

Summary of and Comments on ICRP Committee 1 Task Group Report "Low-dose Extrapolation of Radiation-Related Cancer Risk" December 2004

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ICRP Task Group's Purposes of the Report

- To consider evidence relating to cancer risk at low LET (Linear Energy Transfer) radiation doses at levels below current exposure standards (US public 100 mrem/yr; occupational 5000 mrem/yr)
- To focus on dose-response linearity for all cancers as a group, not individually
 - Reconfirm LNT (Linear No-Threshold hypothesis of [radiation] dose-response) and extrapolate from it.
- Conclude it is unlikely a "universal safe threshold" dose level will be found (though note, with scientists' conservatism, that some specific instances of a "safe threshold" may exist)
- Support continued use of modeling and risk assessment in radiation standards setting (We do not.)

Chapter 2 reviews Epidemiological Studies. Epidemiology identifies spatial correlations between patterns of cancer incidence (or other disorders) in a population and the presence of a radiation source, but does not address the causative biological processes and mechanisms of the radiation impact(s) at cellular, molecular, or DNA levels. Hence, it may show relationships but its explanatory power is limited.

The focus is on (a) Hiroshima/Nagasaki Life Span Study (LSS), establishing a dose-related risk among A-bomb survivors; (b) modeling of dose-related rad risk; (c) extrapolation of estimated risk to other potentially exposed populations; (c) projection of the risk to end of life; and (e) extrapolation of risk estimates downward, from the bomb survivors' moderate-to-high doses to the more common situations of low dose and protracted doses that may actually be experienced by workers and public.

The report finds that risk of mortality/morbidity from all solid cancers is proportional to dose down to c.100 milliGray, which equals 10 rads, and which may not be considered a "low" dose). At the lower doses, cancer risk is termed "obscure" by ICRP, due to many confounding factors. A negative [and to us disappointing] conclusion of this Report is the conclusion that use of extrapolation will be continued by ICRP for estimation of radiation risks at lower dose levels, including at 1mGy/yr (100millirad/yr) from non-medical, man-made sources.

Chapter 3 reviews Low-dose Risk Biology. The framework for risk analysis lies in the fundamental role of radiation-induced DNA damage in inducing mutations and chromosome aberrations, and their critical involvement in the pathogenesis of cancer. Radiation damage characteristically involves multiple lesions within close spatial proximity. "Such clustered damage can be induced even by a single radiation track through a cell." [Page 10, lines 17-18] [How, then, we may ask, can it be claimed that there is a "safe threshold dose"?)

The Report states that, despite "a vast array of damage response mechanisms that facilitate the repair of DNA damage and removal of damaged cells, these mechanisms are not fool-proof. Moreover, clustered radiation-induced lesions pose a particular problem and current emerging evidence suggests that closely spaced lesions" can compromise the repair machinery. On this basis, there is not any strong evidence for a radiation dose below which all radiation-induced damage can be repaired with fidelity. Whilst many of the cells containing such radiation-induced damage may be eliminated by damage

response pathways involving cell cycle checkpoint control and apoptotic pathways, it is clear from analysis of cytogenetics and mutagenesis that damaged or altered cells are capable of escaping these pathways and propagating." This further argues against the likely possibility of a threshold for radiation-induced cellular effects." (p.81 lines 22-32)

Chapter 4 addresses Cellular Consequences of Radiation-induced Damage, including chromosome aberrations, and somatic cell mutations. "The processing and mis-repair of radiation-induced double strand breaks (DSBs), particularly complex forms, are responsible for chromosome/gene alterations that manifest as chromosome aberrations and mutations. Current understanding of mechanisms and quantitative data on dose and time-dose relationships support a linear dose response at low doses (LNT) for total cancer risk." (Page 10, lines 26-31)

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Further, the authors conclude, "... the emerging results with regard to radiation-related adaptive response, genomic instability, and bystander effects suggest that the risk of low level exposure to ionizing radiation is uncertain, and a simple extrapolation from high dose effects may not be wholly justified in all instances." (p. 10-11 lines 32-33, 1-2) "The current view regarding formation of chromosome aberrations is that "the majority of radiation-induced chromosome aberrations are produced by the misrepair of DNA double-strand breaks (DSB) quite possibly those involved in complex DNA lesions (multiply damaged sites)." (p. 99, lines 15-18) The authors caution that more research is required on the mechanisms, extent of activity in vivo, and interrelationships to provide certainty before including them in risk estimation at low dose levels. As for radiation-induced somatic cell mutations, they state that "mutagenesis is essentially a result of the attempts of the cell to repair damage" and that "the mutations are much more complex than originally thought," as also are dose rate effects.

