CONF-8607379--Summs.

DE89 011529

FINAL REPORT

ASA Conference on Radiation and Health

Coolfont VI

Coolfont Conference Center
Berkeley Springs, West Virginia

July 20–25, 1986

With Support From: U.S. Nuclear Regulatory Commission
U.S. Department of Energy

Chair: Jerome Wilson
National Cancer Institute

May 1988

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SIXTH ANNUAL
ASA CONFERENCE ON RADIATION AND HEALTH

Coolfont Conference Center
Berkeley Springs, West Virginia
July 20-25, 1986

Conference Chairman:	**JEROME WILSON** National Cancer Institute
Conference Vice Chairman:	**ETHEL GILBERT** Battelle Pacific Northwest Labs
Conference Committee:	**EDWARD FROME** Oak Ridge National Laboratory
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With Support From: National Cancer Institute, N.I.H.
National Institute of Environmental Health Sciences
U.S. Department of Energy

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FOREWORD

In keeping with the previous ASA Conferences on Radiation and Health, this conference upheld its purpose which is to foster interaction among scientists from various disciplines associated with the problems related to the health effects of radiation. The conference was held at the Coolfont Conference Center in Berkeley Springs, West Virginia. The relatively small size of the conference and the relaxed schedule permitted time for informal discussion beyond the framework of formal presentations.

A special effort was made to have this conference reflect the multidisciplinary nature of the program through sessions in laboratory-based biology, statistical methodology, radiation research, epidemiology, and nuclear power issues. In addition to our usual format, we invited a couple who was in Russia at the time of the Chernobyl accident to discuss their experience in a special afternoon session. (Afternoons are usually free for informal discussion, reading, and recreation.)

The Organizing Committee consisted of Ethel Gilbert, vice-chairperson, Battelle Pacific Northwest Laboratories; Edward Frome of Oak Ridge National Laboratory; Charles Land, National Cancer Institute; Bernard Pasternack, New York University Medical Center, and Elizabeth Kelley of Los Alamos National Laboratory.

Each session consisted of two speakers and one discussant. The sessions included discussions of molecular mechanisms of oncogene activiation, chromosome abberations associated with cancer, chromosome damage, dosimetry from chromosome damage, atomic bomb dosimetry reassessment (DS-86), uranium health effects, nuclear power plant studies, internal emitters, and dogs exposed to plutonium. The new reassessment of the atomic bomb data suggests that neutrons make a small contribution to the total doses for T65 doses. The nuclear power plant studies represent mainly preliminary and planned studies, therefore, a panel discussion format allowed for presentation of some limited data from Northeast Utilities Mortality Registry by Jeanne Loughlin from Epidemiology Resources Inc. in Boston, Massachusetts; the Commonwealth Edison Company Program by Joan S. Chmiel from Northwestern University Medical School in Chicago, Illinois; Ontario Hydro Nuclear Workers' Mortality Experience by Lois Green from the Health Service Department of Ontario Hydron in Toronto, Canada, and a presentation of the plans and implementation of a feasibility study of nuclear power plant workers at Calvert Cliffs by the Radiation Epidemiology Branch of the National Cancer Institute, presented by Robert Goldsmith from the Department of Energy.

The wrapup session was led by Michael Fry who provided an excellent summary of events and shared some of his insight into the basic biological issues raised during the conference. Papers prepared by each speaker are included in this report. The program and list of participants are provided in the appendix.

Professional support was provided by the American Statistical Association through Richard L. Anderson, ASA representative to the conference; Fred C. Leone, ASA Executive Director, and Ede Denenberg, ASA Conference Coordinator. The crucial financial support needed to bring scientists from around the world and the United States was generously provided by the National Cancer Institute, Department of Energy, and the National Institute of Environmental Health Sciences.

Jerome Wilson
Conference Chairman

PREFACE

Richard L. Anderson, Statistical Consultants, Inc.

The 1986 ASA Conference on Radiation and Health (Coolfont VI) continued the procedure established in 1981 of holding forenoon and evening sessions, leaving afternoons free for discussion and relaxation. One exception was made this year in that Michael and Marie Stoline were invited to discuss the Chernobyl Disaster on Monday afternoon. This challenging session, added after the original program had been arranged, even attracted local press coverage. Jerome Wilson chaired the Conference, ably assisted in the program formulation by Ethel Gilbert (chair for Coolfont VII), Edward Frome, Charles Land, Bernard Pasternak and Elizabeth Kelly.

The program consisted of the following topics: a general overview of radiation and health problems; cytogenetics and radiation (human and animal studies and statistical analysis of dose-response curves); uranium and health effects, including continuing emphasis on radon, which has attracted considerable national interest lately; epidemiologic studies of workers at nuclear power plants and an uranium processing plant; the latest assessment of atomic bomb dosimetry.

The Conference was partially supported by the National Cancer Institute, the National Institute of Environmental Health Sciences and the U.S. Department of Energy. Unfortunately no graduate students applied for fellowships to attend Coolfont VI. Conferees were requested to solicit prospective fellows for Coolfont VII; the ASA was advised to advertise these fellowships in non-statistical journals as well as AMSTAT NEWS and to do this at least by February.

These Coolfont Conferences provide an excellent environment for an interchange of ideas and information in an assemblage of scientists from a variety of disciplines. Unfortunately there is one important factor which limits this interchange: language. In order to overcome the difficulty of statisticians understanding nuclear scientists and nuclear scientists understanding statisticians, I suggested one of two procedures: each group prepare a set of commonly used terms with definitions which would be understood by the other group(s); have an introductory session in which each group attempts to explain its language to the other group(s).

This problem of communication is even more serious when scientists attempt to explain their research efforts to the general public. The Coolfont Conferences on Radiation and Health should be ideal forums for development of a language which could be understood by the general public as well as different scientific groups.

RADIATION AND HEALTH: AN OVERVIEW

Arthur C. Upton, New York University Medical Center

In the ninety years since ionizing radiation was discovered, a wide variety of biological effects of irradiation have been observed. These range from effects that appear promptly after exposure to effects that do not appear until years, decades, or generations later. The effects also vary greatly in the severity of their impacts on health; no effects have been discovered as yet that are inherently beneficial to normal individuals.

For purposes of radiological protection, radiation effects are classified into two categories: stochastic and nonstochastic (ICRP, 1977). Those in the former category are viewed as probabilistic phenomena, varying in frequency but not severity with the dose, while those in the latter category are viewed as deterministic phenomena, varying both in frequency and severity with the dose. Stochastic effects are known or presumed to be inducible by damage to only one of the many cells in an affected organ. These include gene mutations, chromosome aberrations, carcinogenic effects, and teratogenic effects. Nonstochastic effects of radiation, on the other hand -- such as cataract of the lens, impairment of fertility, and depression of the bone marrow -- require the killing of many cells in the affected organs. Hence they vary in severity with the extent of cell loss, and their thresholds of detectability depend on the sensitivity with which the consequences of cell damage or loss are measured.

Because a nonstochastic effect is induced by irradiation only when the dose is large enough to exceed the relevant threshold, an attempt is made to set radiation protection standards at subthreshold levels, so as to prevent nonstochastic effects altogether. With respect to stochastic effects, on the other hand, which presumably have no thresholds, radiation protection standards are intended merely to limit their rates of occurrence to levels that are socially acceptable.

Our knowledge of the dose-response relationships for radiation effects of the various types is derived largely from studies of human and animal populations irradiated at relatively high doses and high dose rates. Consequently, estimates of risks at low doses and low dose rates must be derived largely by interpolation and extrapolation, based on assumptions about the shapes of the relevant dose-effect relationships and mechanisms of injury (UNSCEAR, 1977; NAS, 1980).

As concerns nonstochastic effects, our knowledge of dose-effect relationships is based largely on radiotherapy experience (i.e., 20-35 exposures given in 4-7 weeks), and quantitative data for the late-occurring effects are relatively fragmentary. Furthermore, the radiotherapeutic observations pertain mainly to elderly patients, whose response is not typical for the population as a whole. While the threshold for a detrimental nonstochastic effect appears to lie well above 25 Sv in most adult tissues, it is appreciably lower in growing tissues, the lens of the eye, the hemopoietic system, and reproductive organs (ICRP, 1984).

As concerns carcinogenic effects, it is clear that the carcinogenicity of radiation depends on the tissue exposed, conditions of exposure, sex and age of the exposed individual, and other factors. Although neoplasms have been induced by radiation in most types of tissue, they vary in their morphology and in their times of onset, depending on the age and sex of the exposed individual. The long induction period for radiation carcinogenesis and the modifying effects of other agents acting after irradiation imply that the induction of cancer is a multistage process, in keeping with experiments on radiation-induced cell transformation *in vitro* (UNSCEAR, 1977; Upton, 1984). Although the variations with the dose and time are consistent with multistage models of tumor initiation, tumor promotion, and tumor progression, the tendency for the tumors to resemble their spontaneous counterparts in age-distribution points to interactions between radiation and other carcinogenic risk factors which are as yet poorly understood. Also poorly understood are species- and organ-differences in susceptibility to radiation carcinogenesis, which bear no consistent relationships to corresponding "spontaneous" cancer rates (Upton, 1985). The molecular nature of the steps involved in radiation carcinogenesis, although yet to be fully elucidated, is being rapidly explored through advances in somatic cell genetics and molecular biology; existing evidence indicates that the process may involve the activation of oncogenes and/or the inactivation or loss of anti-oncogenes, through chromosomal rearrangements, point mutations, and other effects of radiation on DNA. Furthermore, in contrast to these mechanisms of carcinogenesis, which result from the absorption of radiation by the tumor-forming cells themselves, abscopal effects resulting from irradiation of other cells also may contribute to carcinogenesis under certain conditions (Upton, 1984).

Genetic effects of radiation on germ cells, while well documented in experimental animals, have yet to be demonstrated in human beings. Nevertheless, gene mutations and chromosome aberrations in human somatic cells have been studied extensively and are consistent with those observed in other species (UNSCEAR, 1982).

Teratogenic effects of various types have been observed in human beings and experimental animals, but systematic dose-response data are available for relatively few such effects as yet, especially in human beings. The existing evidence is noteworthy, however, in indicating that the human brain may be particularly sensitive to damage at certain stages in embryonal development (Otake and Schull, 1984).

