower in areas of higher background radiation than in lower radiation areas (Health Phys. 40: 625, 1981; 44: 207, 1983). The implied benefits, if authentic, should be observed generally. Mortality rates for 48 US states, ca. 1960, vs mean background radiation levels show correlation coefficients for: cancer of respiratory organs (ICD 160-164) of $r = -0.428$ ($p < 0.01$); total cancer, $r = -0.277$ ($p < 0.10$); CVD renal diseases, $r = -0.362$ ($p < 0.05$); "white" birth rate, $r = +0.542$ ($p < 0.001$); "non-white" birth rate, $r = +0.244$ ($p < 0.10$); "white" infant mortality rate, $r = +0.335$ ($p < 0.05$); median age, $r = -0.188$ ($p > 0.10$). For leukemia for those <25 yr, $r = +0.402$ ($p < 0.01$); for those ≥ 25 yr, $r = -0.114$ ($p > 0.10$); for all ages, $r = +0.038$ ($p > 0.1$). Since low-level radiation stimulates many natural functions (T.D. Luckey, Health Phys. 43: 1, 1982), and alleviates some forms of arthritis (W.N. Hubbard et al., Brit. Med. J. 284: 1915, 1982), diabetes mortality was examined. For diabetes mortality rate for 43 urban areas vs. background radiation, $r = -0.286$ ($p < 0.10$). This suggests some benefit from radiation, and needs further investigation. Could radiation stimulate synthesis or release of insulin or neurotransmitter hormones involved in homeorhesis? Could such activities explain in part lower cancer and CVD mortality rates in higher than in lower radiation areas, and longer survival of experimental animals exposed to elevated radiation? Theoretical and speculative foundations for such epidemiological results will be discussed.

NP

BIOLOGICAL RESPONSE TO LOW DOSES OF ALPHA PARTICLES.

Werner Hofmann (Division of Biophysics, University of Salzburg, Erzabt-Klotz-Str.11, A-5020 Salzburg, Austria)

Radon therapy in radon spas, i.e. exposure to low doses of alpha particles, has been quoted frequently as a representative example of the existence of hormetic or "biopositive" effects at low doses of ionizing radiation. Because of the high LET of alpha particles cellular targets can receive doses up to some hundreds of rads, dependent on target size, thus far beyond the low dose region. Therefore, at the microscopic level, the probability for the occurrence of hormetic effects in cellular targets is extremely small.If we adopt, however, a system's analysis point of view, i.e. consider the system "stem cells-differentiated cells" as a macroscopic control system, then the reproductive death of a single cell can stimulate the mitotic activity of the stem cell pool. This may lead either to "positive" reactions, e.g. repopulation of tissues or stimulation of the immune system, or to "negative" reactions, such as tumor promotion. Thus there exists a strong correlation between concurrent beneficial and harmful radiation effects at the macroscopic level, having presumably different time patterns. The interference of other environmental factors in radon spas, however, makes it nearly impossible to attribute unequivocally the observed beneficial effects to radiation alone.

A DOSE RESPONSE AMONG A-BOMB SURVIVORS EXPOSED TO LOW LEVEL RADIATION.

Hiroo Kato (Radiation Effects Research Foundation (RERF), 5-2 Hijiyama Park, Minami Ward, Hiroshima City 730, Japan), William J. Schull (Center for Demographic & Population Genetics, University of Texas, Health Science Center, P.O. Box 20334, Houston, Texas 77225), Akio Awa (RERF), Mitoshi Akiyama (RERF) and Masanori Otake (RERF)

A long term cohort follow-up study of approximately 110,000 A-bomb survivors and controls has been carried out by the Atomic Bomb Casualty Commission (ABCC) and its successor, the Radiation Effects Research Foundation (RERF). Among A-bomb survivors exposed to 1 rad or more, a majority (79%) numbering 38,000 were exposed to less than 50 rads. Thus examination of the dose responses for radiation effects among those exposed to low dose levels should provide a fairly good chance to detect phenomena of radiation hormesis if it is present. The dose responses, within the low dose range, for cancer incidence, frequency of chromosomal aberrations, measures of immune response, and frequency of mental retardation among children exposed in-utero were investigated. 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.

