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Commissioner, U.S. Nuclear Regulatory Commission
before the
NRC Workshop on Site Characterization for Decommissioning
Rockville, Maryland
November 29, 1994

In Search of . . . Background

It is a pleasure to be here this morning at the NRC Workshop on Site Characterization for Decommissioning. I'm so pleased to see so many in attendance because I think that the issue of decommissioning is one of the most significant issues on the Commission's plate, one that will have long lasting and far reaching impacts.

Introduction

As you know, the NRC is undergoing a lengthy process aimed at formulating radiological criteria for the decommissioning of NRC-licensed facilities. During that process, extensive discussions have focused on four possible approaches to this task: (1) establishing an annual risk or dose limit for an individual; (2) establishing an annual risk or dose goal; (3) requiring use of the best available technology; or (4) requiring return of the site to background radioactivity. While many commenters preferred a risk-based or dose-based standard, many others favored the "return-to-background" approach.

The proposed rule attempts to accommodate both groups by establishing a dose limit for release of the site of 15 millirem per year Total Effective Dose Equivalent (TEDE) for residual radioactivity distinguishable from background with further reductions As Low As Reasonably Achievable, or ALARA.

First, an aside. To make life easier, I will usually use the quantity total effective dose equivalent expressed in units of mrem. But for brevity's sake, I will use the term "dose" when speaking of total effective dose equivalent.

The objective expressed in the proposed rule is to cleanup up to dose levels that are indistinguishable from background. Return to background!

Sounds good, doesn't it? On the surface, this seems like a relatively easy, common-sense approach: for example, survey a nearby spot unaffected by a nuclear facility, use that radiation level as a baseline, clean up the contaminated site to that level, and . . . voila! The site is decommissioned, the method indisputable, the job completed.

But, as we all know, the devil is in the details. And in this case, the devil could produce a series of torments for those involved in returning a site to background.

I'd like to discuss some of the details with you this morning, particularly the details that are relevant to determining what background is and how it is measured. But I'd also like to place this discussion of the details within the broader context of a regulatory decision-making process.

Risk-Based Decision-Making

The decision-making process I'm referring to is "risk-based" decision-making, a process gaining popularity both in the Clinton Administration and in Congress, and widely advocated by the most recent Supreme Court member, Justice Stephen Breyer. Let me say at the outset that as far as I know this particular mode of making decisions was not followed in any rigorous way in formulating the proposed rule. Nevertheless, for reasons which I hope will be clear later in this talk, it may offer a useful framework for working out the details of a decommissioning program.

Risk-based decision-making allows for the assumption that the resources available for limiting risks are not inexhaustible and seeks to ensure that the resources which are available to society as a whole will be put to the best overall use considering risk, cost and benefit. It can be divided into three basic components as illustrated by the following Sydney Harris cartoons: (1) risk assessment, (2) selection of an acceptable level of risk, and (3) risk management. In the context of decommissioning, risk assessment is an evaluation of the hazard associated with residual radioactivity remaining at a site released for unrestricted or restricted use. Selection of an acceptable risk level involves weighing the benefits of lowering risk to a certain level against the costs and may involve comparing the risk at issue with other similar risks confronting society. Risk management consists of a regulatory process designed to keep the risk below the level found to be acceptable.

Risk Assessment

As the NRC begins to formulate a regulatory program to manage the risk associated with sites cleaned up to levels of radiation contamination that are indistinguishable from background, it might be useful to revisit Step 1 of the risk-based decision-making process: risk assessment. Perhaps this can most easily be done by reviewing the levels of radiation to which humans are typically exposed and the health consequences of those levels.

Broadly speaking, the average American's annual radiation dose is attributable to two sources: naturally occurring radiation which, in the U.S., produces about 82% of the dose, and anthropogenic radiation which produces the remaining 18%. Humans are bathed in a sea of naturally-occurring radiation which has been present since the formation of the earth. About 56% of the average annual dose is from radon and its decay products. Another 11% is from other internal sources, mainly from inhalation and ingestion of food and water which contain naturally occurring radioactive elements. The remainder is from external sources, about 7.5% from cosmic rays and about 7.5% from terrestrial gamma ray sources such as uranium, potassium, and thorium, that are present naturally in soil and rocks.

Just to complete the picture, let's look at the anthropogenic sources. About 11% of the average annual dose comes from medical x-rays, about 4% from nuclear medicine, and about 3% from consumer products such as smoke detectors. The small remainder is from fallout from weapons testing, and occupational exposures at various nuclear facilities.

The proposed rule defines "background radiation" as:

> radiation from cosmic sources; naturally occurring radioactive material, including radon (except as a decay product of source or special nuclear material); and global fallout as it exists in the environment from the testing of nuclear explosive devices or from past nuclear accidents like Chernobyl which contribute to background radiation and are not under the control of the licensee.

Although naturally-occurring radiation and fallout from atmospheric weapons testing and the Chernobyl accident are present everywhere, each of these components of what I'll refer to as background, and the corresponding dose delivered, is by no means constant. Background levels fluctuate significantly due to various physical phenomena that differ from place to place and change with time at any given place. For example, over the long-term, cosmic radiation varies by about 10% over the 11 year solar cycle. Seasonal cycles produce changes in soil moisture, rainfall, snow cover, and evapotranspiration that cause variations in the dose from terrestrial gamma radiation, fallout and radon. Many sporadic geophysical phenomena, volcanic eruptions or earthquakes for example, can also introduce radioactivity into the environment.

Temporal variations can also occur over the short term. Rain, for example, will wash out radon and other radionuclides from the air causing an immediate rapid increase in dose that typically decreases exponentially after the rain stops. Doses from radon typically exhibit a diurnal cycle due to local climate conditions.

Radiation varies spatially. The dose from cosmic radiation is a function of both latitude and altitude. The population of the city of Denver, at an altitude of a mile receives an annual cosmic ray dose that is a factor of 2 higher than the U.S. average. Terrestrial gamma radiation, including fallout, varies from place to place because of differing amounts of uranium, potassium and thorium in the earth's surface material and can easily differ by a factor of 10 across the country. Granite, for example, contains higher than average uranium concentrations and

monazite sands can have particularly high concentrations of thorium. Furthermore, humans sometimes alter soil content with fertilizer which contains varying amounts of potassium-40. Spatial variations occur locally as well; the well-known Reading Prong in New Jersey provides an interesting regional example. The average annual dose from gamma radiation is approximately 50 mrem but if one resides closer to the rock formations along the prong, the annual dose can be much greater. About sixty miles away at the New Jersey shore, the gamma radiation dose levels fall to less than 10% of the average measured over the Prong.

Even in the immediate environment of a typical facility site (this happens to be Shoreham, Long Island), significant fluctuations occur (Figure 1). For this site with an annual average terrestrial gamma dose of about 35 mrem, when measured simultaneously, levels varied by more than 50% over a distance of only a mile within the site boundary, and the areas within a 4- or 5-mile radius of the site exhibited variations with even greater extremes.

This site in rural New Jersey, used as a background monitoring station, is only 50' by 200' (Figure 2). And even within such a small area, simultaneously measured terrestrial gamma radiation dose levels, which average about 125 mrem per year, differ by as much as 30% from spot to spot. That translates into differences of close to 40 mrem per year.

Other local variations occur due to the types of houses and buildings in which people live and work. Persons living in a wood frame house usually receive lower doses than persons living in an all brick house because, even though brick is a better shield of outdoor radiation, it has higher concentrations of naturally occurring radioactivity than wood. Persons working in granite and marble buildings may receive higher doses due to the radioactivity in the stone. Even moving from a rural to an urban setting may increase an individual's annual dose, due to the level of radioactivity present in concrete. The dose from cosmic rays can be measurably higher on the top floor of a high rise than on the ground floor. Measurements in a 12 story building in Manhattan indicated a cosmic ray dose on the ground floor one third that on the 12th floor, due principally to the shielding effect provided by many stories of concrete from the building in question as well as adjacent structures. In addition, a person's annual dose from radon can vary dramatically, by a factor of 10 or more, depending upon where they are and the adequacy of ventilation.

To further complicate matters, these temporal and spatial variations can be interdependent. For example, determining the average annual dose received from terrestrial gamma radiation cannot be done simply by measuring differences in soil concentration, since it is also affected by weather conditions. Moreover, usage must be considered and can result in what is often referred to as technologically enhanced natural background radiation. Finally, the actual dose to particular humans is heavily dependent upon the specific external and internal pathways of exposure.

Obviously then, there is no single number that represents the annual dose to U.S. citizens from background. But for perspective, it is useful to know that the average annual background dose for the U.S. population is about 300 mrem with about 200 mrem from radon, about 40

mrem from other internal sources, about 25 mrem from cosmic rays and about 25 mrem from terrestrial gamma rays. The average annual dose from fallout is less than 1 mrem.

However, because of the many factors that cause both spatial and temporal variations, the annual U.S. dose from background can easily range from 100 mrem for people who live in well-ventilated wooden houses on sandy soil at sea level to about 1000 mrem for people living in the Denver area, a factor of 10 (Figure 3). At the Shoreham site, annual doses from terrestrial gamma radiation differed with location alone by as much as 25 mrem per year. At the small New Jersey site, the equivalent spot to spot difference was as high as 40 mrem per year. It is in the context of these variations that the selection of 15 mrem over background as the acceptable annual dose for residual radiation from a decommissioned site must be viewed. For additional perspective, consider that we rarely choose our residences or domestic habits based on exposure to background radiation, yet the choice to live in a brick rather than a wood-frame house can increase one's annual dose by 45 or 50 mrem. A gas stove can deliver about 15 mrem per year to the lungs due to naturally occurring radioactive elements in the gas and a single flight across the U.S. yields about 4 mrem. A Denver resident can receive double the cosmic ray dose, triple the terrestrial dose, quadruple the radon dose, and a higher intake of radionuclides in drinking water compared to persons living in a coastal region--and if the house is not well ventilated the total dose could be still higher!

Selection of an Acceptable Level of Risk

To place the risk from exposure to background radiation in context, let's look at some general risks to the population. About 33% of the general population in the United States die of heart disease and about 23% die of cancer. Non-cancerous lung disease (7.7%), strokes (6.7%) and accidents (4.3%) also figure strongly as major causes of death (Figure 4). Comparing these causes of death, all of which carry a risk of greater than 1%, with the elective or accidental risks faced by selected groups or by the general population illustrates the complexity of adding societal choice to risk-based decision-making in terms of selection of an acceptable level of risk (Figure 5). Smoking one pack of cigarettes daily will result in death from a related cause for about 28% of smokers and a motorcyclist has about an 11% lifetime chance of dying in a motorcycle accident. By comparison, the average American's risk of dying in an air accident is several orders of magnitude lower, about 0.02%.

As I said earlier, the annual dose from natural background in the U.S. ranges from 100 to 1,000 mrem with an average of about 300 mrem. When relating these annual doses to risk, the risk assessment models developed by the International Commission of Radiological Protection (or ICRP) are usually applied. The ICRP performs risk assessments for both deterministic and stochastic effects of exposure to radiation based on research reports of radiation effects on tissues and animals, as well as on human epidemiology studies and modeling. For the purposes of radiation protection, the ICRP *assumes* a linear non-threshold dose-effect model and basically extrapolates to estimate the probability of harm resulting from low doses and dose rates where there is little, if any, human health effects data.