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Dudley T. Goodhead, Medical Research Council

SUMMARY

A crucial difference between ionising radiation and chemical insult is that radiation interacts in the form of discrete tracks resulting in very inhomogeneous deposition of energy within irradiated cells [1-3]. By comparing the biological effectiveness of different radiations, early radiobiologists were led to simple mechanistic models to describe the action of radiation on cells. In particular, induction of chromosome aberrations by radiations of low linear energy transfer (LET), such as γ-rays, showed a curvilinear dose-response, while induction by high-LET radiations, such as slow neutrons, showed a steeper linear response. This led readily to mechanisms based on a one-track (linear) mode of induction of aberrations and a multi-track (dose-squared or higher power) mode [4]. It was usually assumed that the same basic process was involved in both modes, i.e. the production of sub-lesions which subsequently interact over a long distance (∿ μm) to produce the final observable lesion (aberration). The long-distance was required to allow sufficient contribution from multiple tracks at moderate doses. This one-track, multi-track mechanism allowed simple extrapolation to low doses and low dose-rates by identifying the linear term in the dose-response. The mechanism also allowed a ready explanation of the general qualitative features of the variation in relative biological effectiveness with LET of different radiations.

Because of the clear importance of DNA and chromosomes to cellular function, the above concepts were extended to cell killing, cell mutation, cell transformation and in vivo carcinogenesis. They still play a major role in the underlying philosophy of a great deal of radiobiology and radiation protection.

However, there is now evidence to show that these simple mechanisms are not of general applicability and that they may not be appropriate even for the simple in vitro cellular systems from which they were developed. The low dose-rate extrapolation has been found to be at fault in numerous investigations. However, for this presentation I shall concentrate only on studies which probe the spatial aspects of the mechanisms. These, too, show that extrapolation on the basis of the early models may be misleading.

γ-rays, X-rays and neutrons usually do not provide a precise method of studying the spatial aspects of sub-cellular mechanisms of action because they each produce a broad spectrum of secondary particles of widely different energies, ranges and LETs. However, in the last decade mammalian cell experiments have become possible with much more well-defined components of these radiations. Three particular methods which have probed the biologically critical distances are, in chronological order, (a) ultrasoft X-rays, (b) correlated heavy ions and (c) epithermal neutrons.

(b) Correlated particles (pairs of deuterons or triplets of protons), produced by stripping accelerated molecules, have been used at Columbia University to investigate interactions over distances down to ∿ 50 nm [5,6]. They show that there is very little 1-track interaction over distances $\gtrsim$ 100 nm.

(c) Monoenergetic 24 keV neutrons produce within the irradiated cells a very limited spectrum of predominantly low energy recoil protons of mean range ∿ 300 nm. Very recent experiments at AERE, Harwell, have shown that the shortness of the tracks does not prevent them from efficiently producing one-track (linear) damage [7]. This is contrary to expectations of the early models and to associated extrapolations based on results for higher energy neutrons.

(a) Ultrasoft X-rays (0.28-5 keV) produce within the irradiated cells only very low energy electron 'track-ends' similar to those which occur as a significant component in any low-LET irradiation. They have been used since 1974 in a series of mammalian cell investigations at the MRC Radiobiology Unit [8] and very recently also at a few other laboratories. The lowest energy ultrasoft X-rays produce electron tracks of range only $\gtrsim$ 7 nm (containing only about 12 ionisations) which, according to the early ideas, should be biologically ineffective and virtually incapable of inducing one-track damage. Yet in all biological systems tested to date, including induction of aberrations [9], mutations [10], killing [11], and DNA double-strand breaks [12], these very short tracks have been found to be very effective and to show a large linear component of induction.

It seems clear therefore that the early mechanistic ideas are not satisfactory. One-track damage is apparently determined predominantly by very localized properties of the track over nanometre distances. This fact has now been acknowledged by nearly all mechanistic biophysical models of radiation action [13], there is of course still substantial uncertainty and disagreement as to the nature of the critical localized properties. Two important consequences are:

(1) By contrast, multi-track effects must act over much larger distances if they are to be observable at moderate doses. Therefore, there is apparently a clear difference in mechanism between 1-track and 2-track modes. It may therefore be misleading to attempt to infer details of one from the other.

(2) For further identification of the critical localized properties of individual tracks and for comparison of radiations, it is essential to consider the very microscopic stochastic structure of radiation tracks over nanometre distances. In this region average quantities such as LET provide very poor descriptions of radiation quality.

Energy deposition by radiation is highly inhomogeneous over dimensions of DNA structures (even at extremely high doses) up to entire cells (at low doses) [3]. Inhomogeneities at the cellular and tissue level may be even greater for radionuclides such as α-particle and Auger-electron emitters. At the subcellular level the detailed microscopic structure of radiation tracks is dominated by stochastics as a consequence of the probabilistic nature of the atomic interaction

processes of the primary and secondary particles. These tracks can now be studied in some detail by Monte-Carlo simulation methods. It is clear that most atomic damage within DNA, or an entire cell, is irrelevant to the cell's fate, so it is a major challenge of the present time to identify those types of damage which are of critical biological relevance. This can be approached by attempting to correlate the relative biological effectiveness of radiations with particular microscopic properties of their tracks in the hope that this will lead to closer identification of important features of the tracks and their mechanisms of damage. But a subjective choice must be made amongst the wide variety of possibilities.

One such choice is the deposition of a cluster of energy in very small volumes, possibly involving DNA or DNA-related structures. For example, random scoring of frequency distributions of energy deposition in small cylindrical targets has led to the finding that the deposition of $\sim$ 100 eV in a $\sim$ 2-3 nm sized target correlated well with the observed biological effectiveness of low-LET radiations, including ultrasoft X-rays [14]. Furthermore the deposition of $\sim$ 300 eV in a $\sim$ 5-10 nm sized target apparently correlates well with the production of the qualitatively different damage produced by high-LET radiations [15,16]. These quantities can therefore form the basis of a working hypothesis for the biologically critical properties of radiation tracks.

Finally, it is worthwhile to consider again the relative roles of one- and multiple-track action in single cells. A radiation dose-response relationship can usefully be divided into 3 regions [13]:

(1) Low doses: Guaranteed one-track effects: This region covers only the very low doses (or dose-rates) for which it is highly improbable that more than one track will pass through a given cell or cell nucleus (in a relevant time). For a spherical cell nucleus of about 8 μm diameter this region extends up to $\sim 2 \times 10^{-4}$ Gy of γ-rays or $\lesssim 10^{-2}$ Gy of neutrons [3,17]. This is the region of prime relevance to radiation protection. Yet there are virtually no direct mammalian radiobiological data, in vitro or in vivo. Can we safely extrapolate into this region from regions (2) and (3) below? (The region will be pushed to even lower doses if multiple-cell effects are involved.)

(2) Intermediate doses: Assumed (?) independent track effects: This common assumption is made over the region where dose-responses appear to be linear, despite the fact that tens or hundreds of tracks may pass through the cell nucleus in a short time. There are reasonable amounts of radiobiological data in this region, especially at its upper end. However there are now also accumulating amounts of data which show that the tracks do not always act independently, for example when a dose-rate dependence is seen in this region. Such effects of interference between tracks could come about by increased or decreased repair (by induction or inhibition) or, less likely, by interaction between damage. Such observations seriously question the usefulness of extrapolations from region (2) to the low-dose region (1). They also show that linear extrapolation to low-doses for risk estimation may not always be conservative as is commonly assumed.

(3) High doses: Multi-track interference effects: In this region the dose responses are visibly non-linear. Here there is a great deal of radiobiological data. However, it is of very limited direct interest in radiation protection except in so far as it can give us some information on mechanisms which may also be involved in the intermediate-dose region (2). For example, can some repair processes be dose-dependent, say by induction or saturation [18]? The main contributions to the visible multi-track interference may well include dose-dependent repair, interaction of damage, and cell sterilization where proliferative ability is included in the assessment.

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RESULTS OF THE A-BOMB DOSE REASSESSMENT - A PRELIMINARY GLANCE

William H Ellett, National Research Council-National Academy of Sciences

Discussants: DISCUSSION

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For the last several years, Japanese and American scientists have been developing a new dosimetry system for estimating the organ doses received by the A-bomb survivors at Hiroshima and Nagasaki. This work has resulted in a new computerized system, designated DS-86, which was installed at the Radiation Effects Research Foundation (RERF) in April of 1986 and which is now in use. A bi-national collaborative report documenting this dose reassessment is presently being edited by Dr. William Roesch and is scheduled for publication by RERF in early 1987. In the same time frame, the DS-86 system and its documentation will be reviewed by the NAS-NRC Panel on the Reassessment of A-bomb Dosimetry, chaired by Dr. Frederick Seitz, and by a counterpart senior committee in Japan, chaired by Dr. Eizo Tajima.

The steps in the development of the DS-86 system are described in a recent review (E185) which can be used as a general reference for the dose reassessment. In addition, a start has been made towards comparing organ dose estimates obtained via the DS-86 system with those made with the T65 dosimetry which RERF has used for the last two decades. Even though organ dose estimates for the individual survivors are not available at the time of writing, it is possible to approximate how the estimated collective dose to the survivors will change upon adoption of the new dosimetry.

A major perturbation introduced by DS-86 is a much smaller collective dose due to neutrons at Hiroshima than was the case for the T65 dosimetry. But it is best not to be too simplistic when considering the ramifications of the new dosimetry. There are a number of offsetting factors, some of which increase and others decrease the estimated organ doses of the A-bomb survivors, relative to the T65 dose estimates.

The yield of the Hiroshima bomb is now believed to be about 20 percent greater than that assumed previously. A really precise estimate is beyond the investigators' capability and the actual yield is not known within ±20 percent. The revised yield, as well as a number of other factors related to radiation transport, indicate that gamma ray doses in air at Hiroshima were somewhat larger than estimated by T65. For example, at 1,100 meters from ground zero, a distance within which survivors received about half of the total population dose equivalent, the gamma ray dose in air was estimated as 156 rad by T65 (Mi68). The new estimate at this distance is 256 rad. For neutron doses, again in air, the reverse situation occurs: the T65 estimate is 106 rad; that by DS-86, 12 rad. At Nagasaki changes in the estimated doses, in air, are smaller. At 1,100 meters, T65 yields 589 rad (gamma) and 19.5 rad (neutron); DS-86 yields 498 rad (gamma) and 7.6 rad (neutron).

