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Environmental Mutagen Society
Risk of Low Dose/Low Dose Rate Ionizing Radiation to Humans Symposium
37th Annual Meeting
Genetic and Environmentally Induced Genotoxicity: Causes and Impact
September 16-20, 2006
Hyatt Regency Vancouver
British Columbia, Canada

Final Report, Agenda and Abstracts
November 11, 2009

The low dose symposium thoughtfully addressed controversy of risk from low dose radiation exposure, hormesis and radon therapy. The stem cell symposium cogently considered the role of DNA damage and repair in hematopoietic stem cells underlying aging and malignancy and provocatively presented evidence that stem cells may have distinct morphologies and replicative properties, as well as special roles in cancer initiation. In the epigenetics symposium, studies illustrated the long range interaction of epigenetic mechanisms, the roles of CTCF and BORIS in region/specific regulation of epigenetic processes, the impact of DNA damage on epigenetic processes as well as links between epigenetic mechanisms and early nutrition and bystander effects.

Sunday September 17, 2006

2:00 PM–4:50 PM Risk of Low Dose/Low Dose Rate Ionizing Radiation to Humans Symposium Chairpersons: William F. Morgan, University of Maryland and Jeffrey L. Schwartz, University of Washington

2:00 PM–2:20 PM	An Introduction to Low Dose Radiation Effects *Speaker: William F. Morgan, University of Maryland*
2:20 PM–2:30 PM	The Spontaneous Mutation Rate is the Apparent Threshold for Ionizing Radiation *Speaker: Robert C. von Borstel, University of Alberta*
2:30 PM–3:00 PM	Cancer Risks at Very Low Dose: Why Did the U.S. and French National Academics Come to Directly Opposite Conclusions? *Speaker: David J. Brenner, Columbia University*
3:00 PM–3:20 PM	BREAK
3:20 PM–3:50 PM	Radiation–Induced Neoplastic Transformation *In Vitro*, Hormesis and Risk Assessment *Speaker: J. Leslie Redpath, University of California—Irvine*
3:50 PM–4:20 PM	Toxin or Medicine? Radon Therapy in the U.S. and Europe *Speaker: Barbra E. Erickson, California State University*
4:20 PM–4:50 PM	Response to Low Dose Radiation: Impact on the Dose–Response Curve *Speaker: Antone L. Brooks, Washington State University*

An Introduction to Low Dose Radiation Effects. Morgan, WF. University of Maryland School of Medicine, Baltimore, MD, United States.

While the health risks associated with high dose exposures to ionizing radiation are well established and irrefutable, the potential risks of low dose, low dose rate exposures are controversial and the subject of intense debate. A panel of experts convened by the US Academy of Science recently reviewed the literature in this area and in their BIER VII report concluded that all radiation exposure is potentially associated with some risk, albeit at very low doses a very small risk. They recommended that a linear non-threshold extrapolation from high doses, where there is consensus between radiation exposure and associated health effects, to low dose was prudent. At almost the same time another panel of experts assembled by the French Academy of Science reviewed what is presumably the same data and concluded that there could well be a threshold for radiation induced health effects at very low doses. The goal of this symposium is to bring together investigators to address current issues in low dose radiation research and how these might impact on human health risks for radiation induced cancer and hereditary effects.

The Spontaneous Mutation Rate is the Apparent Threshold for Ionizing Radiation. von Borstel, RC. University of Alberta, Edmonton, AB, Canada.

The induction of cancer by ionizing radiation is most often an exponential increased incidence of cancer in relation to the amount of exposure (cf. Brenner et al., 2003). An argument has been made by the National Academy of Science Committee commentary, that available biological and biophysical data supports a "linear, no-threshold" risk model, which says that the smallest dose of low-level ionizing radiation has the potential to cause an increase in health risks to humans. (BEIR VII-Phase 2, 2006). The assumption is made that extrapolation of an exponential curve to zero exposure will have an effect at any point on extrapolation above zero. It is impossible for an expression of exponentially accumulated data to go through zero on a log-log plot. Thus the “apparent threshold” can be considered as the spontaneous mutation level for spontaneous cancers. On a log-log plot, the exponential line can be extrapolated to the background radiation level, with Drosophila sperm, for example, extrapolating for 5 decades below the spontaneous rate. This indicates that the spontaneous lethal mutations in the X-chromosome, induced by background radiation, is about 1 radiation-induced mutation in 100,000 spontaneous mutations. There are no DNA repair mechanisms in Drosophila sperm. For human cancer, with background radiation of 3.6 mGys/yr, extrapolation of the linear component of dose-action data suggests that the background radiation might induce about 2 to 5% of all cancers over a lifetime. This assumes DNA repair mechanisms are functional.

Cancer Risks at Very Low Doses: Why did the US and French National Academies Come to Directly Opposite Conclusions? Brenner, DJ. Columbia University, New York, NY, United States.

In 2005, both the US and French National Academies published learned reports on the cancer risks associated with low doses of ionizing radiation. The US report, BEIR-VII, concluded that “*A comprehensive review of available biological and biophysical data led the committee to conclude that the risk would continue in a linear fashion at lower doses without a threshold and that the smallest dose has the potential to cause a small increase in risk to humans*”. By contrast, the French Academy report concluded that “*At low doses and low dose rates of ionizing radiation, the pro-apoptotic effect dominates and the damaged cells, of which there are only a few, can be eliminated or controlled*”. Two very different views of the effects of very low doses of radiation. We will discuss how and why these two bodies came to such opposite conclusions, and reassess what we do and don't know about cancer risks at very low radiation doses.