Using ICRP's method of risk assessment, the average annual 300 mrem dose from background produces a lifetime risk of fatal cancer of slightly less than 1 in 100, or approximately 0.82%. The corresponding lifetime fatal cancer risk for 100 and 1000 mrem are approximately 0.27% and 2.7%, respectively (Figure 6).

So how would an additional increment of 15 mrem change the public's risk from natural background? Looked at in isolation, 15 mrem per year over a 70-year lifetime would result in a risk of about 0.04% yet another decade lower on this log scale. When added to the risks associated with low, average, and high annual doses from background it is barely distinguishable (Figure 7). Indeed 15 mrem represents 5% of the average annual dose and is lost within the range of background which spans a factor of 10.

It is perhaps useful to note that for members of the public, the NCRP recommends an annual limit of 100 mrem for continuous exposure and an annual limit of 500 mrem for infrequent exposures due to all anthropogenic sources and recommends that ALARA be practiced below that. They further recommend that where there are multiple sources, no single source or set of sources under one control should result in an individual being exposed to more than 25 mrem annually.

What does one conclude from all of this? The limit of 15 mrem, including 4 mrem from drinking water which in itself is material for a lengthy lecture which I won't attempt to address here, carries a risk that is a small increment over the risk from background itself. Given that the risk is small and masked by the variation in the risk over the range of background doses, one must ask what all this should imply for the third or final component of risk-based decision-making, risk management.

Risk Management

The major questions for risk management are: (1) What is it that will be measured or used to represent "background" at a particular decommissioning site? (2) What will be measured to determine compliance with the 15 mrem limit? and (3) What margins of error or what uncertainties will be considered acceptable in determining compliance?

The difficulties involved in answering these questions become apparent when a site's decommissioning efforts are broken down into a series of steps and the complications that can exist with each step are examined. The overall process consists of, first, an analysis of the activities that have been performed at the site to be decommissioned; second, an assessment or survey to establish what represents background and a survey of the site to determine the degree of cleanup required; third, cleanup; fourth, a resurvey of the site; and, finally, release of the decontaminated site.

Each of these activities can be further broken down into sub-steps. For example, the person performing an analysis of the activity at the site must ask a series of questions: (1) Did the licensed activities involve single or multiple radionuclides? (2) With respect to each

radionuclide, does it also exist in background or is it only produced as a result of licensed activities at the site? (3) For each radionuclide, are there single or multiple pathways that may result in exposure to humans?

Surveying also has multiple sub-steps. Survey methods and the required number of surveys of each type must be determined to establish the background level or levels. The corresponding number of site surveys that will be necessary to establish the level of residual radioactivity on site with reasonable confidence must be determined and the background surveys and initial site surveys must then be performed.

The site is now ready for cleanup. Based on the analysis and survey results, the appropriate methods must be chosen and cleanup performed with periodic re-surveying to determine the level of progress until the release criteria are met and the site is ready for release.

Let's consider a few examples of how this process actually works. First, consider a simple example in which the residual radioactivity involves a single, non-naturally occurring nuclide. For simplicity's sake, postulate that the radionuclide has only one pathway of exposure. This will result in a single set of surveys, presumably a single method of decontamination, and a straightforward path toward releasing the site.

For a second example, let's consider a slightly more complicated scenario, involving multiple naturally occurring nuclides, at least one of which is known to result in human exposure via several pathways. This analysis is still relatively simple, but the surveys will be somewhat more complex. In this situation background will have to be established in a manner that accounts for variability, and that will differentiate quantitatively between background radiation and that produced by site activities. The clean-up may also be somewhat more complex due to the multiple nuclides and pathways of exposure.

The third scenario, unfortunately, may be the most realistic picture for most licensees, including reactor facilities. In this case, the analysis may involve a whole spectrum of radionuclides, some, but not all, of which occur in background. It may also involve a variety of interrelated pathways of human exposure. As a result, establishing background becomes much more complicated, even for a site with a detailed pre-operational survey. Multiple elements of spatial and temporal variation will complicate this scenario further, requiring a higher number of surveys and sometimes multiple methods to achieve the necessary degree of confidence. The decontamination of such a site, of course, will be correspondingly more difficult, involving multiple clean-up methods and, quite possibly, repeated attempts, with re-surveys performed as necessary until the criterion of 15 mrem above background has been met and the site is ready for unrestricted release.

How does this affect cost, certainly an element in risk-based decision-making? Survey costs alone, not even considering cleanup costs, will vary based on the complexity of the situation considering the number of surveys taken and the quality of those surveys in terms of the degree of confidence required, or level of uncertainty considered acceptable.

Consider the cost per sample of various radiation measurements likely to be used in any major decommissioning effort (Figure 8).[1] Assessing the potential radiation dose to humans for a multi-nuclide site could require a complete pathway analysis, including measurements of external gamma dose; air, soil and vegetation samples; and samples of surface water, drinking water, and precipitation. Obviously, to attempt to sample and measure every cubic meter of the relevant environment would be both impractical and prohibitively expensive. Instead, a sampling strategy must be developed combining radiation survey readings over large areas with selective sampling and analysis at representative locations, using the results of past measurement programs as appropriate.

Even with an efficient sampling strategy, however, the cost of performing surveys just to establish background can escalate sharply depending on the degree of uncertainty that is acceptable, which will directly influence both the survey methods employed and the number of surveys taken. In general, measuring smaller doses means increasing costs as more sophisticated techniques are employed.

Similarly the costs of site surveys and decontamination increase based on the background criteria employed and the level of sensitivity and confidence desired. For some radionuclides, the detection limits of standard laboratory instruments can be reached, causing the survey costs to rise dramatically as sophisticated research techniques become necessary. For naturally occurring radionuclides or those present in residual levels from weapons fallout, it may be virtually impossible to distinguish the contribution of site activities given the spatial and temporal variations in background discussed earlier.

Just as an example, consider the cost of measuring cesium-137 in soil (Figure 9).[2] At dose increments of about 30 mrem per year or higher, the cost is about $50 per sample. The cost roughly quadruples when trying to measure at levels of 10 mrem per year or less--based on the need for more sensitive laboratory methods--and increases dramatically again, to about $500 per sample, when measuring at a level of 0.3 mrem per year, which requires sophisticated research techniques. Because cesium-137 is present in residual radioactivity from weapons fallout, the typical levels and degree of variability make the cost of measuring this radionuclide at dose increments of 0.1 mrem per year more or less indeterminate.

What all this reveals is that every assessment of dose due to either natural or anthropogenic radiation will entail some degree of uncertainty. Whether that uncertainty stems from spatial or temporal variations, the limitations of the measurement technique, or the ability of the analyst to interpret data, it is still uncertainty, and it can never be entirely eliminated. Now let's review how the compliance process might work. First, background (χ_o) must be

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[1]NUREG-1496, Vol 2, "Generic Environmental Impact Statement in Support of Rulemaking on radiological Criteria for Decommissioning of NRC-Licensed Nuclear Facilities," Appendices, p. A-44, August, 1994.

[2]NUREG-1496, Vol 2, "Generic Environmental Impact Statement in Support of Rulemaking on radiological Criteria for Decommissioning of NRC-Licensed Nuclear Facilities," Appendices, p. A-53, August, 1994.

determined. But, unless it is zero, this is clearly not well-defined and carries an uncertainty (σ_0). To determine if cleanup is sufficient, the site must be surveyed to determine what remains (χ_1) which may or may not include natural background as discussed earlier. This, too, of course, carries an uncertainty (σ_1). Compliance requires that what remains after cleanup not contribute more than 15 mrem above background.

In addition, the proposed rule requires that further reductions be made As Low As Reasonably Achievable. Defining ALARA, in this framework, might be much more problematic than when working with higher, more readily measurable doses. Can ALARA be assigned a cost-per-dose-increment value, as is done for occupational exposures? Is it simply a matter of vague principle? And how will it take into consideration other risks, such as those associated with the decommissioning activities themselves? These are the questions of the risk management phase of risk-based decision-making.

Now let us return to the framework of risk-based decision-making which is premised on balancing risk, cost, and benefit. To implement the 15 mrem criterion, as well as ALARA, in this context, one needs to ask at least two fundamental questions:

1) How should both background and residual radioactivity be defined or measured in practical terms, and what degree of uncertainty will be considered acceptable? Recall from the examples of our earlier discussion that if one takes into account spatial or temporal variations of background, not to mention measurement uncertainties, the sigma may easily be of the same order as, or even multiples of, the 15 mrem criterion.

2) The second question follows naturally from the first: given that the risk associated with a 15 mrem residual dose adds very little to the risk of exposure to background and indeed is buried in the noise of the natural variations of that background, then how much money and effort should be spent not only to clean up to this level, but to assure compliance?

Conclusion

These are among the questions that we, as regulators, licensees, and members of the public must consider as we proceed toward final decommissioning rulemaking. And remember, I've only touched the surface. For example, we haven't even discussed the proposed 4 mrem criterion for the water pathway and the associated risk management scheme necessary to assure compliance. These are challenges of risk-based decision-making as we all go in search of background.

In this endeavor, I would urge that we be ever mindful of our goal as captured in the NRC's mission, that is, "to help assure that the use of nuclear materials is carried out in such a way that public health and safety, the common defense and security and environment are protected," and that we be mindful of the principles of good regulation, namely, independence,

openness, efficiency, clarity, and reliability. This is our challenge as we strive to protect the citizens of our nation and fulfill our responsibilities as stewards of our planet. I, for one, welcome the challenge, daunting as it may seem, and I look forward to the contributions and participation of all parties as we proceed toward what I hope will be rational and responsible final rulemaking.