NP — No Presentation - author unable to attend conference.

INCREASED FERTILITY OBSERVED IN MALE MICE EXPOSED TO LOW DOSES OF IONIZING RADIATION IN A REGION OF HIGH NATURAL RADIOACTIVITY

A. Léonard[1,2], M. Delpoux[3], R. Meyer[1], G. Decat[1] and E.D. Léonard[2]
[1] Laboratory of Mammalian Genetics, Department of Radiobiology, CEN/SCK, B-2400 Mol, Belgium ; [2] Catholic University of Louvain, Belgium ; [3] Paul Sabatier University, Toulouse, France

Three month old male mice of the BALB/c strain have been maintained on the floor of a hut built at a site of the Southwest France where the dose rate of γ radiation amount to about 10 mrad/h. Due to the sensitivity of the mice to low temperatures, the exposure was restricted to the summer period and was repeated with new animals during three successive years.

The first year, the animals received 13 rad, the second year 15 rad and the third year 45 to 63 rad. After the exposure the animals were mated in laboratory. The fertility of the males exposed to 13 rad, 15 rad or 45 rad was increased above the control values but was reduced for the animals receiving 63 rad. Since histological study of the testes suggests that the germ cell population was normal one has to conclude that the variations in fertility result from physiological effects.

RADIATION HORMESIS - ITS EXPRESSION IN THE IMMUNE SYSTEM

Shu-Zheng Liu, XH Liu, XY Li, GZ Xu (Norman Bethune Univ. of Medical Sciences, 6 Xinmin St., Changchun, Jilin, P.R. China)

The nature of health effects of low level ionizing radiation has been a problem of considerable controversy. Epidemiologic survey in an area of high natural radioactivity in Guangtong, China disclosed a lower cancer mortality rate in comparison with a matched control population. At the same time immunologic studies of the inhabitants showed an increased reactivity of T lymphocytes in response to PHA. There was also an increase in the percentage of B cells. The percentage of T_γ cells (suppressor T cells) was not changed, but there was a tendency towards increase in unscheduled DNA synthesis in the lymphocytes. Small doses of whole-body irradiation (WBI) in the range of 2.5-7.5 rad showed a stimulatory effect on the PFC of the spleen in white mice (50% increase) and in C57BL/6 mice (100% increase). At the same time the reactivity of thymocytes to interleukin 1 was increased in the same dose range, but there were no significant changes in the reactivity of splenocytes to interleukin 2. A study of the effects of small doses on NK cells and the effects of continuous low-level radiation on various aspects of the lymphokine cascade is underway. It is suggested from the present investigation that small doses of ionizing radation 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.

IONIZING RADIATION IS ESSENTIAL FOR OPTIMAL MICROBIC GROWTH RATES

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Endogenous ionizing radiation was eliminated by culturing microbes in chemically defined media with no added radionuclides. Exogenous radiation was decreased ten fold in the RER vault at Argonne (ANL). E. coli showed decreased growth rates in medium with ^{39}KCl when compared with natural (N) KCl in either ambient (A) or subambient (S) radiation environments. This was caused by a toxicant in Oak Ridge (OR) ^{39}KCl. With either heat treated OR ^{39}KCl or USSI ^{39}KCl in the medium, growth rates were comparable with that of ^{N}KCl in either A or S environments.

Preliminary experiments at UMC and in literature showed that protozoa grew at rates which were slower in S than in A. At ANL growth rates of Tetrahymena pyriformis were comparable with either ^{39}KCl or ^{N}KCl in the A incubator; in the S incubator growth rates were consistently less with USSI ^{39}KCl than with ^{N}KCl in the medium. Growth rates with USSI ^{39}KCl in the ANL-S incubator were clearly proportional to the amount of radiation from a ^{137}Cs source.

In an A incubator at UMC Reactor, with ^{N}KCl, the optimum amount of radiation from a ^{60}Co source was determined for an alga, a photosynthetic bacterium, and a nonphotosynthetic bacterium. Surprisingly, the optimum rate of continuous radiation was about 10 rads/hr for each species.

The composite of these results suggests that ionizing radiation is essential for optimal performance in modern organisms. Perhaps vestigeal systems remain from the first organisms which lived when clouds and volcanic ash occluded sunlight and ionizing radiation was about10 times greater than now.