Of particular interest, recent studies on "induction of so called 'bystander effects' in cells not directly irradiated, and the development of genomic instability in the non-irradiated progeny of irradiated cells many generations after exposure, have served to challenge the conventional view that only those cells directly traversed by radiation are targets for cellular effects of radiation including cell killing, and the induction of chromosomal aberrations and mutations." (p. 103, lines 15-20) The authors note, too, that multiple low-dose exposures may not have an additive effect on a cell, responding similarly post-repair to a second low dose exposure as previously thought. Rather, the cell may, or may not, demonstrate an "adaptive response." The responses may be complex and may affect the shape of the dose-response curve for low doses and low dose-rates in human populations. It has been suggested that a prior "priming dose" may have an "adaptive" impact on cell response to a subsequent exposure. Effects may be positive or not.

Radiation-induced genomic instability is the term applied to "a type of instability in individual cells that is transmitted to their progeny, leading to a persistent enhancement in the rate at which genetic changes arise in the descendants of the irradiated cell after many generations of replication." It is noted

that "genetic endpoints studied have included malignant transformation, chromosomal aberrations, specific gene mutations, and cell survival." (p. 107, lines 7-13) Among the delayed consequences cited is that "a persistently increased rate of cell death has been shown to occur in cell populations many generations after irradiation...variously referred to as occurring as a result of 'lethal mutations' or 'delayed reproductive failure.'" (pp. 109, lines 7-10)

It is suggested that these phenomena – genomic instability, bystander effect, and adaptive response may complicate understanding of dose response at low doses, and, thus, downward linear extrapolation from high doses may be misleading in the low dose range. The possibility is also raised of differing tissue response, as well as the biological effects of DNA irradiation upon individual cells.

Chapter 5 addresses the important role of animal models for precise dose and dose rate controls, genetic background, and other modifiers of dose response.

Recent studies support significance of "early events involving DNA losses targeting specific genomic regions harboring critical genes."

"Dose response for tumorigenesis and life-shortening in lab animals appear to support linearity, and support a dose and dose rate effectiveness factor (DDREF), for reduction of estimated risk per 19-24 unit dose based on acute, high-dose data, in the range of about 2 when data are extrapolated to low doses from effects induced by doses in the range of 2-3 Gy (200-300 rad). Extrapolation [at 1Gy, (100rad)] would result in lower DDREF values." (p. 11, l. 19-24)

Chapter 6 addresses quantitative uncertainty analysis, including uncertainty distribution for excess relative risk per Gy (ERR.Gy), allowing and not allowing for the possibility of a universal threshold. Other major uncertainty factors cited are excess relative risk per Gy, statistical variation in estimated ERR @ 1Gy for Atomic Bomb Casualty Commission survivors (ABCC), and Dose and Dose Rate Effectiveness Factor (DREF) at low doses and dose rates

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Conclusions in the final Chapter 7 could be interpreted as recognition that much of the full report (e.g., discussions of recent findings on mechanisms of radiation damage in Chapters 3 and 4) is venturing into new realms for radiation research. The conclusions are cautionary, carefully worded by some very careful scientists, but clear about the importance of their recommendations that there is much yet to be learned about low-level radiation impacts. They didn't use the term "precautionary principle" outright but it was implicit in their conclusions.

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JHJ conclusions

** Reconfirmation of the linear no-threshold dose-response relationship is a positive but no longer enough, given the recent low-level radiation research. High-to-low linear extrapolation, dose modeling, and reliance on risk assessment for radiation standards and regulation should be discontinued.

** Certainty about single radiation track damage to a single cell alone should halt any regulatory efforts to return to "safe threshold," or to proceed with deregulation, exemptions, exclusions from control, or release, recycle, or reuse of any radioactive waste.

** Chromosome aberrations, mutations, double strand breaks, imperfect cell repair, genomic instability, bystander effect, and adaptive response -- all -- also alter basic understanding of low-dose and dose-rate effects and strengthen the public need for far stricter standards and regulation.

** There must be a far stronger public demand for much more basic research at much lower dose levels, necessary for protection of public health, genetic integrity, and the quality of the environment and all its occupants.

** The Precautionary Principle should be adopted by all regulatory agencies immediately, practiced, and fully enforced. No more radioactive wastes should be produced for military, power, or commercial uses.

Additional comments

Neither the executive summary, introductory nor final chapters are really representative of the positive research findings and discussions in Chapters 2, 3, and 4. It's almost as if the report was framed to be skimmed by nuclear proponents, reading the summary, introduction, and conclusion, but not digging into the important content in the central chapters. I hope this Report, labeled "Draft," will survive with its central chapters intact. (NIRS, New England Coalition, and Sierra Club submitted comments to ICRP.) We hope you'll compare the draft with the final version.

This summary doesn't -- really can't -- begin to do justice to those central chapters, but I hope it will be of use for activists at this crucial time as the nuclear industry tries to revive.

The complete Draft ICRP Report, "**Low-dose Extrapolation of Radiation-Related Cancer Risk**" can be found, viewed, and downloaded by googling "ICRP." Open the first reference, point to "News and Drafts," then click on "Draft Reports." The document will be shown at the bottom right in blue; click on it to read or begin downloading. 212 pages.

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