It is not always appreciated, however, that tissue doses in air are a misleading parameter for describing the A-bomb survivor experience. Almost all of the survivors who received appreciable doses were inside of houses that provided much better shielding than previously assumed. The new dosimetry estimates that gamma ray transmission into Japanese houses was about 50 percent vis-a-vis the 90 percent estimate for T65. On the other hand, estimates of neutron transmission have not changed much, 38 percent in DS-86 vis-a-vis 32 percent in T65.

Finally, one must consider the self-shielding provided by the body itself to the organs within. This varies for each particular organ with the orientation of the survivor at the time of exposure, a factor not considered in T65. The self-shielding of gamma radiation was overestimated in T65. The NAS BEIR III Committee (NAS80) used an average gamma ray transmission factor of 0.5 to internal organs in assessing the A-bomb survivors data. DS-86 indicates that 0.78 would be a better value for this average. DS-86 also predicts greater average transmission for neutrons, 0.31 vis-a-vis 0.22 for T65. However, the DS-86 system does not utilize average values of self-shielding when information on the survivor's orientation and posture is available. Rather, individual dose estimates are made for 14 of the internal organs of each survivor.

The net result of this is that the collective organ doses are now estimated to be smaller in both cities but not by very much--probably less than a factor of 2. At Nagasaki, where neutrons are a minor

consideration, estimated organ doses are about 30-40 percent smaller with DS-86 dosimetry than with T65. At Hiroshima, the situation is not clear-cut, since comparisons must be based on a dose equivalent that takes into account the increased biological effectiveness of neutrons as compared to gamma radiation. That is, since neutron doses were estimated to be relatively large at Hiroshima with the T65 dosimetry, the difference between DS-86 and T65 for organ doses depends heavily on what weighting factor is used for the neutron component. In actuality this weighting factor probably changes with dose level, diminishing at higher doses. In analyses which assumed a linear response function, the BEIR III Committee (NAS80) used a constant weighting factor of 11.3 for neutrons relative to gamma radiation, a value not too different from the quality factor of 10 for fast neutrons advocated, until recently, by the ICRP.[1]

To calculate the collective dose at Hiroshima, d[illegible]cussed below, I have used a weighting factor of 10 for neutrons, but this should be viewed as a default choice in the absence of informative data on the effectiveness of neutrons for inducing cancer in humans. (No doubt the A-bomb survivor data will be analyzed extensively to throw some light on this question; but such efforts are quite likely to be doomed to failure because of the high correlation between the gamma ray and neutron doses received by the individual survivors.)

In addition to an arbitrary weighting factor for neutrons, several other approximations were made in this preliminary calculation of the collective internal dose. I have restricted the "exposed" population to those 33,832 Hiroshima survivors in the RERF Life Span Study sample located between 700 and 2,200 meters from ground zero. Survivors further away contribute almost nothing to the collective dose and are usually considered unexposed. Survivors closer than 700 meters (43 persons) should, like all high dose survivors, have their shielding histories reviewed before they are included in analyses of the Life Span Study sample. Based on the distribution of exposed persons at Hiroshima and their average T65 doses, as given in M168, I calculate that the collective organ dose equivalent to the "exposed" population at Hiroshima was about 1.5 x 10^6 person rem. Using average values for self-shielding and structural shielding--not the individual organ dose estimates-- DS-86 dosimetry yields a collective organ dose equivalent of about 1.1 x 10^6 person rem, see figure 1.

Of more interest, perhaps, is the way the distribution of the collective dose changes with the new dosimetry. Almost all of the dose response information at Hiroshima and Nagasaki comes from those few thousand survivors who had T65 doses to internal organs of more than 50 rem. These survivors were relatively close to ground zero, within 1,200 meters or so, and it is in this range that the new dosimetry makes the largest difference. For example, at Hiroshima, a quarter of the collective T65 dose to internal organs was received by 609 survivors who had an average internal dose of 620 rem. With DS-86 dosimetry, 827 survivors received a quarter of the DS-86 collective dose and have a much more believable average dose of about 350 rem. Similarly for the second quartile of the collective dose, T65 yields an average internal dose of about 280 rem, DS-86 yields 170 rem. It is clear that the changes in the dose estimates will vary with distance and therefore with exposure level. This raises our anticipation as to what DS-86 dose response functions at Hiroshima will look like following the dose reassessment. With a bit of luck, we should know fairly soon.

[1] At the low dose levels relevant to radiation protection practices, the ICRP now recommends a quality factor of 20 for neutrons.

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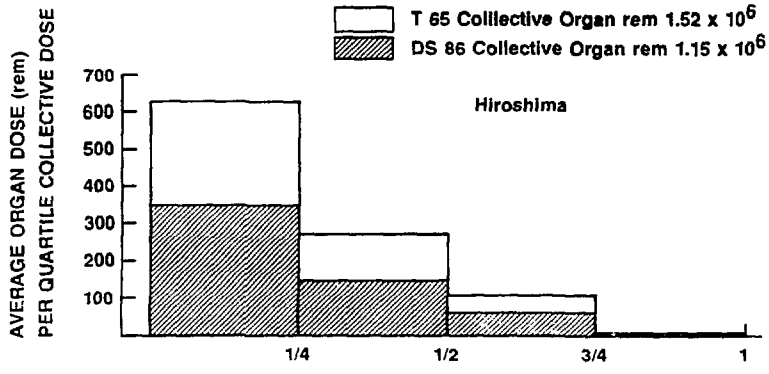
Background information on the dose reassessment is available in two workshop proceddings published by RERF, Hiroshima, Japan. Copies of these proceedings are available from the RERF Office, Commission on Life Sciences, National Research Council, 2101 Constitution Avenue, N.W., Washington, D.C. 20418:

US-Japan Joint Workshop for Reassessment of Atomic Bomb Radiation Dosimetry in Hiroshima and Nagasaki. Proceedings of a workshop held at Nagasaki, Japan, 16-17 February 1983 (edited by D.J. Thompson), (Hiroshima: Radiation Effects Research Foundation).

Second US-Japan Joint Workshop for Reassessment of Atomic Bomb Radiation Dosimetry in Hiroshima and Nagasaki. Proceedings of a workshop held at Hiroshima, Japan, 8-9 November 1983, (Hiroshima: Radiation Effects Research Foundation).

T 65 Comparison to DS 86 Average Organ Rem by Quartile Assuming Q = 10 for Neutrons.



DS86 A NEW DOSIMETRY FOR THE HIROSHIMA AND NAGASAKI ATOMIC BOMBS

Dale Preston Radiation Effects Research Foundation

Estimates of the risk of radiation effects in Japanese A-bomb survivors are crucial to our understanding of the health effects of radiation and to attempts to set standards for radiation protection. In order to produce reliable estimates of the risks associated with radiation exposure among A-bomb survivors it is important that we have accurate estimates of the doses received by individual survivors. In the late 1970's and early 1980's a scientists raised questions[1,2] about the tentative 1965 dosimetry system (T65D) which had been used by the Radiation Effects Research Foundation (RERF) and its predecessor, the Atomic Bomb Casualty Commission (ABCC) to compute dose estimates for individual survivors. As a result of these questions a joint US-Japan committee was established to review all aspects of the dosimetry for the Hiroshima and Nagasaki atomic bombs. In April 1986, after over four years of work, the committee approved a new dosimetry system, christened DS86, for use by RERF.

In this presentation I will briefly describe the the new dosimetry system and discuss how this system will be used by RERF to compute organ dose and exposure kerma estimates for individual survivors. I will also very briefly summarize some early results on how these new dose estimates will affect risk estimates for leukemia and nonleukemia non-cancer mortality and the rate of chromosome aberrations. All results discussed herein should be regarded as extremely preliminary. RERF is in the process of preparing a series of reports which will discuss in detail the various topics I will mention here. The results based upon DS86 mentioned briefly below are based upon analyses carried out by Professor D. A. Pierce, Dr. A. Awa, and myself.

The Life Span Study Cohort

Studies of radiation effects at RERF are based upon the Life Span Study (LSS) cohort which, as currently defined includes about 120,000 persons, 93,000 of whom were within 10,000 m of the hypocenter in either Hiroshima or Nagasaki at the time of the bomb (ATB). The remaining 27,000 people in the cohort were not in either city ATB. Various ABCC and RERF reports describe the original construction of and various extensions to the LSS cohort.[3,4]

T65D Dose Estimates

In the late 1960's the T65D system[5] was adopted as the official dosimetry system. With some minor revisions, T65D doses have been used in all ABCC/RERF analyses since about 1970. T65D FIA kerma estimates are computed using city-specific parametric functions of the distance from the survivor location to the point at which the bomb exploded.

T65D transmission factors for exposure kerma estimates were computed in various ways including: the nine parameter model for persons inside Japanese houses or wooden tenements; the globe method for persons who were outside but shielded wholly or partially by buildings or terrain (Nagasaki only); the globe method for persons inside concrete buildings (Nagasaki only); ad hoc assignment for more difficult situations, particularly Nagasaki factory workers. Gamma and neutron transmission factors of one were used to compute exposure kerma for all Hiroshima survivors beyond 1600 m from the hypocenter at the time of the bomb (ATB) and all Nagasaki survivors beyond 2000 m. Using the T65D system dose estimates have been computed for about 90,000 survivors in the LSS cohort.

The T65D system does not contain estimates of transmission factors for the computation of organ doses. However, in the 1977 Kerr[6] published transmission factor estimates for a number of organs. Although most major RERF analyses of the LSS data are based upon exposure kerma rather than organ dose, Kerr's transmission factors have been used in a limited number of analyses.

The DS86 System

During the course of its work the US-Japan Committee for Reassessment of the A-bomb Survivor Dosimetry has reviewed all major aspects of the dosimetry. Among other things the factors considered include: weapon yield; location of the epicenter; the initial radiation spectrum, radiation transport through air; shielding provided by Japanese houses; self-shielding for organ dose estimates; and comparison of in-situ measurements with values predicted from current theoretical and computational results.

The DS86 dosimetry system which RERF received in April 1986 resulted from this work. The DS86 system is much more complex than was T65D. The system includes information needed to compute FIA kerma estimates for survivors in either city who were within 2,500 m of the hypocenter ATB.