RADIATION HORMESIS MAY BE NURTURE BY IONIZING RADIATION

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The general nature of hormesis distinguishes this phenomenon from nurture, in which specific agents evoke specific responses. Growth is stimulated by many agents: radiation, electric current, antibiotics, dyes, or heavy metals. The results are not additive unless one of the agents is essential. The J dose-response curve, or its $\curvearrowleft$ inverse used in physiology, does not distinguish between a hormetin and an essential agent, such as vitamin A or Fe. The direction of the curve below ambient levels is important. There is no effect from withdrawal of the hormetin, the curve is horizontal. A deficiency develops following withdrawal of the essential agent, the curve becomes negative. A third possibility is that all quantities of the agent produce harm; then withdrawal would produce beneficial effects, i.e., reduced radiation, below ambient levels, would lead to less cancer, morbidity and mortality.

Recent experiments indicate that ionizing radiation is essential for optimal microbic growth rates which decrease when radiation is below ambient levels. Thus, the complete dose-response curve is a parabola with the general formula of $X = Y^2$. Conformation of these results with human cell cultures, the experiments are presently in progress, would profoundly affect current concepts. Then the evidence for radiation hormesis could be interpreted as providing optimal doses or levels of ionizing radiation as an essential agent. Attempts to reduce ambient levels of ionizing radiation for most populations would be counterproductive for any persons or agencies concerned with optimal health. Indeed, methods to safely increase ambient levels of ionizing radiation need to be examined within this decade.

HORMESIS OF ALPHA RADIATION AND ITS ROLE IN CANCER AND AGING

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Alpha particles are exceptionally effective in killing cells. Goldman (1976) posed the question, "If alpha particles are so efficient at killing cells whose nucleus they traverse, why is such radiation so effective a carcinogen?" This dilemma can be resolved if, in the multistage process of cancer induction, the role of alpha radiation is that of cancer promotion by killing cells (Martell, 1983). Radiation-induced tumors arise focally in small tissue volumes, and it is likely that there is a threshold dose for this process. In view of these and other considerations, current dosimetry models for lung cancer induction by radon progeny have serious shortcomings, and radon decay products at natural levels and in soluble chemical form make only a minor contribution to human cancer.

There are possible salutary effects of natural alpha radiation exposure, which contributes to the mitotic activity of cells and to the elimination of damaged cells. However, reduced exposure to inhaled and ingested alpha emitters should give rise to an increase in life span. In aging as well as in malignancy the breakdown takes place in small tissue volumes--effects not due to natural alpha radiation exposure alone.

Goldman, M., 1976, "An overview of high LET radiation effects in cells", The Health Effects of Plutonium and Radium, W.S.S. Jee, Ed., J.W. Press, Salt Lake City, 751.

Martell, E.A., 1983, "Bronchial cancer induction by alpha radiation: A new hypothesis", Proc. 7th Int. Cong. Radiat. Res., Amsterdam, July 3-8, Paper C6-11.

IS THERE A PROTECTIVE EFFECT FROM RADIATION IN RADIOLOGISTS?

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The observed effect of radiation in radiologists practicing during the early years of this century is an increased risk of cancer mortality. However, an examination of the changes in the shape of the age-specific mortality curve for entrants into the specialty after 1940 suggests that this group exposed to lower doses of radiation may actually start in their early ages with risks which are below those of other physician specialists. Eventually their preferred mortality experience is erased and their rates are higher than those of other groups. Some of this effect is due to a reduced cancer risk in younger ages with a sharp increase in rates after age 50. Several possible explanations for this observation will be suggested.

CANCER INCIDENCE vs. α-PARTICLE DOSE*

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Dose-response relationships will be presented on cancer incidence vs. α-particle dose in mice, rats and beagles. The usual response seemed approximately linear between lifetime incidences of 0 and 30% for bone sarcomas induced by α-particles. In beagles that developed bone sarcomas after ^{239}Pu injection, the lowest average skeletal dose was only 2 rads. The possibility of a threshold below 2 rads was not investigated.