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RELATIVE TERRESTRIAL GAMMA RADIATION LEVELS (MAY 1974)

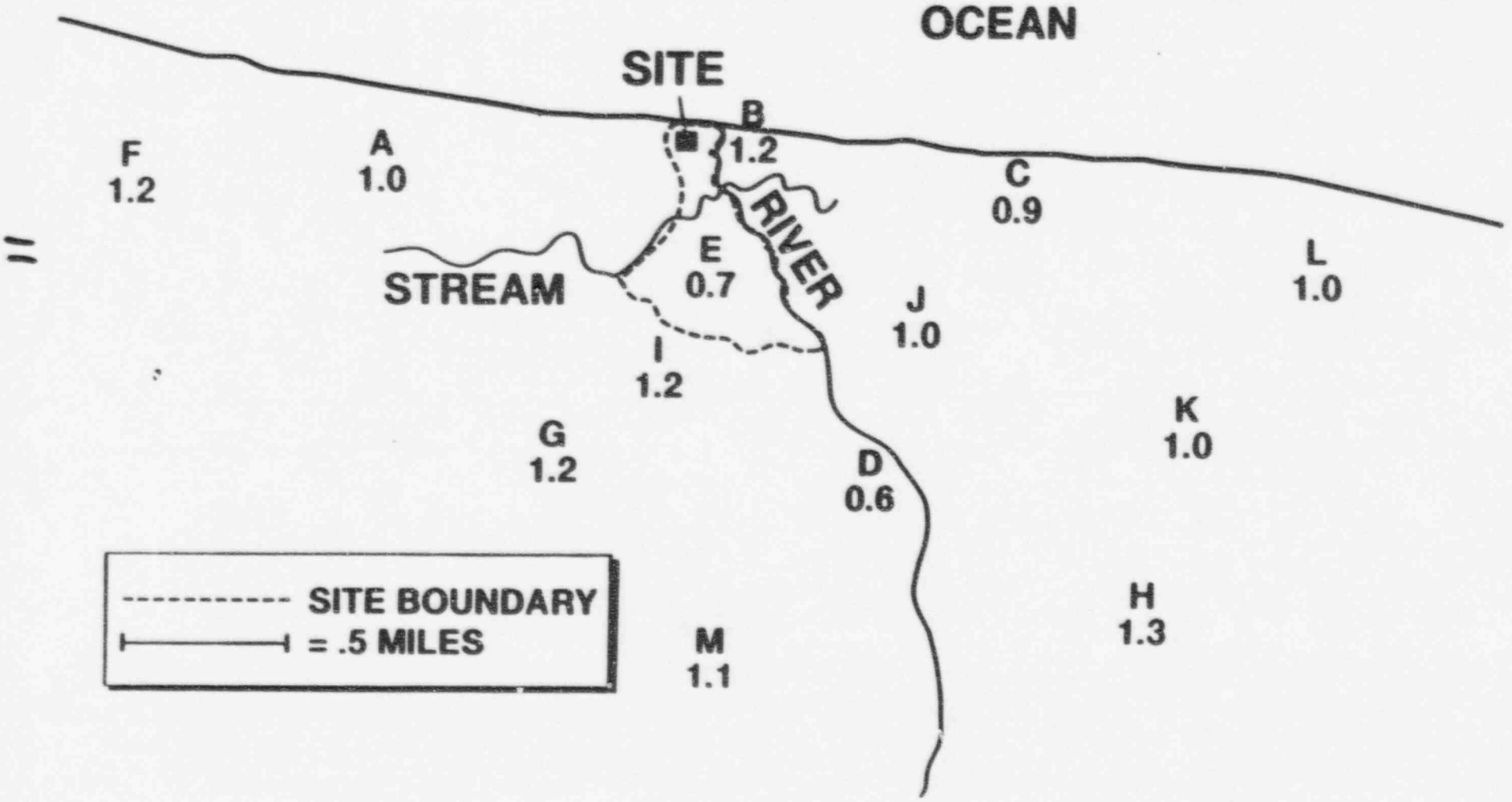


FIGURE 1

RELATIVE TERRESTRIAL GAMMA RADIATION LEVELS (SEPTEMBER 1974)

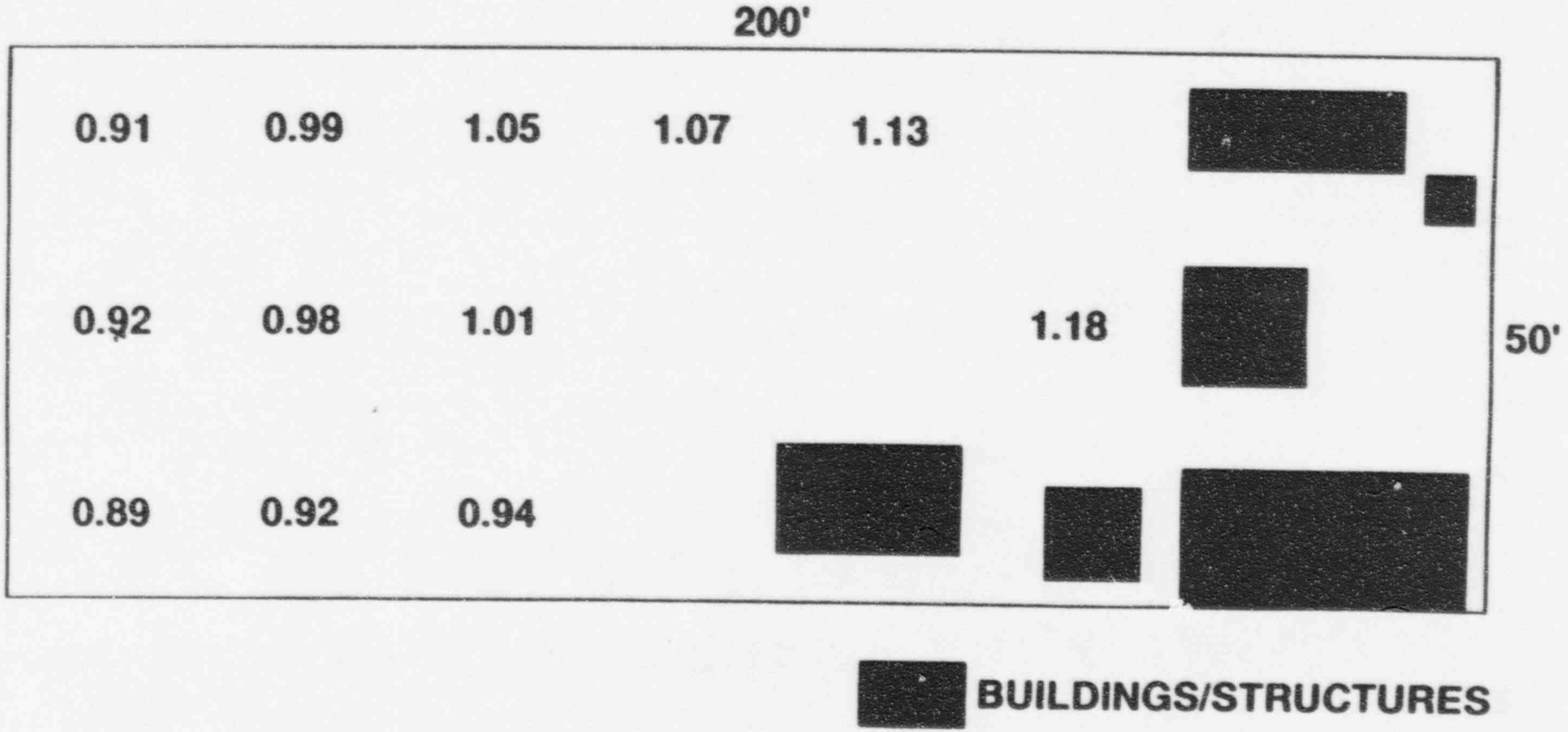
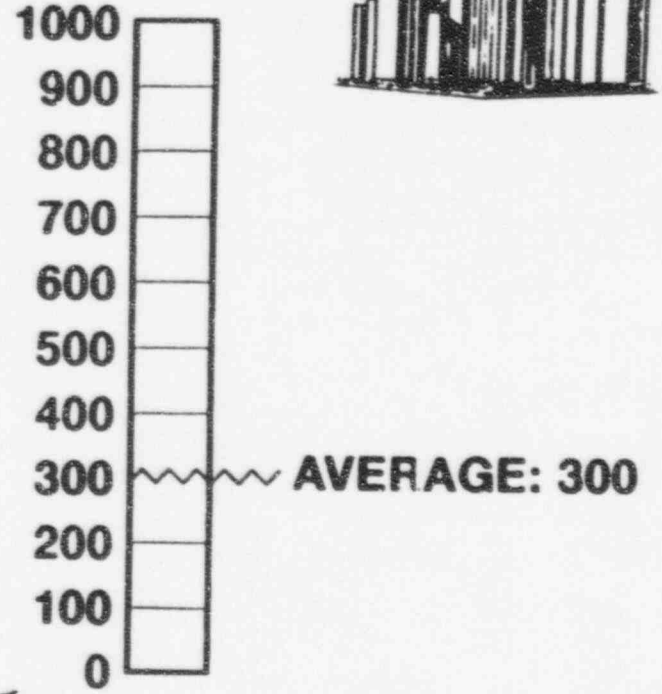


FIGURE 2

RANGE OF ANNUAL RADIATION DOSE: NATURAL SOURCES (MREM)



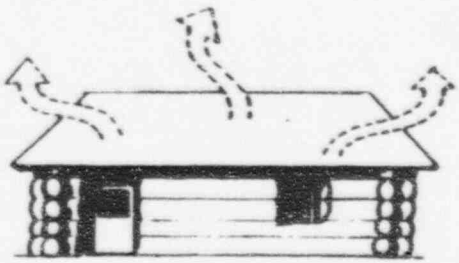


FIGURE 3

LIFETIME MORTALITY RISKS
(PERCENT OF GENERAL POPULATION)

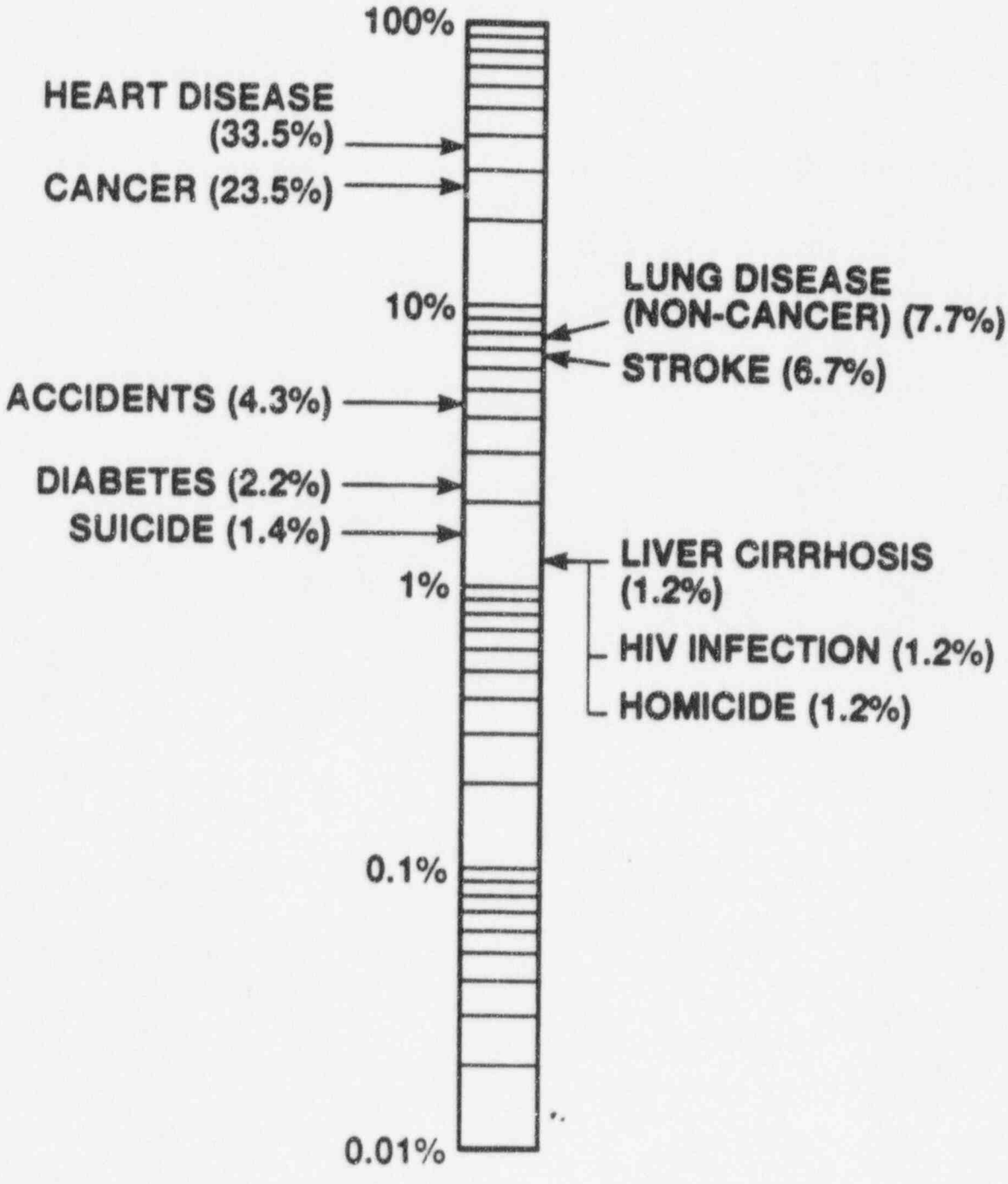


FIGURE 4

LIFETIME MORTALITY RISKS
(PERCENT)