DS86 exposure kerma can be computed

for some groups of survivors with DS86 FIA kerma estimates. These groups include people who were inside Japanese houses or wooden tenements who have T65D nine parameter data (about 14,000 in the LSS), people who were outside but shielded by light structures and have T65D globe data (4,000 people in the LSS), and people with detailed shielding histories who were in the open and unshielded ATB (1000 people in the LSS).

It is not currently possible to compute DS86 exposure kerma estimates for survivors with shielding histories who were outside shielded by terrain or inside of factory buildings. The number of survivors with shielding histories in these groups are small (about 1000 members of the LSS), but they are quite important since a large fraction of the Nagasaki survivors with T65D exposure kerma estimates in the range of .5 to 2 Gy are included in these groups.

The DS86 system system includes information which allows the computation of doses for 15 organs. Organ doses can be computed for any survivor with a direct DS86 exposure kerma estimate. The organ dose calculations take into account sex, age, and orientation of the survivor.

The doses produced by DS86 are more detailed than the T65D doses in that there are separate estimates of prompt and delayed gamma and neutron dose components as well as estimates of dose due to gamma radiation induced by the passage of neutrons through the surrounding external shielding or tissue.

The computations are complicated. The system does not include simple parametric formulas for FIA kerma or transmission factors. Rather the system begins with a description of the angular and energy dependent distribution of the FIA radiation environment at the survivor location and combines this information with detailed descriptions of transfer functions associated with particular shielding configurations to produce modified distributions which reflect the effect of external and self-shielding. Appropriate soft tissue kerma and organ dose response functions are then used to produce the final estimates. The computations and data manipulation required to produce kerma and four organ dose estimates for one survivor take about one minute on the relatively fast mainframe at RERF.

As the foregoing discussion indicates, the DS86 system can be used to compute direct exposure kerma and organ estimates for only about about 20% of the survivors in the LSS. An important part RERF's work with DS86 is the development of procedures which allow us to impute DS86 dose estimates for additional survivors. We have developed procedures which allow us to impute doses for about 80% of the survivors in the LSS. The subcohort for whom new doses have been computed includes: the 19,000 people with direct DS86 estimates; about 30,000 people but whose estimated DS86 exposure kerma is less than 0.5 cGy; and about 27,000 survivors without shielding histories who were probably located inside Japanese houses or tenements ATB. This subcohort will be used in initial reassessments for selected endpoints of radiation effects in A-bomb survivors.

Work is continuing on the development of the DS86 system. This work will result in small (but important) additions to the number of survivors for whom DS86 dose estimates can be computed directly and in refinement of some of the data used in the dose calculations. It is unlikely that near term enhancements to DS86 will have much impact on individual dose estimates or substantially increase the number of survivors for whom direct DS86 dose estimates can be computed.

The Impact of DS86

As a result of the dose reassessment virtually all aspects of the dosimetry for the Hiroshima and Nagasaki bombs have been revised. In general terms, the major changes have resulted in FIA gamma kerma estimates for Hiroshima survivors which are about 30% higher than T65D estimates for survivors within 1000 m of the hypocenter and about 60% higher for survivors at 2000 m. There was a reduction of about 90% in Hiroshima FIA neutron kerma. In Nagasaki, the gamma DS86 FIA gamma kerma estimates are about the same as the T65D estimates while the neutron kerma are reduced by about 60%.

DS86 gamma transmission factors for Japanese houses and tenements are about .45 on the average compared with a T65D average of over .9. Neutron transmission factors do not differ appreciably between the new and old dosimetries. On the average for Hiroshima survivors with direct DS86 estimates DS86 gamma exposure kerma estimates are lower than T65D estimates for survivors within 1200 m from the hypocenter and slightly greater for more distal survivors. In Nagasaki, DS86 gamma exposure kerma estimates are substantially lower than the T65D estimates. Because of the reduced FIA neutron kerma estimates DS86 neutron exposure estimates kerma in both cities are less than the T65D estimates.

It appears that for many organs the DS86 transmission factors will be about 30-40% higher than the T65D values. Detailed comparisons of organ dose estimates for individuals have not been made, but it appears that differences between T65D and DS86 organ dose

estimates will be smaller than the differences seen for exposure kerma estimates.

No detailed analyses of the data for specific endpoints have been completed at this time. In addition, it is impossible to summarize the complex issues involved in analyses of radiation dose-response with a single statistic.

With this caveat firmly in mind, preliminary results for leukemia and nonleukemia cancer mortality indicate that DS86 risk estimates based on total (gamma plus neutron) exposure kerma are about 50% higher than corresponding T65D estimates. It is clear that it will be impossible to use the A-bomb survivor data to produce accurate estimates of the neutron RBE. However, because of the reduced proportion of the total dose received by individual survivors which was due to neutrons the estimated effect per Gy of gamma radiation is much less sensitive to changes in the neutron RBE than it was when T65D doses were used.

Results for comparative analyses of recent data on chromosome aberrations collected by Dr. A. Awa parallel those for cancer mortality mentioned above. Based on DS86 exposure kerma estimates, the aberration rate per Gy is estimated to be about 50% higher than the estimate based on T65D kerma. There is no evidence against linearity of the dose response in either city when DS86 estimates are used. The general comments made above about RBE and the effect per Gy of gamma radiation also apply to the chromosome aberration data.

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APPLICATIONS AND LIMITATIONS OF CYTOGENETIC EVALUATIONS AS AN INDEX OF RECENT OR PREVIOUS RADIATION EXPOSURES

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Numerous studies have been conducted to derive dose response relationships for chromosomal breakages and rearrangements in human lymphocytes exposed to various radiation qualities. These have demonstrated that the yields of asymmetrical ("unstable") rearrangements, such as rings and dicentrics, are adequately described by the so-called "linear-quadratic" dose response model following exposures to low-LET radiations, whereas aberration yield varies predominantly as a linear function of dose after exposures to high LET radiations such as fission spectrum neutrons. In vitro exposures of human lymphocytes have also been employed in experimental protocols designed to define and quantify the effects of dose fractionation and protraction on aberration induction, and to derive estimates of "repair time" for radiation induced lesions in DNA.

Because the frequencies of aberrations induced in vitro are quantitatively and qualitatively identical to those induced in circulating lymphocytes of exposed persons, these in vitro "calibration" curves may be employed as standards for estimating "equivalent whole body dose" in persons having recent radiation exposures. Indeed, cytogenetic methodology is routinely employed by laboratories around the world as a "biological dosimeter" in accidents involving real or suspected overexposures (Lloyd 1984). Although the kinetics of aberration induction in human cells have been extensively investigated, relatively less is known regarding biological and physical variables that may affect the long-term survival of radiation damaged lymphocytes. Information on the lifespan of lymphocytes bearing various types of chromosomal aberrations has been obtained in extensive follow-up studies of British patients treated with fractionated X-radiation for arthritis of the spine (ankylosing spondylitis) between about 1940 and 1970 (Buckton 1983). These studies shown have that the frequencies of lymphocytes with unstable aberrations diminish dramatically over the first four years after radiotherapy and very gradually thereafter. The proportion of lymphocytes bearing translocations, inversions, and deletions (i.e. "stable" aberrations) remains relatively constant for up to about 30 years after exposure. Detailed evaluations in Japanese A-bomb survivors who received acute whole body exposures have demonstrated that the average frequency of lymphocytes bearing persistent aberrations can be correlated with estimated radiation dose in populations exposed over 30 years previously (Awa et al. 1978).

In ongoing studies we are examining the frequencies of stable and unstable chromosomal aberrations in cultured lymphocytes of patients who received partial-body radiation exposures 20-40 years ago. The study populations include control subjects and persons who received radiation treatment for enlarged tonsils; women treated surgically or those who received fractionated and/or protracted radiotherapy for carcinoma of the cervix; patients who underwent multiple fluoroscopic examinations during treatment for disease of the lung; and, lastly, adults selected from a cohort of persons whose thymus glands were irradiated in infancy. Our objectives are to explore the relationship between the frequencies of aberrant cells and dose received, adjusting for other biological or physical factors such as region of body exposed, age at exposure, time elapsed since exposure, radiation quality, and modality of dose delivery.

To date, we have completed cytogenetic evaluations of 200 T lymphocyte metaphases from each of 73 persons who received average bone marrow doses of about 7 rad as treatment for enlarged tonsils and from an equal number of persons who did not receive radiation therapy. Cytogenetic studies are also complete in 98 women treated by radium implants or external beam for cervical cancer more than 20 years ago, and in 26 patients treated by surgery alone. Preliminary statistical evaluations have demonstrated that increases in the proportion of cells bearing chromosomal aberrations are apparent for upwards of 20 years postexposure. The majority of aberrations observed are of the stable type in both study populations. A strong dose response relationship has been observed in the irradiated cervical cancer patients with a weak suggestion that more chromosome damage occurred in women who were older at the time of radiotherapy.

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Supported by NCI-DOE Interagency Agreement Y01 CP-10504 and by Contract DE-AC05-76OR00033 between Department of Energy, Office of Energy Research and Oak Ridge Associated Universities.

STATISTICAL ANALYSIS OF CYTOGENETIC DOSE-RESPONSE CURVES

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"My object all sublime
I shall achieve in time --
To let the punishment fit the crime,
The punishment fit the crime."
William Schwenck Gilbert

The Mikado's ambitious goal should always be borne in mind, if not actually heeded, by practicing applied statisticians when faced with a new data set. The first step in data analysis, as in forensic pathology, should be to reconstruct the circumstances of the generation of the occurrence under investigation, in hideous detail if possible, and to determine not only the time and place of the heinous deed but, more importantly, to interrogate those involved in order to elicit in the minutest detail, not only the values of the recorded results, but the subtleties of procedure and circumstances which could have had an effect on the result and the nuances of meaning attached to the terminology (not to say jargon) with which the results are described.

This session was meant to be a lesson in returning to basics, in the sense of modeling the data analysis on the original counts which the cytogeneticist actually makes -- counts of aberrations seen. Under appropriate assumptions (which are actually frequently met in practice), these counts can be shown to follow a Poisson probability mass function with a mean value that depends on several parameters, some of which may be assumed and others tested for.

The research reported here postulated a very general form of the mean value function which could accommodate a number of special cases; in particular, both continuous exposure and split-dose exposure types of experimental designs are subsumed. The generality of the mathematical model allows one, for example, to test whether the data are consistent with specific models that would arise from conjectured biologic mechanisms (such as one- or two-tract hit models).