In humans exposed to α-emitters, the dose-response seems approximately linear for liver cancers in the Thorotrast patients, lung cancers in the Uranium miners, and head-sinus carcinomas (but not bone sarcomas) in the Radium dial workers. However, a shallow linear component to the bone-sarcoma response in the Radium dial workers cannot presently be excluded.

Supported by DOE contract DE-AC02-76EV-00119.

RADIATION HORMESIS IN PLANTS

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There is a large number of reports of stimulation of plant growth by exposure of seeds or plants to low doses of ionizing radiation. The reported effects include increased height, weight, growth, flowering and yield. The magnitude of the effect(s) is usually small, being about ± 10% of control values and the effect is often not reproducible. None has been independently confirmed. The level of exposure reported to induce such effects is about an order of magnitude greater than that reported for similar hormetic responses in animals. There is no understanding of the mechanism(s) of such increased responses or of the physical factor(s) pertinent to induction of the effect(s).

THEORETICAL PHYSIOLOGICAL BASIS FOR RADIATION HORMESIS

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ABSTRACT-- Excitation and ionization of DNA by X and gamma radiation is known to degrade its structural integrity. The demonstrated higher susceptibility of the Adenine-Thymine nitrogenous base pairs to damage by ionizing radiation is postulated to play an important role in the initiation of the apparent hormetic effect of low level radiation exposure. The promoter and operator regions of specific regulatory gene loci exhibit a very high incidence of Adenine-Thymine base pairs compared to the Guanine-Cytosine base pair configuration. There is evidence that radiation induced damage to these loci stimulate the derepression of regulatory genes involved in the repair and synthesis of DNA. There is also evidence to suggest that this mechanism is capable of allowing the cell to bypass regulatory controls. Expression of these derepressed genes may provide a substantial survival advantage over control group cells when subsequently exposed to higher levels of ionizing radiation. Active and passive control mechanisms of genetic damage are discussed with regard to the induction of adaptative advantages associated with isozyme production.

OBSERVATIONS OF PLANT AND ANIMAL STIMULATION RESULTING FROM NUCLEAR DETONATIONS.

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An engineer's review of unusual effects of nuclear weapon tests relating to stimulation by detonations at the Nevada Test Site and the Pacific Proving Grounds from 1953 to 1961. Observations were stimulation of desert plants around detonation sites, stimulation of tropical vegetation near ground zero, shellfish, rodent, and test animals near ground zero and their survival years after initial acute and chronic exposures.

CRITICAL VALUES OF LET, DOSE RATES, AND DOSES FOR RADIATION HORMESIS

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The existence of radiation hormesis is still in doubt, but it would be worth while continuing further research. In this note a certain kind of clue for such research is suggested.

Critical values of LET, dose rates and doses, below which radiation hormesis might occur but above which it is rather unlikely, are discussed. Comparison of α and β activities, such as ^{226}Ra and ^{90}Sr, would be very interesting. For plants and in dry conditions, such as seeds or bulbs, critical dose rates may be much higher.

Although the argument in this note is highly speculative and the results should therefore be regarded as very tentative, there still seems to be a certain type of systematics among the experimental data which may possibly account for the observations.

EVIDENCE THAT CELL PROLIFERATION IS INFLUENCED BY BACKGROUND RADIATION OR EXPOSURE TO VERY LOW GAMMA CHRONIC RADIATIONS.

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Investigations performed in our laboratory have shown that background radiation or a chronic irradiation given at a very low dose rate can stimulate the proliferation of a single cell organism, Paramecium tetraurelia; same effect was observed in the blue alga, Synechococcus lividus. For background radiation, telluric radioactivity and cosmic rays are both involved in this biological effect, as it was demonstrated by experiments carried out on earth, in an underground laboratory, in air-borne balloon flights or in space. Changes in growth rate depends of external and internal factors. Furthermore this cellular effect is limited to very low doses, that suggests an adaptation of living organisms to background radiations, i.e., to a natural environmental factor. Results of previous investigations carried out on Synechococcus will be discussed.