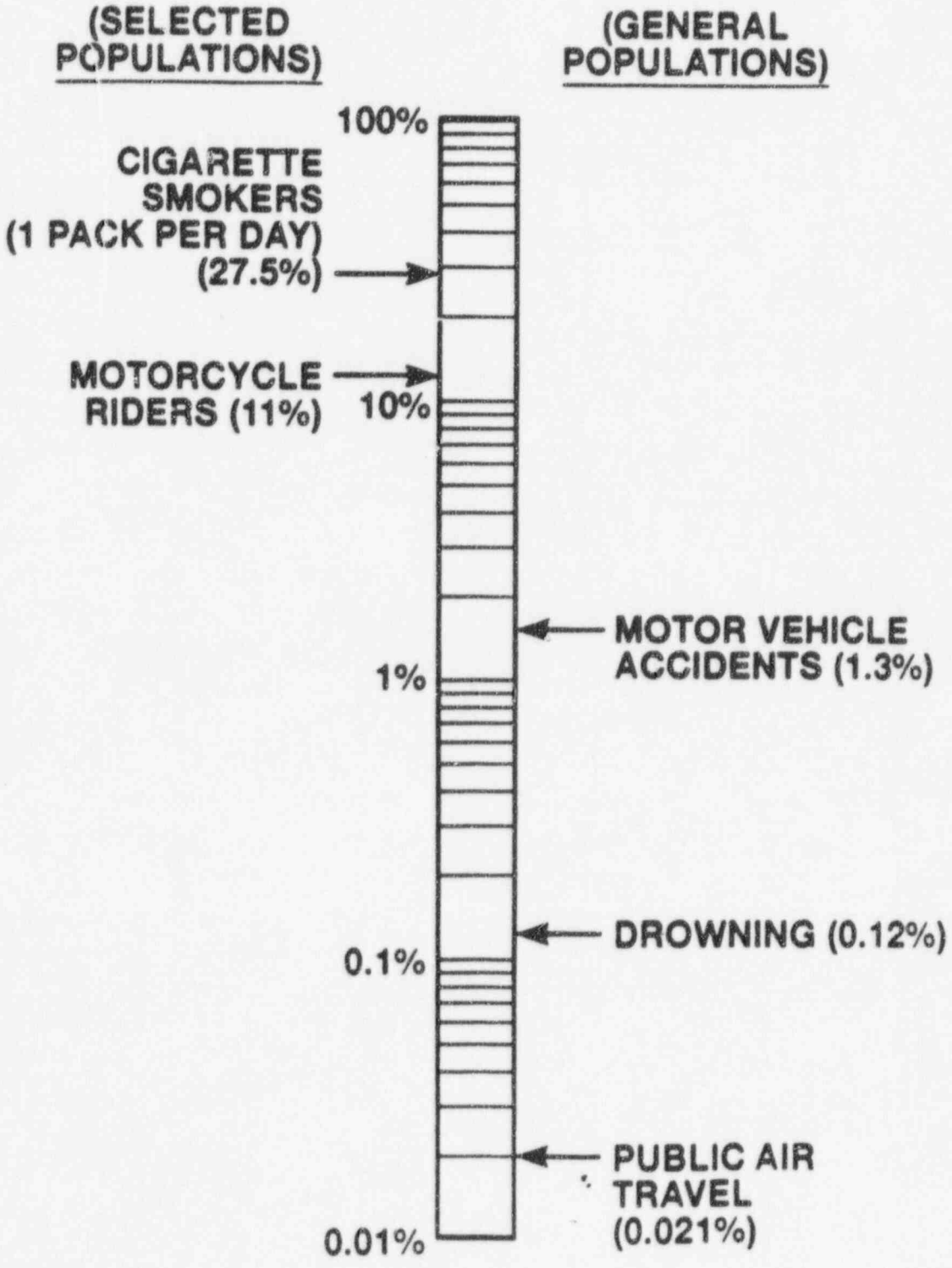


FIGURE 5

LIFETIME MORTALITY RISKS
(PERCENT)

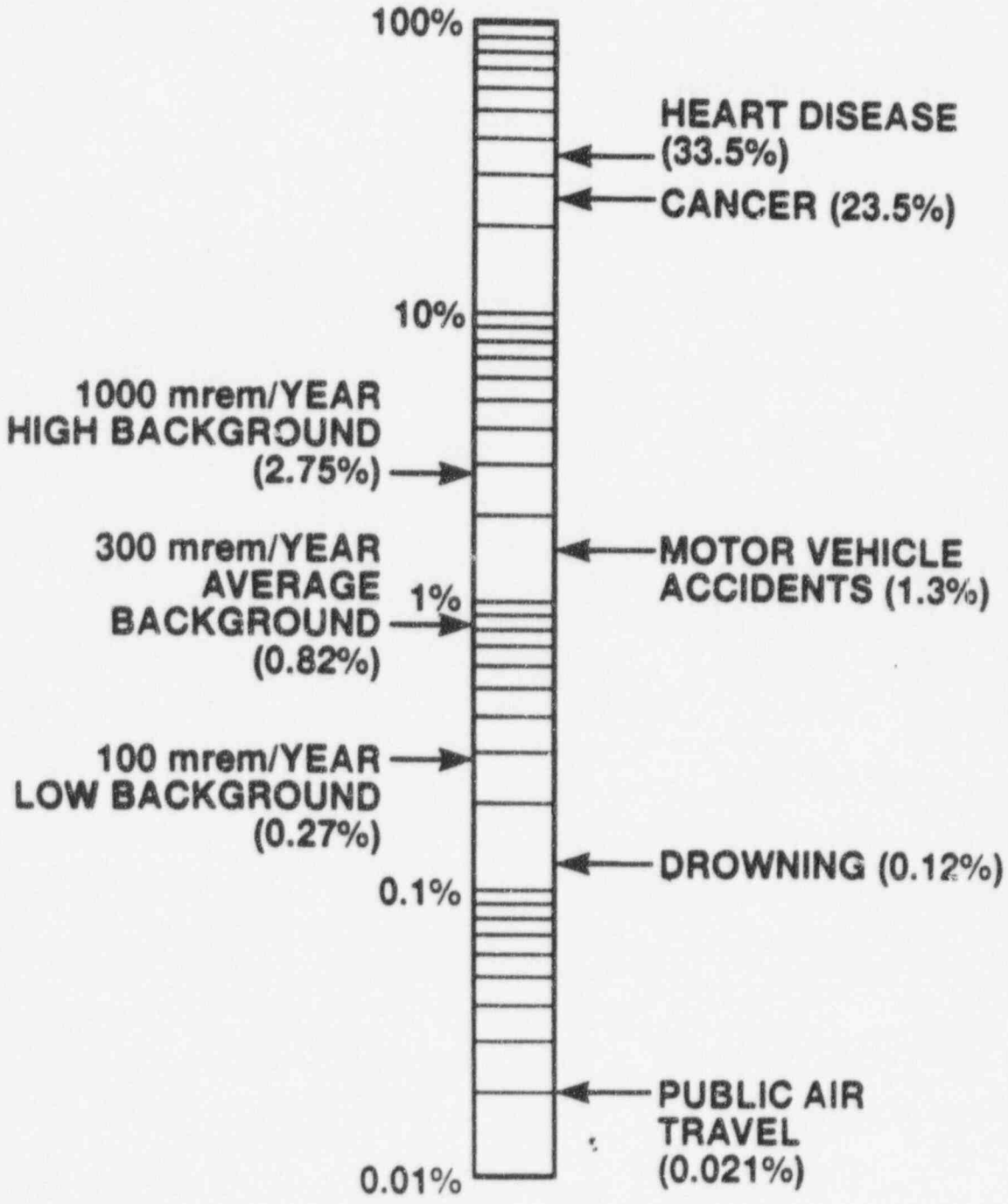


FIGURE 6

LIFETIME MORTALITY RISKS
(PERCENT)