Several data sets were used for illustration. In particular, one analysis allowed a nested sequence of models in which it was possible to test sequentially related sub-hypotheses about parameters using a natural partition of the deviance function.

For the biologically oriented in the audience, clarity might have been improved with the expanded use of graphical materials for illustration (in contrast to algebraic), though with some illustrative material, this would be hard to accomplish.

The bottom line of this session perhaps illustrates Michael Fry's analogy of the tendency to search for lost keys under the lamp-post, since that is where the light is. With most cytogenetic data of this sort, many analysts would, and have (myself included) expressed the results in terms of cells with aberrations per 100 cells examined, thus casting it into a binomial model framework, then appealing to asymptotic normality and using standard regression techniques, with or without a variance-stabilizing arcsine transformation. (In the illustrations I have seen, incidentally, the use of this transformation does not seem to affect the conclusions drawn.) The results of the modeling effort presented here allow one to go one step closer to the original data in the analysis. This may or may not make a difference in the conclusions, but one would never know the answer to that question without the opportunity to give it a try. This methodology makes it possible to give it a try.

URANIUM AND RADON MODELS

Nacmi H. Harley, New York University Medical Center

The models I would like to discuss are a metabolic model for internally deposited uranium and a comparison of lung cancer risk models for determining the health detriment from exposure to environmental radon daughters. In the case of an internal emitter such as uranium the models which are emerging appear to be realistic and organ burdens can be calculated with some degree of confidence. We have investigated uranium uptake as this is not well established. In the case of lung cancer risk projections from environmental exposure based on miner epidemiology, it is the model which is not well established and the "best" model awaits the complete follow-up of the cohorts.

The uranium model is being developed in collaboration with Herta Spencer, M.D., Hines Veteran's Administration Hospital, Hines IL, and Dr. Isabel Fisenne, U.S. Dept. of Energy, Environmental Measurements Laboratory (EML). We are currently attempting to develop a realistic biological (compartmental) model for uranium based on patient input/output studies and measured organ burdens also from environmental exposures. Dr. Spencer is in charge of a metabolic ward at Hines V.A. hospital and, in a pilot study, 4 patients were given their standard diet plus water, aliquots of which were sent to EML for ^{238}U and ^{234}U analysis along with all excreta. This area has naturally elevated uranium in water. The patients had essentially a constant natural uranium intake in their diet (20 mBq ^{238}U/day) but the water intake varied from 6.3 to 26.4 mBq ^{238}U/day. The data have not been fully analyzed as yet but it appears from the intake to urinary excretion ratios that the fractional uranium uptake from water is higher than that from the diet.

Dr. Fisenne has recently analyzed tissues from deceased New York City residents and determined the uranium organ burdens in lung, liver, kidney, vertebra, blood cells and plasma.

With these data and the New York City daily diet, water and air concentrations for uranium, it is possible to construct a metabolic model for uranium. Although the uranium content was constant with age for liver and kidney in the NYC autopsy specimens, the uranium content in vertebra and lung in these samples showed an increased concentration with age from 15 to 65 years by a factor of 2 and 3 respectively. Using the ICRP lung model for retention (primarily in lymph nodes), and measured New York City air concentration, the modeled increase in lung content with age showed good agreement with the measurements. The increase in vertebra could not be modeled assuming conventional bone turnover rates. It is postulated that mineral loss with age accounts for the apparent increase in uranium concentration in vertebra, in other words, bone is lost while the uranium remains.

This is a continuing project and additional patient data are being obtained by Dr. Spencer at Hines VA Hospital to verify and extend the initial findings of dietary and water uptake.

Modeling of lung cancer risk from radon daughter exposure is of current interest because of the recent finding of high environmental exposures from indoor air. Lifetime risk was calculated using a modified absolute risk model developed to be consistant with the age of appearance of lung cancer and the observation that lung cancer risk appears to be higher for miners exposed at older ages, even after accounting for the higher age specific mortality at older age. The higher risk at older age is accomodated by introducing an exponential decrease in attributable risk with time post exposure. This model is shown to be consistant with the observed excess cancer in miners (who have continuous exposure for about 10 years) and for environmental exposure of nonsmokers. A relative risk model calculation was presented to show that a relative risk coefficient of 0.01/WLM applied over the same 10 year interval for the miners yields an estimated 50% lung cancer deaths in the U.S. miner cohort, for example, which is not consistent with the observed data of less than 10% mortality (EPA recently adopted a range of coefficients of 0.01-0.04/WLM and a relative risk model for their risk estimates).

A recent NIOSH publication (Hornung and Meinhardt, 1986) shows that an exponential reduction in the relative risk coefficient with time post exposure is necessary to explain the observed mortality pattern in the U.S. cohort. Introducing this factor into the relative risk model of lung cancer mortality for continuous exposure for various time intervals up to whole life improves the agreement with observed miner mortality significantly.

NORTHEAST UTILITIES MORTALITY REGISTRY

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Northeast Utilities (NU) is a holding company organized in 1966 to integrate its operating subsidiaries. NU's principal operating subsidiaries are the Connecticut Light and Power Company, the Hartford Electric Light Company and Northeast Nuclear Energy Company. NU operates three nuclear plants, Millstone 1, Millstone 2 and Connecticut Yankee, with a fourth, Millstone 3, scheduled to begin operating soon. In addition, NU is part owner of three other nuclear units: Yankee Rowe, Vermont Yankee and Maine Yankee. The utility serves approximately 3 million people in Connecticut and Western Massachusetts. Their total energy output is derived mostly from nuclear power (57%) with the remainder from oil-fired stations (32%), coal-fired stations (7%) and hydroelectric facilities (4%).

Epidemiology Resources Inc. (ERI) was hired by NU to study the health effects of employment at a nuclear utility. Our initial approach was to conduct a mortality study of NU employees hired since the start of nuclear operations in 1966; the project has since evolved into an ongoing mortality registry.

We identified deaths among NU workers who were employed on or after January 1, 1966 and who died in the interval from January 1, 1966 through December 31, 1983. Deaths were ascertained by review of personnel files and benefits and compensation records. Both active and inactive files in a warehouse were reviewed. As each death notice or death certificate was found, we recorded employment information including date of hire, date of separation, reason for separation and whether or not the employee was ever a nuclear worker at NU or elsewhere. Nuclear work was defined initially by work location and job title. Nuclear employment status was then verified by cross-checking with a list that was available from the NU Health Physics monitoring system of regular, permanent employees who ever were issued dosimeters. Individual dose data were not available. Any death certificates not available from company files were requested from the appropriate states. All causes of death were coded according to ICD-9 by a professional nosologist.

Of the deaths identified for study, less than 3% were confirmed to have been nuclear workers. Since 89 percent of the deaths were in white men, the analyses were restricted to this group.

We used the mortality odds ratio (Miettinen and Wang, 1981) to estimate the mortality rate ratio (RR) for employment as a nuclear worker. The mortality odds ratio compares the odds of having been a nuclear worker in the case group of deaths with the odds of having been a nuclear worker among control deaths. Each deceased worker was characterized according to whether he was considered a nuclear worker by NU, i.e. according to whether he was issued a dosimeter. We selected as controls those decedents who died of circulatory disease, a cause of death that was most numerous and one that we assumed to be unrelated to nuclear employment. Both crude and adjusted estimates were calculated.

Preliminary findings were discussed at the meeting.

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ONTARIO HYDRO NUCLEAR WORKERS' MORTALITY EXPERIENCE

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Ontario Hydro is a public utility responsible for the generation of electric power for the province. Over one-third of the power produced is through nuclear generation.

Two mortality studies are underway. These studies were initially set up to monitor the health of nuclear workers. The studies provide information on 1) mortality by place of work and 2) mortality by radiation dose. Both were designed and are analyzed by an external epidemiologic consultant, Dr. T.W. Anderson. The population for both studies is active employees who contribute to the pension plan and pensioners. Notification of death is via the insurance company covering employee benefits. Cause of death information usually accompanies this notification and there is some verification with the appropriate vital statistics records. The measure used is the Standardized Mortality Ratio (SMR): the study populations are standardized to the general population of Ontario. Detailed person-years are not available: denominator figures are derived from the mid-year populations.

Mortality by Place of Work 1970-1984. SMRs are calculated for the total study population and three subdivisions - Nuclear (those working in the nuclear generating stations), Thermal (those working in the thermal generating stations), and Other (all other employees), totalling approximately 332,000 man-years. The categorization by Place of Work is according to current work location or, in the case of pensioners, the work location from which the individual retired. It is not necessarily reflective of an employee's career with the Corporation. Over the time period of the study there have been 2,662 deaths, of which 69 are categorized as Nuclear.

The Nuclear SMRs for four broad categories and all causes are:

	SMR	Observed
Neoplasms	61	(13)
Circulatory	61	(21)
Accidents	81	(32)
All Other Causes	17	(3)
All Causes	61	(69)

The Nuclear group has steadily increased in size since the study began: it is a relatively young population with 69% of its population currently less than 40 years of age.

Mortality by Radiation Dose 1972-1984. The study population for this analysis includes active pensionable employees and pensioners who are on the Radiation Dose Register. This population is not completely analogous to the Nuclear population in the aforementioned analysis as it includes anyone who has been designated as an Atomic Radiation Worker (ARW) since 1972. In 1985 there were about 6,900 individuals included in the mortality study by radiation dose and information is readily available by year on whole body doses (external and internal), skin and cumulative lifetime dose. The radiation doses against which mortality is assessed are the cumulative whole body lifetime doses which include that received both during employment with and prior to Ontario Hydro. As of 1985, calculations were based on an approximate total cumulative dose of 28,000 rem and approximately 57,500 man-years. There have been 101 deaths in this population over this 13-year period. Average total cumulative dose per person is 4.05 rem over the 13-year period. The corresponding number for those with a record of exposure is 5.12 rem; there are 1,448 individuals included in this analysis who have "zero" dose.

The SMR for malignant neoplasms is 64 and is based on 23 deaths: 14 lung, 2 liver, 1 pancreas, 1 bladder, 1 stomach, 1 leukemia, 1 colon and 2 disseminated.