Radiation-Induced Neoplastic Transformation *In Vitro*, Hormesis and Risk Assessment. Redpath, JL. University of California Irvine, Irvine, CA, United States.

Introduction: The shape of the dose-response curve for the cancer-relevant endpoint of neoplastic transformation *in vitro* has been explored for low-LET radiation in an attempt to gain insight into radiation risks at low doses (<100 mGy). Methods: The HeLa x skin fibroblast neoplastic transformation assay system has been used along with following high dose-rate low-LET radiation sources – Cs-137 gamma rays, 60 kVp x-rays, 28 kVp x-rays, 232 MeV protons – as well as low dose-rate photons from I-125 decay. Results: At intermediate to high dose-rates, all low-LET radiation sources demonstrated a J-shaped dose-response curve with evidence for a threshold dose in the range 100-200 mGy. At lower dose-rates of 1 and 2 mGy/min there was evidence for a similar threshold but at higher doses the induction curve was 1.5x less steep than at the intermediate to high dose-rates. At the very low dose-rates of 0.2 and 0.5 mGy/min there was no induction, and evidence for possible suppression, up to 1000 mGy, the highest dose that was examined. Mechanistic studies imply a role for upregulation of DNA repair, as well as hyper-radiosensitivity of a transformation-prone subpopulation, in the apparent hormetic response at low doses. Discussion: It is apparent from these studies with this assay system that J-shaped dose-response curves for low-LET radiation exposure are possible. This suppressive (hormetic) effect of low doses (<100 mGy) to levels below those seen spontaneously has been seen in other *in vitro*, as well as *in vivo*, assays. The implications of this are that low doses of low-LET radiation may be beneficial, a conclusion that does not support the linear no threshold model currently utilized by regulatory agencies. Epidemiologic studies on human subjects do not have the statistical power to demonstrate such a hormetic effect at low doses of low-LET radiation, however neither do they have the power to rule it out, at least for certain cancers such as leukaemia and breast cancer.

Toxin or Medicine? Radon Therapy in the U.S. and Europe. Erickson, BE. California State University, Fullerton, CA, United States.

There is a growing recognition in the United States and Europe that health care is driven to a significant extent by consumer choice and demand. As consumers, many people favour pluralistic health care that includes a variety of choices in addition to mainstream conventional medicine. This paper examines one such alternative: radioactive radon therapy, a treatment considered dangerous by the Environmental Protection Agency (EPA) and one that is not supported by conventional American biomedical standards. Radon is believed by its proponents to have analgesic and anti-inflammatory properties, and it is used to treat a wide variety of conditions, including arthritis, rheumatism, fibromyalgia, psoriasis, asthma, and bronchitis. In the United States radon therapy is available only in four old mines located in south western Montana, where people self-treat without medical supervision. In Europe, however, radon therapy is offered at selected clinics and spas in the form of inhalation, bath or steam, usually under the supervision of a medical doctor. This paper is based upon my research in Montana radon health mines during the years 1997 through 2005, and two visits to European radon health facilities made in 2000 and 2001. Data at the Montana mines were collected through open-ended ethnographic interviews with 64 mine clients, and from 294 questionnaires. Informants were primarily arthritis sufferers using radon to alleviate their pain and symptoms. Data at the European facilities were gathered through interviews with medical personnel. In this paper I compare radon health mine facilities in Montana with selected radon mines and spas in Europe. I discuss the decision-making process by which ill people choose to use radon, and describe how radon is conceptualized as both a toxic and medicinal substance.

Response to Low Dose Radiation: Impact on the Shape of the Dose-Response Curve. Brooks, AL. Washington State University Tri-Cities, Richland, WA, United States.

Extensive research has been conducted over the past ten years to determine the interactions between low doses of radiation (below 0.1 Gy) and biological systems. Many new biological phenomena have been observed. These include adaptive responses, bystander effects, genomic instability and changes in gene and protein expression. Using modern cellular and molecular techniques, the mechanisms behind these observations are being investigated. With this understanding, the impact of these unique responses in the low dose region on the shape of the dose-response curve can be identified and the implications on the extrapolation of radiation risk from the high to low dose regions clarified. It has been demonstrated that unique genes are activated following low doses of radiation, suggesting unique biological responses. Cells and tissues that demonstrate an adaptive or protective response following low dose exposures have unique repair and stress genes up regulated. Identification of these genes is provide a scientific basis for constructing metabolic pathways and determining mechanisms of action. Low dose activation of protective mechanisms suggests the existence of non-linear dose-response relationships for low-LET radiation. Bystander effects have been demonstrated using microbeams. It is possible to identify the cells that are “hit” by ionizing radiation and to measure the biological effects in both “hit” and “non-hit” cells. This impacts the “hit-theory” since non-hit cells show biological responses and requires new paradigms be adapted that run counter to the current linear biophysical models of radiation response. Tissue responds as a whole and not as the sum of the number of cells hit. Genomic instability suggests frequent radiation-induced changes following radiation, not rare mutational events, which challenge the mutation theory of cancer. Such data demonstrate that the initial DNA damage may be linearly related to the radiation dose but that the biological processing of this damage and the cellular and organ responses are very non-linear over biologically important doses. Current biophysical models that suggest that a single ionization interacts with a single cell and resulting in a mutation that then produces an increase risk for cancer must be discarded since the LNTH does not fit the data. Research Supported by Office of Science (BER), U.S. Department of Energy through Grant No. DE-FG02-99ER62787 to Washington State University Tri-Cities.