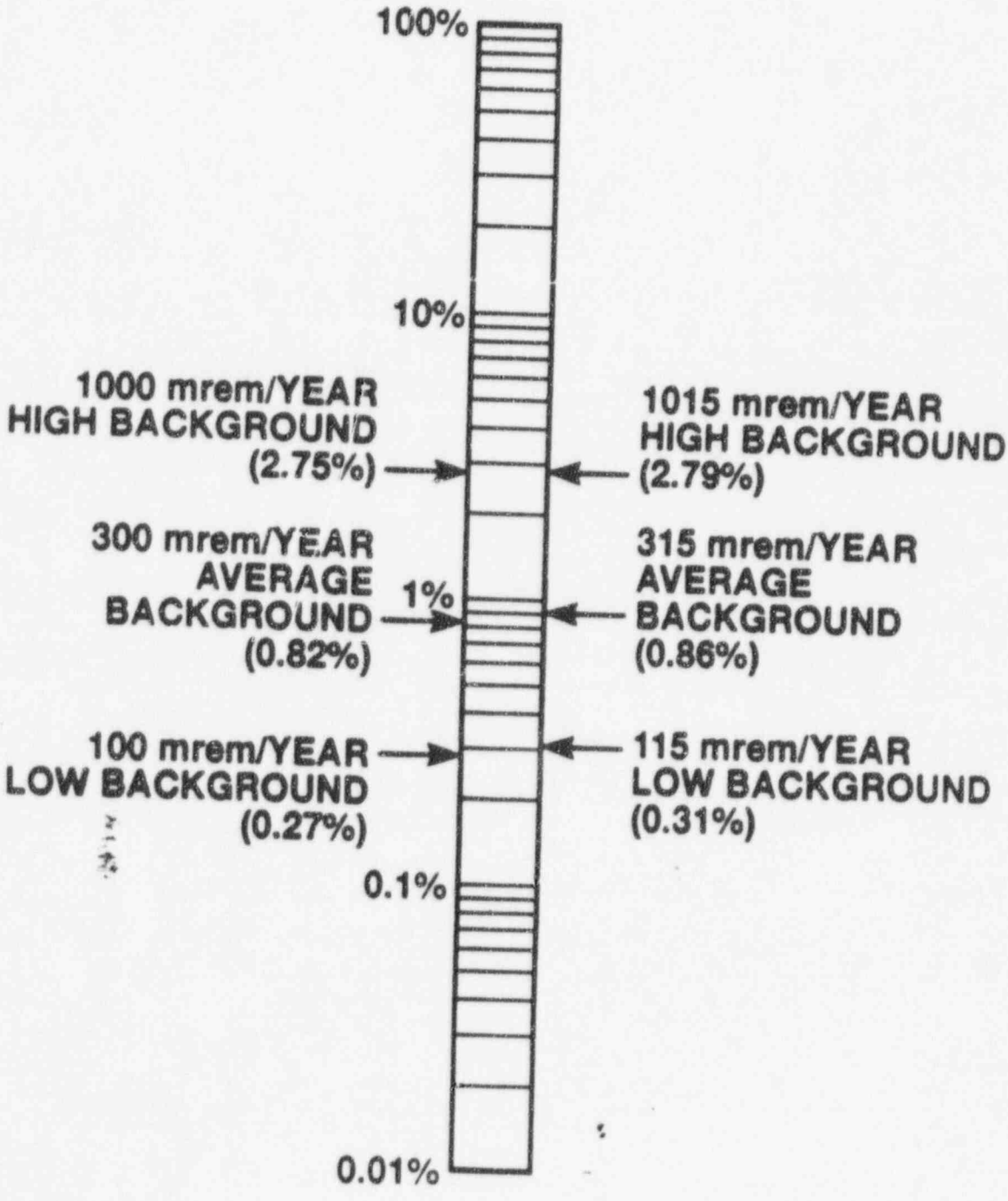


FIGURE 7

ESTIMATED COSTS OF RADIATION MEASUREMENTS

METHOD	COST PER SAMPLE
ALPHA SPECTROMETRY	$300-1000
BETA ANALYSIS	$50-750
EXTERNAL GAMMA EXPOSURE SURVEY	$50
EXTERNAL GAMMA TLD MEASUREMENT	$20
GAMMA SPECTROMETRY	$100-300
RADON MEASUREMENT	$10-20
SOIL SAMPLE COLLECTION	$100-200
SOIL SAMPLE PROCESSING	$100-400
THERMAL IONIZATION MASS SPECTROMETRY	$1000

FIGURE 8

ESTIMATED COST PER MEASUREMENT OF CESIUM-137 IN SOIL

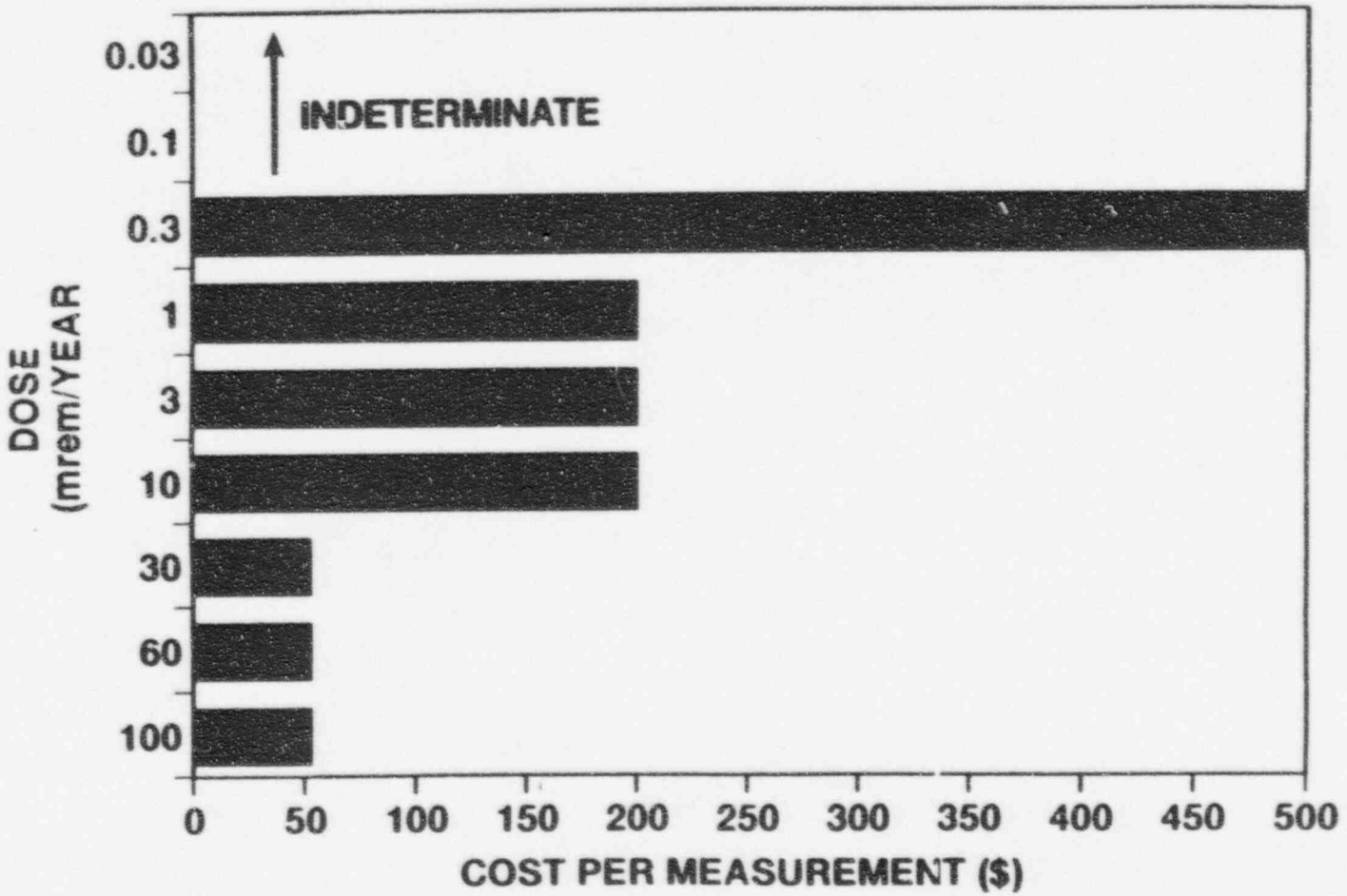


FIGURE 9

BELLE NEWSLETTER

[redacted]ts of
[redacted]asures

[redacted]

Vol. 3, No. 1, July 1994

Belle Office
Northeast Regional Environmental
Public Health Center
[redacted]
[redacted]
TEL. [redacted]
FAX. [redacted]

State of Research and Perspective on Radiation Hormesis in Japan

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ABSTRACT

In 1982, Prof. Thomas D. Luckey of the University of Missouri published a paper in the journal of Health Physics describing radiation hormesis. Radiation hormesis research in Japan has been based on the rationale that if Luckey's claim were to be true, radiation management in Japan has been extremely erroneous.

After results were obtained from various experiments on the health effects of low doses of radiation supporting the hormesis hypothesis, a Round Robin collaborative testing program was initiated on about twenty research plans with more than ten universities in Japan. These activities are categorized as follows: A. Effects of free radicals produced by low dose radiation B. Molecular biological responses to low dose radiation C. Radiation effects on the neurotransmission system D. Stimulative effects of low dose radiation on the immune system E. Epidemiological studies

INTRODUCTION

In the review article "Physiological Benefits from Low Levels of Ionizing Radiation" in Health Physics (December, 1982), Luckey asserted the existence of "radiation hormesis". This resulted in the first International Symposium on Radiation Hormesis at Oakland in California, August 1985. Subsequently, interesting surveys and experiments on the effects of low dose radiation on mammals in Japan have expanded on the body of knowledge which in general have supported Luckey's claim that "low dose radiation is stimulating and essential for life!" The following article will describe various radiation hormesis research findings and the current "Round Robin Radiation Hormesis" research program in Japan which represents a collaborative multiorganizational endeavor involving CRIEPI and various research organizations including various universities.

TOPICS OF RADIATION HORMESIS RESEARCH

Survey of A-bomb Survivors

The follow up data of people who received radiation from the Atomic Bomb show us an interesting feature especially in the low dose range. Figs. 1 and 2 show that about 8 cGy is the optimum dose for the suppression of leukemia through the survey of the people of Hiroshima and Nagasaki exposed to the radiation of the Atomic Bomb. The exposed groups are showing longer lives through the comparison of the death rate of each age between exposed group and non-exposed group (Fig. 3).

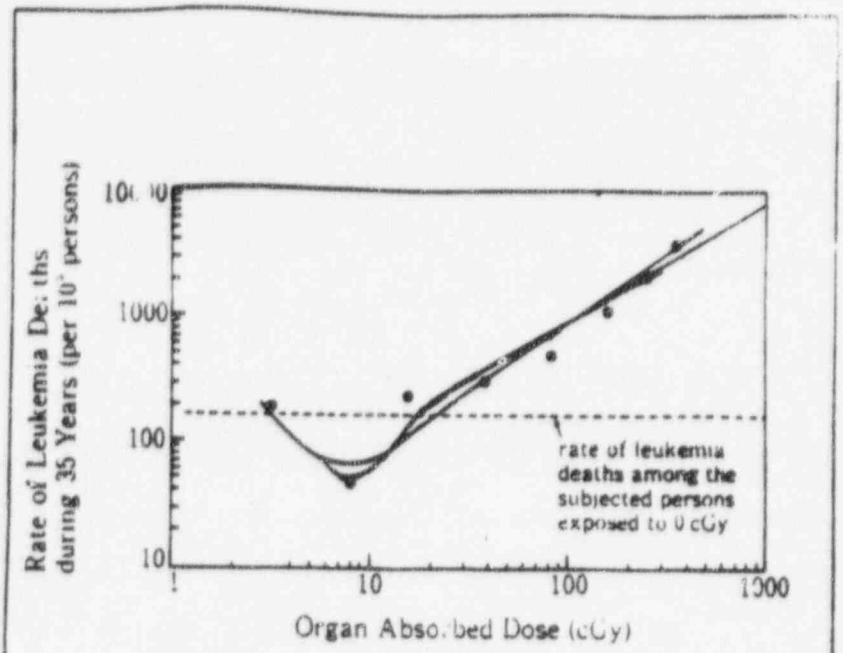

Figure 1 Dose-response relation of leukemia deaths among A-bomb survivors.