For those pensionable employees and pensioners on the radiation dose register, the SMRs for all causes of mortality in four broad categories are:

Dose (Rem)		0	.001 -4.9	5.0 -9.9	10.0 -14.9	15.0 -19.9	20+	Total
Neoplasms	SMR	56	45	128	107	284	0	64
	Obs	(6)	(8)	(3)	(2)	(4)	-	(23)
Circulatory	SMR	70	70	26	32	42	82	65
	Obs	(12)	(21)	(1)	(1)	(1)	(3)	(39)
Accidents	SMR	54	64	124	39	0	87	63
	Obs	(8)	(16)	(5)	(1)	-	(2)	(32)
All Other Causes	SMR	13	29	0	0	171	0	25
	Obs	(1)	(4)	-	-	(2)	-	(7)
All Causes	SMR	54	56	74	44	101	51	58
	Obs	(27)	(49)	(9)	(4)	(7)	(5)	(101)

Limitations of the two studies are:

1) only males are included
2) no examination of cancer incidence, only mortality
3) not analyzable by occupational history or person-years, only by place of work at each mid-year point
4) no attempt to trace those who leave the corporation before becoming pensioners
5) no allowance for latent period
6) no internal control group
7) no adjustment for potential confounders.

Despite the crudeness of methodology, the system that has been established enables us to monitor for unexpected excess risks. Plans will be developed for a definitive analysis of the data once the appropriate latent periods have been exceeded.

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THE COMMONWEALTH EDISON COMPANY PROGRAM

Joan Sander Chmiel, Northwestern University Medical School

The Commonwealth Edison Company Program, also known as the Northwestern Edison Workers Study (The NEWS), is an ongoing prospective epidemiologic cohort study of cancer in workers in an electric utility company. Developed in the early 1980's in cooperation with the Commonwealth Edison Company, headquartered in Chicago, Illinois, the NEWS is an independent research program conducted by faculty and staff of the Northwestern University Cancer Center, Northwestern University Medical School, Chicago, Illinois. Dr. Nathaniel I. Berlin, director of the Cancer Center, is principal investigator for the Edison Workers Study. The program is fully funded by the Commonwealth Edison Company via a contract to Northwestern University. It has been reviewed and approved by the University's Institutional Review Board.

The NEWS evolved during the late 1970's and early 1980's as a result of increased public and private interest and concern over the possible negative effects of radiation exposure in the workplace on the health of individuals in various industries. Other programs that address concerns about occupational exposures have been developed in other industries; this program is being conducted in an electric utility company, Commonwealth Edison, one of the first utilities to explore the feasibility of nuclear power. Edison had the first large-scale privately-owned nuclear plant, Dresden, which has operated for over 25 years. Edison is also the largest nuclear operator in the United States, currently running 5 nuclear plants with 9 reactors. In 1985 Edison's nuclear stations generated over 55 percent of the electric power produced by the company.

The primary objective of the Commonwealth Edison Company Program is to assess over a sufficiently long period of time certain aspects of disease and related risks in workers in an electric utility company. Primary concerns are: (1) mortality from all causes and (2) incidence of cancer. Particular attention is devoted to radiation-related cancers, with emphasis on long-term exposure to low dose radiation. Other facets of the study include collection and analysis of data on job history, nuclear worker radiation data (badge data), smoking history, and demographic data.

Data for the program are collected from several sources: (1) company records stored on tape at Commonwealth Edison; (2) the employee, via completion of a voluntary, self-administered questionnaire; and (3) public death records (e.g. Social Security Administration and the National Death Index). Relevant data from the company records are provided to Northwestern program staff at annual intervals. Included in this information is the name, address, social security number, demographic and employment history for each employee. Also provided for those employees who wear radiation badges is the detailed bi-weekly, annual and cumulative lifetime dose information, job class and station number. Northwestern program staff also receive bi-weekly lists of employees who have left the company and who have died. Death certificates are obtained from Edison or from the appropriate state Bureau of Vital Statistics. Most important is the fact that all information provided to the NEWS is held in strict confidence. No report is sent to Commonwealth Edison that includes information identifying any individual.

In an attempt to maximize employee participation, information requested on the initial (baseline) questionnaire includes only essential data. This includes social security number, name, address, cancer history, smoking history, education history and personal references. Participants are contacted every two years for follow-up and are asked for relevant information about events that have occurred since the time of their last questionnaire. The voluntary questionnaires help identify those employees who have had cancer. Additional information is sought to follow-up on and confirm all reported cancers. In particular, with the participant's written permission, physicians and hospitals are contacted to obtain detailed medical records relating to suspected or reported cancers.

Eligible participants for the cancer incidence program (the "incidence population") are full-time employees of Commonwealth Edison Company, who were employed there on February 1, 1983, or on February 1 of any subsequent year, and who meet a minimum employment criteria (one year). All are mailed questionnaires to determine cancer incidence. As of July 1, 1986, there are 20,756 persons in the "incidence population". Full-time employees who leave Commonwealth Edison are asked to either begin or continue the questionnaire portion of the program. Additionally, these participants are asked to sign a consent form that will permit the Northwestern staff to obtain future radiation (badge) data.

Analysis of the age, race and sex distributions of the 20,756 persons currently in the incidence population shows that this study population is predominately young, white, and male. In particular, 9,898 (47.7%) of these individuals are younger than 35 years old, and an additional 5,361 (25.8%) are ages 35-44 years; only 3,001 (14.5%) persons had attained age 55 or older as of January 1, 1986. Whites totalled 16,826 (81.1%) while only 2,746 (13.2%) persons in the study are black, and 1,017 (4.9%) are Hispanic. The sex distribution shows that 17,768 (85.6%) persons in the current incidence population are male.

The program also includes a "mortality population" for study. This population consists of all employees who were employed at Commonwealth Edison on February 1, 1975, or who started after that date, and who meet the minimum employment criteria described above. It includes the "incidence population". The mortality population is being followed for deaths only. There are currently 26,556

individuals in the mortality population (as of July, 1986).

As in any study of this type, the ultimate success of the NEWS depends on the voluntary and complete participation by all of the employees invited to join the study. Such participation is vital if the study is to produce meaningful results. All participants receive periodic NEWS Letters to keep them informed of the study's progress. To assure the scientific integrity of the study, results of outcome analyses are to be submitted for review periodically to the program's External Advisory Board before being presented in final form to the Commonwealth Edison Company. The External Advisory Board consists of persons from other universities and research centers who are knowledgeable in the fields of radiobiology, cancer, epidemiology and statistics. A member of the International Brotherhood of Electric Workers (IBEW) International Staff, Washington, D.C. also serves on the Board.

All of the 20,756 persons in the incidence population have been invited to join the NEWS cancer incidence study by returning a voluntary short NEWS baseline questionnaire to the study office at Northwestern University. As of July, 1986, only 9,940 (47.9%) of those invited have chosen to return their baseline questionnaire. Analysis of the return rates shows a slightly higher response among older persons; 52.6% of persons ages 55-64 years responded and 55.1% of those older than age 64 responded, in contrast to 45.8% for the 35-44 year age group and 47.1% for those younger than 35 years as of January 1, 1986. Whites have the highest response rate (52.5%) among the racial groups, while 23.9% of blacks and 36.2% of Hispanics have returned their baseline questionnaire so far. The response rates for males and females were approximately the same (48.1% and 46.7%, respectively). It is interesting to note that 63.4% of the 7,426 persons classified as management returned the baseline NEWS questionnaire while only 39.2% of the 13,330 nonmanagement employeees responded to our invitation. Analysis of response rates by type of station where the employee worked shows that 56.0% of the nuclear station employees have returned their baseline questionnaire while only 39.4% of those at fossil fuel stations and 47.9% of the remainder of the employees have responded so far. Response rates analyzed according to years of sevice of the employees shows roughly comparable percentages across all durations of service. While the overall response rate of 47.9% may appear to be hopelessly low, it is worth noting that our rate would have been only 25.7% if we had restricted the study to only one invitation (mailing) per person. With repeat, follow-up invitations to initial non-responders we have almost doubled the baseline response rate. With additional contact and reminders via newsletters and other mailings we are hopeful that additional baseline questionnaires will be returned to our NEWS offices. It is never too late to join in our incidence study.

This prospective longitudinal cohort study of cancer incidence in the Commonwealth Edison employee population is still young and requires many additional years of follow-up before meaningful analysis of cancer incidence can be undertaken. So, while 360 definite or probable cancers have been reported to us as of July, 1986, many of these represent prevalent cancers that were diagnosed in 1982 or earlier years, i.e, prior to the initiation of our study and definition of our initial incidence population on February 1, 1983. Furthermore, when medical records are obtained to verify the diagnoses, a small number of these 360 reported "cancers" must be excluded since later information indicates that the reported case was really not cancer.

A major goal of the NEWS is to relate cancer incidence to radiation exposure in the workplace, in an attempt to determine whether employment in a nuclear power plant is hazardous to the health of employees. The radiation badge data available to us for our NEWS incidence population (through 1984) suggests that only 6.8% of the active employees have a cumulative lifetime exposure of 5 rems or more. The mean lifetime exposure among the "badge wearers" in our study population is approximately 4.33 rems, and among those with detectable lifetime exposures (0.001 rem or more), the mean lifetime exposure is 5.58 rems. Approximately 75.6% of the incidence population had no or mininal (<0.001 rem) recorded radiation exposure. It is easy to deduce that one should not expect to see large numbers of radiation-related cancers in a study population (such as the NEWS) with such low lifetime radiation exposures. It fact, it is relatively straightforward to show that even with a 100% response rate to our questionnaires (and with complete ascertainment of cancer incidence since 1983), our study has very low statistical power for detecting increased cancer incidence (regardless of type) in the current NEWS population. One solution is to expand our study to include additional nuclear power companies and/or to extend the length of our follow-up to well in excess of 20 years. A theoretical projection that we have made shows that with the addition of four companies of Edison's size and employee composition, and with a minimum of ten (10) years follow-up and complete cancer incidence ascertainment, we could detect a 23 percent increase in the incidence of all cancers, with a statistical power of 80% and one-sided significance level of 5%. (This calculation uses the non-exposed or minimally exposed (< 5 rems lifetime exposure) individuals as an internal comparison group for the "exposed" (≥ 5 rems lifetime) subset of the population).