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LOW-LEVEL ALPHA-RADIATION DOSE EFFECTS ON PERIPHERAL BLOOD CHROMOSOMES

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Rn 222 and its decay products are always present in the human environment. Besides the known health hazard of these radionuclides there is also a beneficial effect suggested e.g. in radon spas. In our former investigations on chromosome aberration in blood lymphocytes of people exposed to elevated levels of radon in the atmosphere the dose response curve was not linear but showed a plateau. This effect is most probable due to repair mechanisms triggered by the low-level α-irradiation. This result could be supported by large scale in vitro investigations which hithertoo were carried out only with X-rays and neutrons because of many difficulties using α-irradiation.
We developed a method to irradiate peripheral blood in vitro with a defined amount of short-lived radon daughters. RPMI-Medium was loaded with Rn 222. After eliminating the gaseous radon and measuring the activity of the remaining decay products this medium was added to the blood cultures. Such the lymphocytes were irradiated very homogeneously during the decay of the radon daughters and the accumulated dose could be calculated. This method does not cause any chemical toxic effect from the α-source.
First results of dose response archived by this method will be given and the necessity of a larger study in cooperation with other institutes will be discussed.

WHAT IS HORMESIS AND WHY HAVEN'T WE HEARD ABOUT THIS BEFORE?

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Low doses of ionizing radiation are widely believed to produce effects similar to those observed at high doses; only the incidence (i.e, risk) varies with dose. Furthermore, it is assumed, effects other than those observed at high doses will not occur at low doses. Yet, there have been frequent reports in the literature of "anomalies" at low doses - effects unrelated to toxic effects of high dose exposures. These have been referred to as "hormetic" effects.

It is postulated that hormesis has previously received but scant scientific attention because it conflicts with the conventional paradigm of radiation science and protection.

NP — No Presentation - author unable to attend conference.

FACTORS CONTROLLING THE HORMESIS RESPONSE FROM IRRADIATED SEED.

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Ionizing radiation at very low doses frequently has a stimulatory effect on the growth of organisms. Irradiation of seed prior to planting can stimulate early plant growth, leading to advanced maturity and increased yield of some economic plant species. This technique has received a great deal of research and is now practiced on a large scale in some countries. The unreliability of the response has limited its application. Our research addressed various factors that determine the stimulation response with the goal of developing an ability to predict the occurrence of increased economic yield. Wheat seed (Triticum aestivum) was irradiated at a range of doses (0.5 to 50 Gy exclusive of controls) and grown under growth chamber or field conditions. Radiation from X-rays, ^{192}Ir, ^{137}Cs or ^{60}Co was used to give ranges of photon energy and dose rate. Other experimental factors were seed moisture content, cultivar, various seed-lot characteristics within each cultivar, and post-planting conditions. In several cases plants from irradiated seed emerged more quickly and yielded more than controls. However, there was no consistent relationship between these occurrences and the experimental factors. The prospect of developing the hormesis phenomenon to a predictable technique is discussed.

RADIATION-INDUCED STIMULATION EFFECTS IN LIVING ORGANISMS--Dr. J. Simon, Budapest, Hungary

During the past 30 to 40 years, data and reports showing the increased effects of low-radiation dose-treatments in agricultural production have been announced. The expression, "radiostimulation", originates from Breslavets, 1946, who meant by it the positive biological effects of radiation. These effects may manifest themselves in many ways: in better and quicker germination by sowing seeds; more rapid initial growth; greater yield of green-mass or seedstocks; a richer yield in certain components; in earlier harvest time; increase in resistance to different diseases; and, in general, an increase in vigor.

It is, however, a determinant criterion that the effect is not inherited, but occasionally traceable in the next generation, although to a much lesser degree. It is a completely physiological phenomenon on a very sensitive level. Researchers are in agreement that stimulative effect is modified by several primary and some secondary factors. The following may be considered as primary factors: radiation sensitivity of the organisms; character of radiation--radiation source; dose and dose rate applied, etc. Secondary factors are time of sowing and breeding after irradiation; moisture content; and condition of storage of seeds, etc. The paper will give a short review about the existing hypotheses and explanations of the controlled effects and the mechanism. It also will give a summary of the present practical applications of the industrial-sized machines--mainly mobile units--for the practical stimulation technique in agriculture, especially plant and animal breeding and production. A brief report of the aims and activities of ESNA (European Society of Nuclear Methods in Agriculture) will be included.