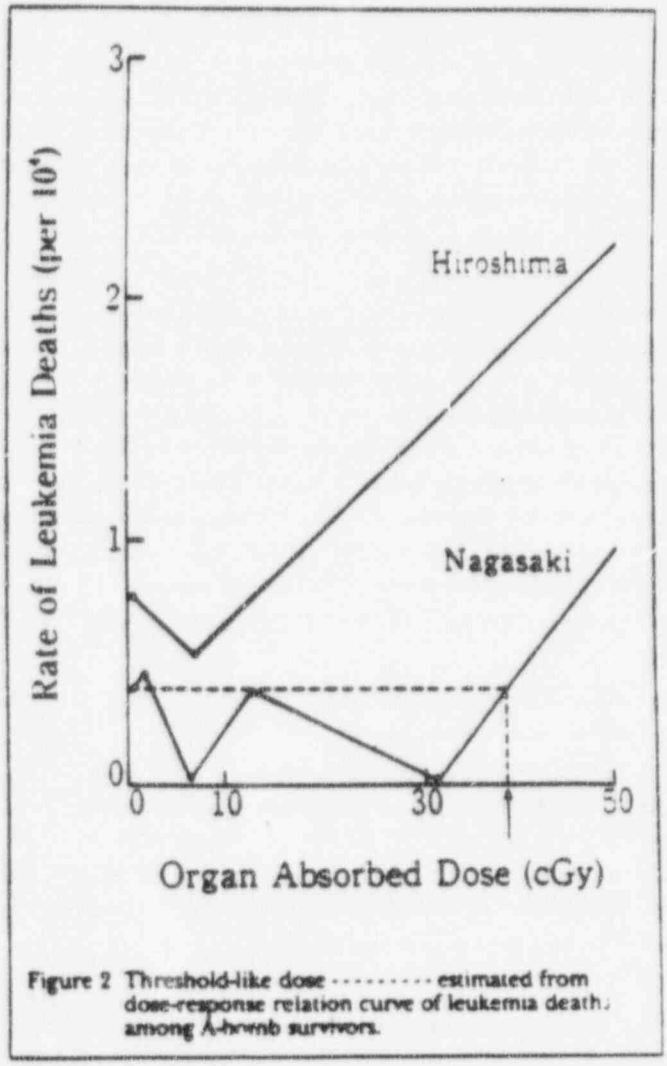

Figure 2 Threshold-like dose ····· estimated from dose-response relation curve of leukemia deaths among A-bomb survivors.

The Beneficial Effect of Misasa Spa

Professor Emeritus of Osaka University Dr. Kondo and Dr. Tanooka, former Chairman of Japan Radiation Research Society, conducted statistical comparisons of cancer of the people of Misasa villages (i.e. high radon levels in drinking water), adjacent villages and all Japan. The result was meaningful as shown in Fig. 4.

Medical Application: Treatment of Cancer

Professor Sakamoto is using radiation hormesis to cure and to suppress the reappearance of cancer in the hospital of Tohoku University. For example, he applied 10 cGy twice weekly for several weeks successfully against liver cancer and lymphatic tumors. He is successfully applying whole body or half body low level dose combined with local high dose irradiation to treat non-hodgkin's lymphoma. The low survival rate of 36% in patients with non-hodgkin's lymphoma after five years of the therapy improved to a 90% survival rate with a low dose treatment schema. Some analytical results demonstrate an increase of the ratio of the helper T cells to suppressor T cells.

Suppression of Lung Cancer

Ishii of CRIEPI and Hosoi of Tohoku Univ. examined the suppression of metastasis by counting lung colonies of mice, (Fig. 5). Ishii also measured the activation of rat splenocytes, as shown in Fig. 6 by low dose radiation exposure.

Cell Rejuvenation

Yamaoka of CRIEPI measured the properties of cell membranes and superoxide dismutase activities. Fig. 7 shown data from some of his experiments.

Radiation Adaptation

Ikushima of Kyoto Univ. examined the radio-adaptive response as shown in Fig. 8. Chinese hamster V 79 Cells were incubated with 5H-Thymidine for 16 hrs (one cell cycle) and irradiated with a dose of 1 Gy of 60Co gamma-rays (0.4 Gy/min). The cells were fixed and assayed for the formation frequency of the micronuclei 6 hrs after irradiation. Misonoo of CRIEPI estimated the optimum irradiation dose for radio-adaptation as shown in Fig. 9.

Zones of Hormesis

Yonezawa of University of Osaka prefecture confirmed two phases of radio-hormetic responses by using a priming dose and survival after a sublethal

dose administration. He found that a low (i.e. priming) dose (i.e. hormetic dose) enhanced resistance to sublethal x-radiation given two months but not two weeks later. (Fig. 10). Opposite results were observed when the primary dose was substantially greater (Fig. 10).

Vitalization of Human Cells

Watanabe of Nagasaki Univ. compared the growth rate of human embryonic cells which had been exposed to a high acute dose or to periodic multiple doses. Cells which received 7.5 cGy/week showed an hormetic response. Fig. 11 shows one of his experimental results.

An Effect on the Neurotransmitting System

Miyachi of Tohoku Univ. discovered an interesting behavior of mice when he initiated the first work of his hormesis research in CRIEPI. The 5 ~ 10 cGy whole body X-ray irradiation to the ICR mice which inevitably fight caused a drastic change of the behavior after seven days. Fig. 12 shows one of his tests results. Moderation of offensive behavior was observed with the isolated-resident versus isolated-intruder paradigm. Significant differences ($p<0.01$) between control and irradiated groups are represented by the asterisk.

Thorotrast Study

Dr. Mori, former principal researcher of National Institute of Radiological Sciences, is directing epidemiological follow up studies on thorotrast patients in Japan. He has indicated no harmful lung effects are observed following a 10 year exposure to 2 Gy via an internal alpha-ray source.

Response of p53

Professor Onishi of Nara Medical College discovered a marked increase of stress protein production by p53 genes. Doses of 10 to 25 cGy were effective. Fig. 13 shows his experimental results.

Importance of Low Dose Steady Irradiation

Prof. Nomura confirmed the importance of steady low dose irradiation for gene repairing activities, giving evidence that steady low dose administration is essential for obtaining beneficial health effects.

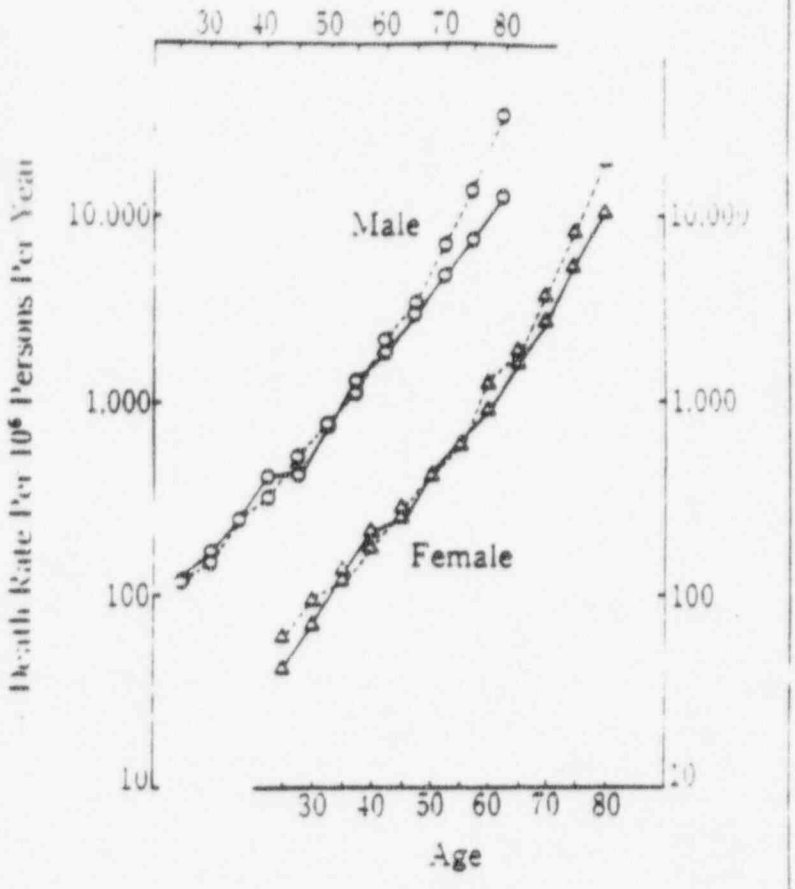

Figure 3 Higher death rate after 55 years old (dotted line) corresponds to the people who were not exposed to A. Bomb living in Nagasaki. Lower death rate after 55 years old (solid line) corresponds to A. Bomb survivors.

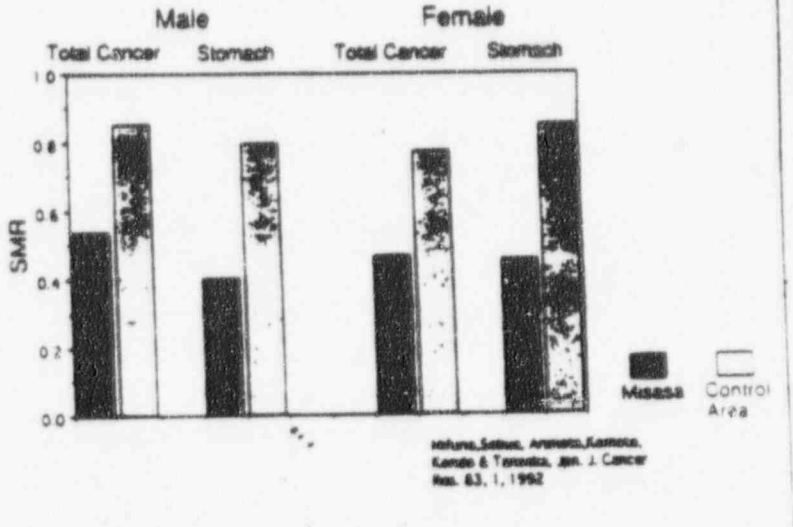

Figure 4 Comparison of standardized mortality ratio. Misasa/control area.

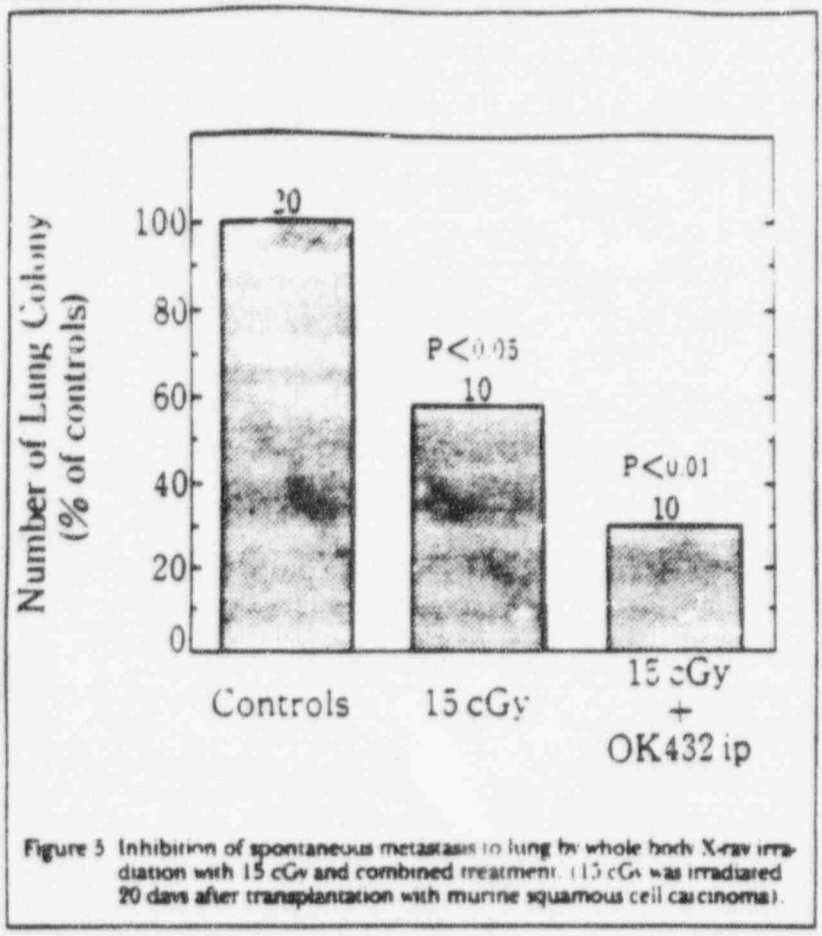

Figure 5 Inhibition of spontaneous metastasis to lung by whole body X-ray irradiation with 15 cGy and combined treatment. (15 cGy was irradiated 20 days after transplantation with murine squamous cell carcinoma).