In summary, the NEWS represents perhaps the only prospective longitudinal cancer incidence study being conducted at the present time in a nuclear power company in the United States. It has had a good beginning, but work must proceed vigorously to increase our response rates, and if possible to expand to other nuclear power companies, so that we can improve the study's statistical power to detect any increased cancer risk that may exist. The NEWS mortality study may add to the information about cancer-related occupational risk, but it also has low statistical power if only the Commonwealth

Edison employees are studied. Despite these limitations, the NEWS is an important study that with time may yield interesting data about cancer in this important occupational cohort.

REFERENCES

Mossman, Kenneth L. (1984), Ionizing Radiation and Cancer. Cancer Investigation, 2(4), 301-310.

Health Protection Program in Illinois (1985). IBEW Journal, 84(8), 7-8.

The NEWS *Questionnaire*

for office use

Social Security Number

Today's Date: Month / Day / Year

Name: (PLEASE PRINT) Last First Middle

Address:

City: County: State: Zip:

Home Telephone: (Area Code)

☐ Check here if you have moved within the last 2 years.

Date of Birth: Month / Day / Year

DIRECTIONS: Please tell us whether you have ever had cancer (Questions 1 to 7) and then answer the questions on the back. Feel free to leave any questions blank that you do not feel comfortable answering.

1. Yes ☐ No ☐ Did you ever have LEUKEMIA?
   If yes, what year? 19__ Comment:
2. Yes ☐ No ☐ Did you ever have LYMPHOMA?
   If yes, what year? 19__ Comment:
3. Yes ☐ No ☐ Did you ever have MULTIPLE MYELOMA?
   If yes, what year? 19__ Comment:
4. Yes ☐ No ☐ Did you ever have HODGKIN'S DISEASE?
   If yes, what year? 19__ Comment:
5. Yes ☐ No ☐ Did you ever have MELANOMA?
   If yes, what year? 19__ Comment:
6. Yes ☐ No ☐ Did you ever have SKIN CANCER?
   If yes, what year? 19__ Comment:
7. Yes ☐ No ☐ Did you ever have any other CANCER? Comment:
   If yes, what year? 19__ Type:
   If yes, what year? 19__ Type:

Office Use only: (__) (__) (__)

PLEASE TURN PAGE OVER

Jan. 85-B3

8. Yes ☐ No ☐ (65) Have you ever worn a badge to measure radiation exposure at any time during your employment at Commonwealth Edison?

9. Yes ☐ No ☐ (66) Have you ever worn a badge to measure radiation exposure at any time other than during your employment at Commonwealth Edison?

10. Yes ☐ No ☐ (67) Have you ever smoked cigarettes?

At what age did you first begin smoking cigarettes? __ __ (68-69)

Average number of cigarettes smoked per day? (Write in 0, if less than 1 per day) __ __ (70-71)

Total number of years you have smoked cigarettes since you first began? (Write in 0, if less than 1 year) __ __ (72-73)

11. Yes ☐ No ☐ (74) Do you now smoke cigarettes?

At what age did you last quit smoking cigarettes? __ __ (75-76)

12. Yes ☐ No ☐ (77) Have you ever used other tobacco products (pipe, cigars, chewing tobacco)?

13. Circle highest grade completed (not including college):

01 02 03 04 05 06 07 08 09 10 11 12 (78-79)

14. Yes ☐ No ☐ (80) Have you received a high school diploma?

15. Yes ☐ No ☐ (81) Did you complete at least 1 year of college?

16. Yes ☐ No ☐ (82) Have you received a bachelor's degree?

17. Yes ☐ No ☐ (83) Have you received a college degree higher than a bachelor's degree?

18. Please list 2 people who do not live with you but who could reach you at some future date. We will contact them only if we cannot otherwise locate you. (Please print.)

Name: _____

Address: _____

City: _____ State: _____ Zip: _____

Home Telephone: (__ __ __) __ __ __ - __ __ __ __
Area Code

Name: _____

Address: _____

City: _____ State: _____ Zip: _____

Home Telephone: (__ __ __) __ __ __ - __ __ __ __
Area Code

THANK YOU FOR PARTICIPATING

EPIDEMIOLOGIC STUDIES

Chair- John Harley, Consultant

The topic of Shirley Fry's talk tonight- Occupational Exposure to Uranium at a Uranium Processing Plant- is one dear to my heart for two reasons.

The first relates to my work during World War II where I was involved with the analytical chemistry of the product of one uranium processing plant. This was the Electrometallurgical Company in Niagara Falls where they converted green salt, UF_4, to uranium metal. The intentional isolation of the individual plants gave us no idea of the overall process, and our best guess was that the uranium was intended for some type of power generation- perhaps in submarines.

The second follows from my early work at the Health and Safety Lab, starting in 1949. The several small plants in the uranium process of the Manhattan Project had no specific radiation safety programs of their own. The Lab furnished industrial hygiene, radiation measurement and even medical services to each group, including the refinery at Mallinkrodt, the oxide and UF_4 plant at Harshaw, the green salt plant at Linde, the metal plant at Electromet, the rolling mill at Simonds and miscellaneous operations. In a few years, the consolidated operations at Fernald and Weldon Springs took over and we were out of the uranium business.

Specifically, our industrial hygienists descended on each plant about twice a year, took hundreds of general air and breathing zone samples and returned the to the Lab for analysis. The data were combined with time studies to give weighted exposures for each job and even for individuals. These data, plus measurements of urinary uranium, were used to develop recommendations for improvements in handling or ventilation to reduce exposures. Since the Government was paying, the recommendations were generally carried out.

In spite of these efforts, the fact that the facilities were old and not intended for such work meant that high inhalation exposures were far from exceptional. Results were usually presented in terms of multiples of the "permissible level"- at that time 50 micrograms of uranium per cubic meter. Urinary excretion was also high, particularly at the operations with soluble compounds at Harshaw, where a milligram per day excretion was often observed. The only effect noted at the time was proteinuria in some workers, but the time of observation was limited.

The records of these studies and the medical examinations have been generally available. Originally they were supposed to be reviewed by Dr. Thomas Mancuso but for the last few years they have been in the custody of ORAU. Tonight, we are going to hear about the epidemiology they are working on for one of these plants- Linde Air Products Co. in Tonawanda, New York. Dr. Fry will make the presentation.

SUMMARY OF COOLFONT VI AND LOOKING TOWARD COOLFONT VII

Ethel S. Gilbert, Pacific Northwest Laboratory

As has been the case in the past, a major strength of this conference is the intermingling of scientists from several disciplines. As a statistician who has been mainly involved in epidemiological studies, I find input from radiobiologists and others who have a better understanding of mechanisms than I, is very helpful. They may be able to suggest analyses that are designed to test specific theories, and that may be more relevant than analyses I would think of on my own. Also, I am well aware that there are many questions that cannot be answered by statistics and epidemiology alone, and thus I appreciate presentations (such as those on Monday and Tuesday mornings) which provide insights with regard to what is going on at the cellular level.

To turn things around, I hope that the biologists and physicists have come away with a greater appreciation of statistics and epidemiology. Human epidemiology studies are our only means of studying health effects directly in man, and thus must play an important role. In addition, statistics has an important role to play in that the theories proposed by biologists and physicists need to be rigorously checked by applying appropriate statistical methods.

A recurring theme in this conference has been the importance of problems related to dosimetry. The effects of errors in dosimetry on analyses of epidemiological and other data is a subject in which I have a strong personal interest. I have recently learned that there are several very good statisticians working on the problem of how to analyze data when it is known that the exposures have been measured with error.

In order to handle this problem, it is necessary to have information on the nature and the magnitude of the errors. I was thus pleased to hear that the new estimates for the doses received by the Japanese A-bomb survivors will be accompanied with error estimates. The discussion of dose measurement errors in the occupational studies discussed on Thursday morning indicated concern for the problem in this context as well.

Estimating doses resulting from internal depositions is especially difficult since it requires understanding the manner in which material is metabolized by man and laboratory animals. This was a recurrent them in the talks presented on Wednesday as well as Thursday evening.

A concept that I found interesting is that a full understanding of dosimetry is very much related to a full understanding of the underlying biology. In addition, dosimetry is not only a question of being able to measure what we have traditionally called dose, but also of learning what we should be measuring to best explain the health effects of interest. These concepts were introduced Monday morning, but came up repeatedly as the week went on.

On Thursday, Dr. Anderson raised two rather important issues, one related to terminology and the other related to simple versus complicated statistics. I think these are important issues, and thus I would like to comment on them further.

With regard to simple versus complicated statistics, we statisticians may on occasion be guilty of using overly complicated procedures when simple ones would have been adequate. Perhaps we do on occasion become overly enchanted with the elaborate tools that are so readily available to us.

On the other hand, many of the data sets we are analyzing are not only complex, but represent enormously valuable resources. These include human data such as the Japanese A-bomb survivor data, data from animal studies such as the dogs exposed to inhaled plutonium, and cytogenetic data. In my opinion, we have to give these data our best. That means using the most sensitive techniques, which in our opinion do the best job of appropriately addressing the questions of interest and of handling the various biases and idiosyncrasies of the data. These methods are not always simple.

However, once we have conducted a so-called complicated analyses, I think we have a strong obligation to try to make what we've done understandable to scientists in disciplines other than statistics. Although it is not easy, I am convinced that even with the most complex of methods, it is possible to describe the essence of what has been done in an intuitive manner. Or, we might say that any method will appear simple and straightforward if it is thoroughly understood and properly explained.

That raises the general question of communication, which I think was also Dr. Anderson's concern in his comments regarding terminology. Whenever we have as diverse a group of disciplines as we have here at Coolfont, there are bound to be communication problems. It is not easy to present a talk which both introduces the basic concepts to the novice, and also presents material which is stimulating to those who have been in the field for many years. I see this as a major challenge, because I think that one of the main reasons for holding this conference is to encourage and enhance communication across disciplines.

On the positive side, I think we have succeeded in bridging many gaps. Our speakers are to be congratulated for presenting talks that in general provided insights for those in many disciplines. However, I also think that with additional effort we could do better. I hope we will work to do even more in the future to meet the objectives of the Coolfont conferences.