THE PHYSIOLOGY OF THE HORMETIC EFFECT

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Comparison of the results of experiments in which animals received protracted low-level gamma ray or x-ray exposure with those in which food was restricted reveal a similar outcome with respect to the slope of the survival curve. This suggests that a mechanism common to both procedures must operate to affect the life-span. It is suggested that the proper exposure to ionizing radiation affects the mechanism controlling the animal's voluntary food intake resulting in a reduction with results on the animal's physiology similar to an involuntary food restriction. The variance in life span exhibited in a survival curve undoubtedly arises from the processes of natural selection and the response to restricted food intake appears to be an adaptation to a lower level of food supply.

EPISTOMOLOGICAL PROBLEMS AT ASSESSMENTS OF CANCERRISKS AT LOW RADIATION DOSES.

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A non-dominant radiation dose may be defined as one, the biological effects of which does not differ from those of other "normally" occurring milieufactors or living conditions. From this definition it can be shown that it is principally impossible to achieve any knowledge of the biological effects, beneficial or not, on an individual or a population exposed to non-dominant radiation doses.

A corollary of this conclusion is, that it is not possible to substitute one conceptual entity (e.g. a biological high-dose effect) by another (mathematics) and achieve a knowledge of a low-dose effect by interpolating the latter to zero. The common requirement that the interpolated formula should be a polynomial, and the discussions whether it should be of the first or second degree is thus nothing but a scientific collapse.

Examples can easily be given on mechanisms by which low radiation doses may counteract or enhance carcinogenic processes.

GROWTH HORMESIS - A BIPRODUCT OF CONTROL

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The stimulatory effect of low levels of a toxicant on biological growth is a commonly observed phenomenon for a wide range of toxicants, and examples are known from every phylum. We have attempted to find an explanation for hormesis in a series of experiments spanning 10 years, involving two unrelated organisms (the colonial hydra Laomedea and the marine yeast Rhodotorula). Our approach has been to consider in a novel way the growth kinetics of these organisms exposed to subinhibitory concentrations of toxic agents, and to corroborate interpretations using simulation models. Our work suggests that growth hormesis is not a specific effect of any toxic agent, but rather a response to the growth inhibitory properties that at higher levels they all share. Growth stimulation is apparently due to a tendency of rate-sensitive growth control mechanisms to over correct to low levels of inhibitory loading.

EFFECTS OF EXPOSURE TO PLUTONIUM AND LOW-LEVEL EXTERNAL RADIATION ON LUNG CANCER RATES

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The National Plutonium Workers Study is concerned with studying workers at Los Alamos National Laboratory, Rocky Flats Plant, and Mound Laboratory who were exposed to plutonium and other forms of radiation. The purpose of the study is to measure adverse health effects, if any, which might arise from exposure. Most exposures occur from inhalation of highly insoluble forms of plutonium oxide, and from animal studies, lung cancer is the most likely outcome. To date, the studies have shown that lung cancer mortality among highly exposed persons is surprisingly low, often significantly lower than national averages. Other types of cancer will also be discussed.

THE TRITIATED-THYMIDINE-INDUCED ADAPTIVE RESPONSE OF HUMAN LYMPHOCYTES TO SUBSEQUENT DOSES OF X RAYS.

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When human lymphocytes are exposed to tritiated thymidine ([^{3}H]dThd), which acts as a source of chronic radiation, the cells become refractory to subsequent doses of X rays. That is, if the cells are X-irradiated at about 46 hrs of culture to induce chromatid breaks observed at 53 hrs in culture, those cells that have incorporated [^{3}H]dThd (which by itself induces chromatid breaks) have fewer aberrations than are produced by X rays alone. This effect is not an artifact caused by delays in progression of irradiated cells to metaphase, nor of selection against cells that have incorporated [^{3}H]dThd. It is suspected that this adaptive response is related to a hitherto undiscovered radiation-induced repair mechanism that depends upon poly(ADP-ribosyl)ation. Inhibition of poly(ADP-ribose) polymerase, which is thought to be necessary for the repair of DNA strand breaks, reverses the adaptive response. This is the first time that such a phenomenon has been found for ionizing radiation.

Work supported by the United States Department of Energy Contract No. DE-AC03-76-SF01012.