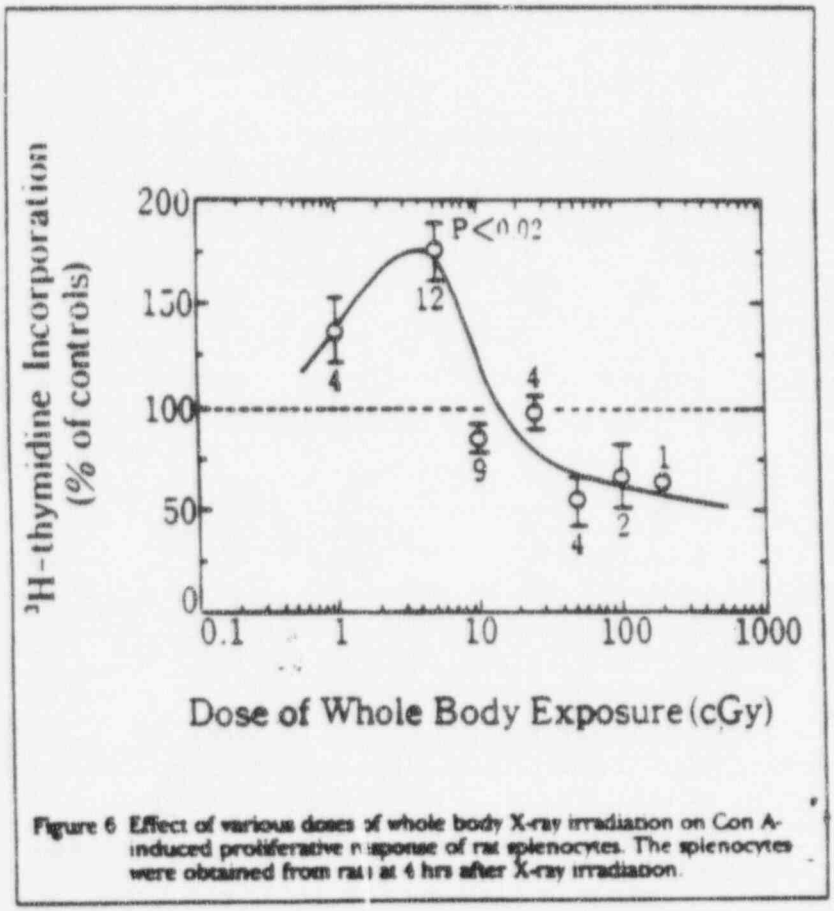

Figure 6 Effect of various doses of whole body X-ray irradiation on Con A-induced proliferative response of rat splenocytes. The splenocytes were obtained from rats at 4 hrs after X-ray irradiation.

THE ROUND ROBIN TESTS PROGRAM

So-called Round Robin Tests Program (1995 - 1996) on Radiation Hormesis being carried out in Japan is as follows:

Studies on Special Biological Responses to Low-Dose Radiation

Anti-Carcinogenesis and Anti-Cancer Effects induced by Low-dose Radiation

Two different groups are working on anti-carcinogenesis effects induced by low-dose radiation (LDR): One is looking at the suppression of leukemogenesis through the augmentation of the immune system by LDR using AKR mice. The other is looking at the suppression of chemical carcinogen (Fe-NTA) induced tumor formation through enhanced SOD (Superoxide dismutase) activity by LDR.

Title & Researcher

1. Anti-Leukemogenesis Test (S. Sakamoto, Faculty of Medicine, Tohoku University)
2. SOD and Possible suppression of Fe-NTA induced Tumor (K. Utsumi, Institute of Medical Science, Center of Adult Diseases, Kurashiki)

Anti-Aging Effects

Two different groups are looking at the possibility of LDR induced increase in longevity of laboratory animals. Possible depressive effects of LDR on the aging process of the immune system and/or regulatory system of energy metabolism are tested using SAM (Senescence Accelerated Mouse) and/or other laboratory animals.

Title & Researcher

1. Possible Depressive Effect of Low-Dose on the Aging Process (Y. Okumura, Faculty of Medicine, Nagasaki University)
2. Low-Dose Radiation and Energy Metabolism Regulation (A. Mori, Faculty of Medicine, Okayama University)

Epidemiological Studies

One group is looking at the possibility of LDR induced increase in longevity of human populations using the data

LDR. intercellular and intracellular signal transduction is examined in this study.

Title & Researcher

1. DNA Damage Repair Mechanisms (T. Ikushima, Research Reactor Center, Kyoto University)
2. Cellular Resp and Signal Transfer (M. Watanabe, Department of Pharmacy, Nagasaki University)

CLOSING

Formation of free electrons and free radicals by ionizing radiation creates many complex chemical reactions followed by significant biological responses. This article describes important research directions that will provide important mechanistic understandings of how cells and organisms adapt to environmental stimuli such as low dose radiation.

ACKNOWLEDGEMENT

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Those University persons who are giving respectful advise and direction to the research are Dr. Luckey (Missouri), Dr. Kondo (Osaka), Dr. Sugawara (Kyoto), Dr. Sakamoto (Tohoku), Dr. Makinodan (UCLA), Dr. Okada (Tokyo), Dr. Sasaki (Kyoto), Dr. Yamada (Tohoku), Dr. Kuboderra (Tokyo Science), Dr. Watanabe (Nagasaki), Dr. Tanooka (National Cancer Inst.), and Dr. Aoyama (Shiga Medical).

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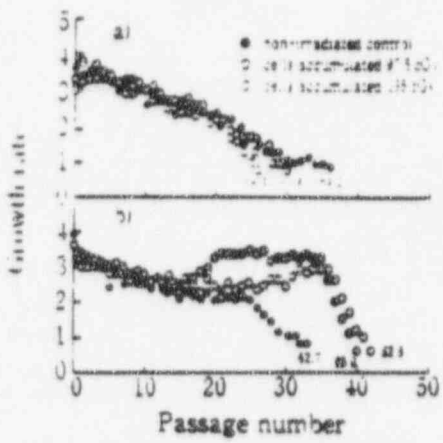

Figure 11 The growth rate at each passage in human embryonic fibroblasts (HE7) irradiated with single dose at passage 0(A) and multiple doses of 7.5 cGy of C_s^{137} gamma-rays (B).

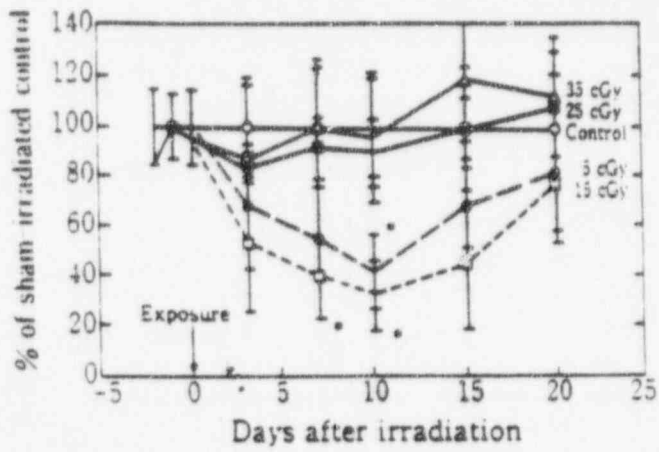

Figure 12 Effect of low-dose X-rays on aggression displayed by isolated resident vs isolated intruder.

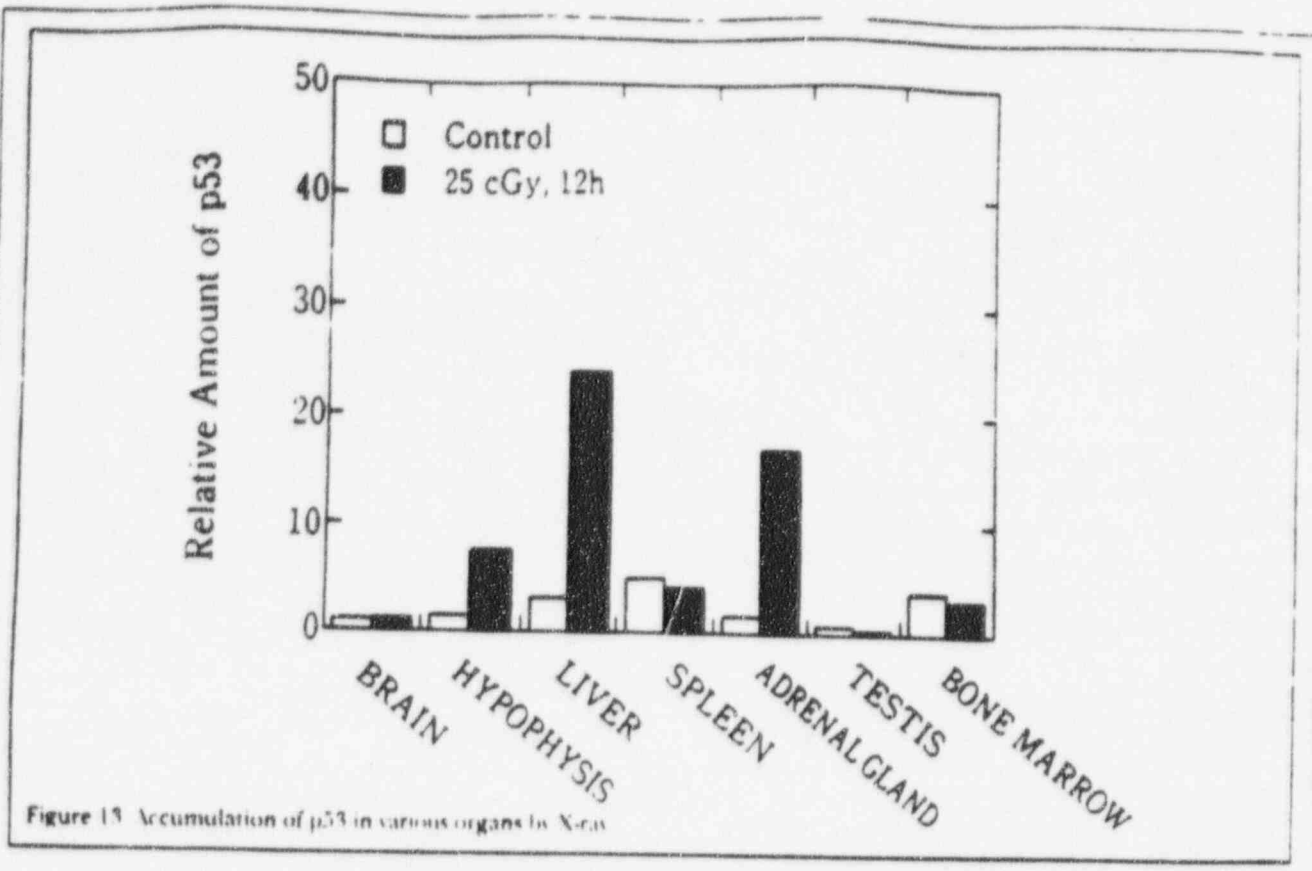

Figure 13 Accumulation of p53 in various organs by X-ray

Spontaneous DNA Damage and Its Significance for the "Negligible Dose" Controversy in Radiation Protection