APPENDICES

CONFERENCE PROGRAM

SUMMARY OF EVALUATIONS

LIST OF PARTICIPANTS

ASA Conference on Radiation and Health

Coolfont Conference Center
Berkeley Springs, West Virginia
July 20–25, 1986

Conference Chairman
Jerome Wilson, National Cancer Institute

Program

Monday, July 21

9:00 a.m. **Overview: Radiation and Health**

Chair: **Charles Land**, National Cancer Institute

Keynote Speaker
Arthur Upton, New York University Medical Center
Microdosimetry
Dudley T. Goodhead, Medical Research Council, England
Radiation Biology
A.M. Kellerer, Republic of West Germany

2:00 p.m. **The Chernobyl Disaster**

Michael and **Marie Stoline**, Michigan State University

7:30 p.m. **Atomic Bomb Dosimetry (Latest Assessment)**

Chair: **Gilbert Beebe**, National Cancer Institute

Atomic Bomb Data (Dosimetry)
William H. Ellett, National Academy of Sciences
Atomic Bomb Data (Analysis)
Dale Preston, Radiation Effects Research Foundation, Japan

Tuesday, July 22

9:00 a.m. **Cytogenetics and Radiation**

Chair: **Michael Bender**, Brookhaven National Laboratory

Radiation and Cytogenetics (Human Studies)
Gayle Littlefield, Oak Ridge Associated Universities
Radiation and Cytogenetics (Animal Studies)
Julian Preston, Oak Ridge National Laboratory

7:30 p.m. **Statistical Methods**

Chair: **Philip Archer**, University of Colorado, School of Medicine

Statistical Analysis of Cytogenetic Dose–Response Curves
Edward L. Frome, Oak Ridge National Laboratory

Wednesday, July 23

9:00 a.m. **Uranium and Health Effects**

Chair: **M. Eisenbud**, University of North Carolina, School of Public Health

Uranium Metabolism
E. McDonald Wrenn, University of Utah
Uranium and Radon
Naomi Harley, New York University Medical Center

7:30 p.m. **Lifespan Study of Dogs Exposed to Inhaled Plutonium**

Chair: **Bernard Pasternack**, New York University Medical Center

Jim Park and **Ethel Gilbert**, Battelle Pacific Northwest Laboratories

Thursday, July 24

9:00 a.m. **Panel: Epidemiologic Studies of Nuclear Power Plant Workers in Canada and the United States: Needs, Status, and Plans**

Chair: **Pat Ashmore**, Health and Welfare, Canada

Panelists:
Study of Northeast Utilities
Jeanne Loughlin, Epidemiology Resources, Inc.
Ontario Hydro Workers
Lois Green, Health and Safety Division, Ontario Hydro
Calvert Cliffs Workers
Robert Goldsmith, Department of Energy
Commonwealth Edison Workers
Joan S. Chmiel, Northwestern University Cancer Center

7:30 p.m. **Epidemiologic Studies**

Chair: **John Harley**, Consultant

Occupational Exposure to Uranium at a Uranium Processing Plant
Shirley Fry, Oak Ridge Associated Universities

Friday, July 25

9:30 a.m. **Conference Wrap-Up**

Open Discussion
Jerome Wilson, Conference Chair
Summary of Events and Prospects for 1987
Ethel Gilbert, Conference Vice Chair
General Overview and Future Problems
R.J. Michael Fry, Oak Ridge National Laboratory

1. WHAT I LIKED MOST ABOUT THE CONFERENCE:

The small group of attendants and the relaxed time schedule which permitted ample time for private discussions. The friendly atmosphere and the perfect organization.

Program good. Good mix of congenial people. Presentation good.

The informality of the meetings while maintaining scientific quality and complete openness and objectivity in presentations and discussions.

Mixture of disciplines, informality, opportunity to meet colleagues with shared interests, good choice of speakers.

Time and opportunities for communication with participants.

The informal atmosphere with ample opportunity for interaction.

Small group facilitates interchange.

Relatively small size seems to encourage lively discussions; good opportunity for interaction between statistician and others involved with radiation studies.

Interactions between biologists, epidemiologists, physicists, and statisticians.

Meeting congenial people, keep up with what is new; good food.

The schedule—9-12 AM; 7:30-9:30 PM.

Interdisciplinary mix of topics. Cytogenetics—a very interesting new area this year.

Interaction of participants; smooth operation, well-coordinated arrangements.

The friendliness and the opportunities to exchange information and views.

Topics were new. I learned a lot. Well organized. Facilities very good. Especially liked the cytogenetics talks.

Congenial atmosphere, opportunity to meet and talk with others in related fields.

2. WHAT I LIKE LEAST:

Can't think of anything I disliked.

I have no complaints. (4)

I found the weather conditions a little oppressive.

Although in some ways a strength, the mix of health physicists, statisticans, and epidemiologists did not seem compatible. Each focussed (as is natural) on their own discipline and seemed disdainful of the other disciplines.

Professional jargon of someone else's profession.

PA System.

The inability to hear people when seated in the back of the room.

No evenings off. Insufficient discussion time.

So little to do in the afternoon.

Long, narrow meeting room and speakers not using microphone.

Suggestion that Coolfont should take place biennially.

Lack of laying groundwork by speakers—this is bad with mixed group. Poor timing by some speakers.

The problems with the air conditioning—too damned cold.

Most people knew each other and their work. Was hard for a new participant to fit in. Some talks too technical—not enough handout material, so non-experts couldn't learn as much as they could have. Five days is too long for a meeting.

Meeting after 10 PM.

3. I WOULD RECOMMEND THESE IMPROVEMENTS:

General topic could be formulated to include one or two problems to be solved or to be intensely discussed during meeting.

Rearrangement of meeting room seating in order for participants to get a clear view of the audio-visual presentations.

It might not hurt to cut the length by one day.

More emphasis on statistical methodology and a little less biology.

It would be good if people could all stay in a more central location.

Have Wednesday afternoon session and Wednesday night free.

A TV in the conference room for use in the afternoons. Along with this, bring the latest issue of Time, Newsweek, Atlantic, etc.

Handouts of viewgraphs.

One or two afternoon tutorials on the basics (one hour each). There could be statistics/epidemiology/dosimetry/radiation measurement etc. in this series.

Avoid days with three sessions. Need amplifier in some cases.

More detailed handout materials. More methodology talks.

We need some new blood, perhaps graduate students could provide this.

4. WOULD I ATTEND ANOTHER CONFERENCE OF THIS TYPE?

Yes. (16)

Possibly.

Not sure. Depends on speakers, topics, and funding availability.

5. OVERALL EVALUATION:

One of the most pleasant and instructive meetings to attend.

Excellent. (6)

Pretty good! (2)

Good. (2)

Very enjoyable, informative, useful in terms of meeting others in this field whom I don't already know.

Very useful and relaxing conference.

Favorable.

Very informative.

Very good conference.

The people invited were excellent mixers.

One of the better meetings.

Highly enjoyable and well worthwhile.

A positive experience.

6. OTHER SUGGESTIONS:

Provide ample time not only for the evening presentations (especially general surveys would need sufficient time to reach the uninitiated).

A week is too long. Hold in the autumn.

It would be nice to have a methodological workshop available using a simplified data base to illustrate computation of methods discussed by speakers (eg., Poisson regression).

Pay for meals rather than part of lodging cost.

Consider 3 1/2 instead of 4 1/2 days—Hear from some that being away from office for full week plus two weekends is difficult.

I would suggest a biennial arrangement of meetings.

New location? Easier to get to, but same type of atmosphere.

7. SUGGESTED TOPICS FOR FUTURE CONFERENCES:

Models and numerical methods in hazard rate analysis (specific problems: initial part of the dose effect relation and RBE as a function of dose) or statistical methods to describe random patterns (of energy deposition; specific problem: can spatial random patterns be reconstructed from auto correlation function?)

Ultraviolet radiation—modelling, epidemiology and biology of UVR effects. Interactions of different agents.

The impact on the field caused by technological advancement—particularly in terms of testing.

Examination of morbidity of nuclear workers.

Problems in environmental radon epidemiology, especially dosimetry and confounding factors (e.g. smoking). Bernie Cohen, University of Pittsburgh, is possible speaker.

Dosimetry in epidemiological studies of radiation workers.

A comparison of methods of survival analysis on a common data base and their ramifications on data interpretation.

Mike Bender hinted at some unsolved statistical problems but did not have time to state them. I would like to see more unsolved statistical-biological problems presented by biologists.

New analysis of Japanese A-Bomb survivor data.

Analyses of RERF A-Bomb survivor data.

The epidemiology, health physics, and radiation effects. People will always have new studies to report.

Extrapolation or scaling from in vitro to animals and animals to humans.

Development of radiation standards; and update on the D.O.E. supported epidemiology; plutonium and uranium registries.

Might have one session on brief updates on previous recent topics. Medical occupational exposures. Genetic epidemiology. Statistical treatment of clusters.

Epidemiologic methods session. Other methods sessions, but with more documentation, etc. (2)

8. PLEASE EVALUATE AS: A=Very Good; B=Good; C=Fair; D=Poor; E=Terrible

Program: A(12); A/B(1); B(5)
Speakers: A(7); A/B(3); B/A(1); B(7)
Discussants: A(4); A/B(2); B+(1); B(5); C(2)
Chairs: A(8); A/B(1); B(9)
Accommodations: A(5); B(10); B/C(1); C(2)
Food: A(9); B(9)
Overall: A(8); A/B(1); B+(2); B(7)

9. OTHER COMMENTS:

Attendants could be asked to list some of their current research problems (especiallly if they relate to statistics or mathematics) on a sheet which is distributed before the conference. This might make it even easier to find overlap of work and methods and to bring materials to conference.

Multiple housing should be carefully assigned. The absence of fans in a non-airconditioned house in mid-summer is very uncomfortable.

Meet every year.

A sound financial base is being established with NRC/DOE/NCI/BTC. This should be a priority to insure the persistence of the Coolfont Conferences and the ability to invite authoritative speakers. Foreign invitees have added an important dimension.

Might be worthwhile having a speaker or two plus discussion on how health statistics are developed—particularly on a national level and also something on the cancer registries.

This field is very small, apparently. It seems hard for a new person to fit in. Conference should be broadened in scope if new people and students are to be attracted. Perhaps a "reading list" should be provided prior to the meeting. This was a worthwhile conference for me—much different than the usual statistics (ASA) meeting.

The conference coordinator did a wonderful job of organizing everything. Program had a nice flow from theory and microdosimetry through in vitro studies and ending with epidemiology studies of occupational exposure.

ASA Conference on Radiation and Health

Coolfont Conference Center
Berkeley Springs, West Virginia
July 20–25, 1986

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