Daniel Billen
Medical Science Division
Oak Ridge Associated Universities

One of the crucial problems in radiation protection is the reality of the negligible dose or *de minimus* concept (1-4). This issue of a "practical zero" and its resolution is central to our understanding of the controversy concerning the existence of a "safe" dose in radiological health. However, for very low levels of environmental mutagens and carcinogens including low doses of low-LET radiations (less than 1 cGy or 1 rad), spontaneous or endogenous DNA damage may have an increasing impact on the biological consequences of the induced cellular response. It is this issue that is addressed in this communication.

The following discussion is intentionally limited to a comparison of low-LET radiation since its effects are due primarily to indirect damage in cellular DNA brought about by OH radicals. Indirect effects of low-LET radiation under aerobic conditions are reported to account for 50-85% of measured radiation damage in cells (5, 6). High-LET radiation, on the other hand, produces unique DNA damage (7) primarily by direct effects (5) which is less likely to be properly repaired (7).

Spontaneous or intrinsic modification of cellular DNA is ubiquitous in nature and likely to be a major cause of background mutations (8), cancer (9), and other diseases (10). The documentation of this intrinsic DNA decay has increased at a rapid pace in recent years and has not gone unnoticed by contemporary radiobiologists. Setlow (11) and more recently Saul and Ames (12) summarized the findings of Lindahl and Karlstrom (13) and others (14) which suggest that approximately 10,000 measurable DNA modification events occur per hour in each mammalian cell due to intrinsic causes.

bases of the Atomic Bomb Survivors Health Survey

Title & Researcher

1. Analysis of Data showing the Longevity Increasing Effect of Low-Dose using Data Base of A-Bomb Survivors Health Survey in Nagasaki (Y. Okumura, Faculty of Medicine, Nagasaki University)

Studies on Mechanisms underlying Low-Dose Effects

Activation of Basic Biological Functions

There are four different groups here. One is looking at organic radicals with long half lives produced by LDR, and their biological/molecular effects. The other is looking at the stimulative effects of fractionated LDR on the proliferation of cultured cells. Using human embryonic fibroblasts, total passages, transformation frequency, mutation frequency and other alterations of cells are examined in this study. The third group is looking at stem-cell activation through apoptosis induced by LDR. The effects of protracted irradiation with low dose rates are examined in intestinal crypts of mice. Using LacZ gene introduced transgenic Mutamouse, somatic cell mutation induced by LDR is being observed by another group. Mutation frequency and spectrum in the introduced LacZ gene are examined after acute and/or chronic LDR.

Title & Researcher

1. Identification of the Initial Radicals induced by Low-Dose (T. Miyazaki, Faculty of Engineering, Nagoya University)
2. Examination of the Inhibitory Effects of Low-Dose on Cell Aging and its Mechanism (M. Watanabe, Department of Pharmacy, Nagasaki University)
3. Stem-cell Activation by Low-Dose through Apoptosis Induction (K. Ijiri, Radioisotope Center, Tokyo University)
4. Specification of the Somatic Cell Mutation induced by Low-Dose using Mutamouse (T. Ono, Faculty of Medicine, Tohoku University)

Activation of Biological Defense Mechanisms

There are five different groups in this study. Two groups are looking at the acquired radioresistance in mice. When the radioresistance appears after conditioning irradiation, how long it lasts and the relation to the recovery of hematopoietic tissues are examined in preirradiated mice. Relationship between stressors, including LDR, and defense mechanisms is also examined in the mice pretreated with stressful stimuli, such as diet restriction, i.p. injection of heavy metals, skin-excision and LDR. Activation of defense mechanisms is also looked at in relation to the stimulation of stem-cell proliferation through apoptosis by LDR. Application of the Altruistic Cell Death Hypothesis to stem-cells in

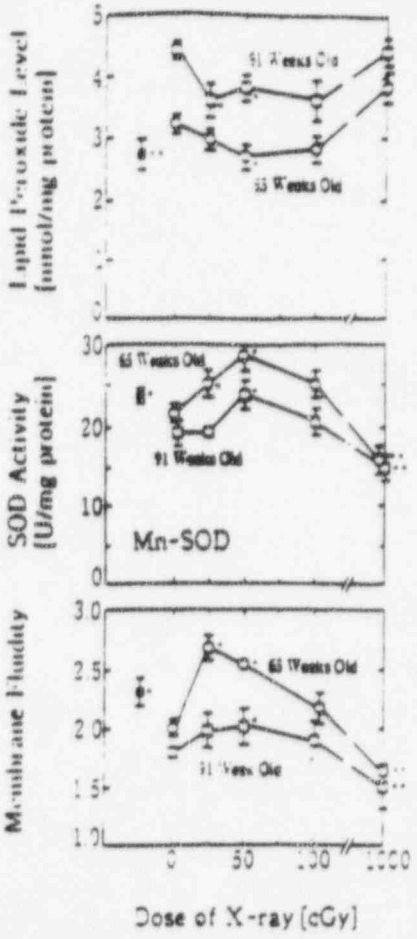

Figure 7 Dose and aging-dependent changes in lipid peroxide (TBARS) level, SOD activity and membrane fluidity (W/S ratio) of rat's brain cortex by X-ray irradiation.

Membrane fluidity was determined by spin-label method using ESR spectrometer. W/S means ratio of weak to strong bands. ○ shows the data from sham-irradiated 7 weeks old control. Each value indicates the mean ± S.E.M. The number of rats per experimental point is 10–12. *P<0.05 and **P<0.01 vs sham-irradiated 65 or 91 weeks old control (t test).

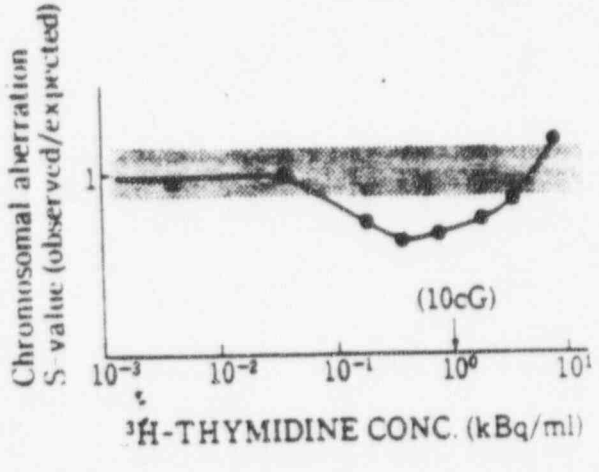

Figure 8 An optional dose range of low-level tritium for the micronuclei induction of radio-adaptive responses

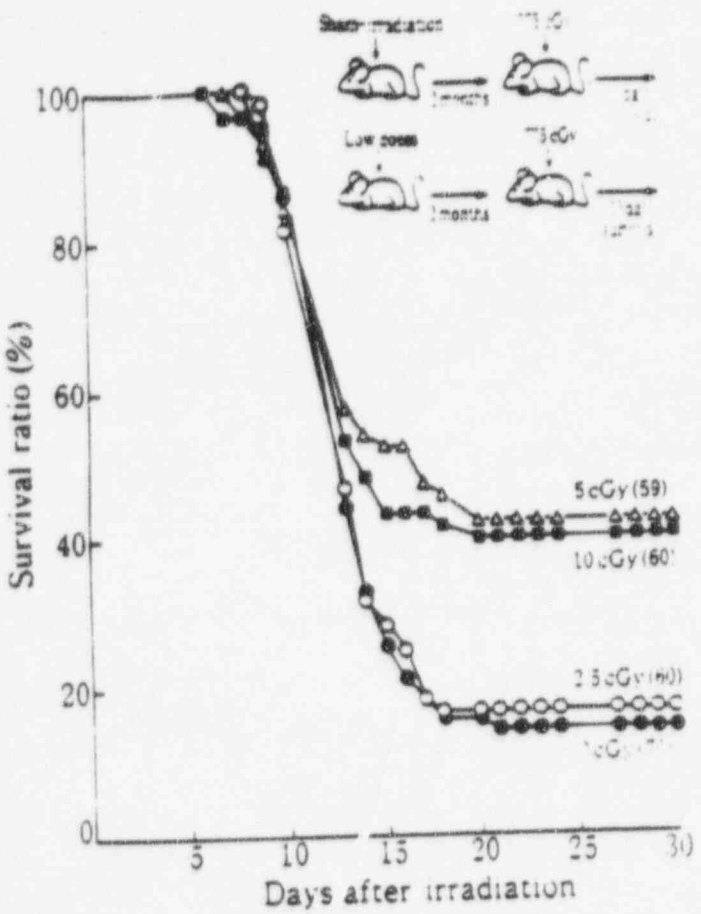

Figure 9 Survival ratios of mice irradiated with low doses 2 months before the second irradiation with 775 cGy of X-rays.

Two types of acquired radioresistance after small doses of X-rays in mice

Priming Dose of X-rays (cGy)	Radioresistance*	
	2 weeks interval	2 months interval
2.5	No	No
5-10		Yes
15		No
20	No	No (1.5 months)
30-50	Yes	No

* Increase in 30-day survival rate after sublethal X-irradiation

Figure 10 Preirradiation with 5–10 cGy resulted in the radioresistance 2 months later. The acquired radioresistance was also observed when the mice were exposed to 30–50 cGy. In this case, the radioresistance appeared 2 weeks later. Preirradiation with the intermediate doses of 15-20 cGy did not result in any radioresistance.

thymus and other hematopoietic tissues are examined in this study.

Depression of aggressive behavior observed in mice irradiated whole-body or partially on the head portion with low dose X-rays suggests the organisms can perceive the LDR through the central nervous system (CNS). One group is looking at the effects of LDR on the immune system, as well as behavior, because the defense mechanisms are closely connected with CNS function. Radicals generated by LDR are detoxified by a detoxification system which includes a group of enzymes, such as catalase, SOD and glutathione peroxidase. An hypothesis that LDR can induce expression of genes and a variety of gene products related to detoxification of radicals is also examined in relation to activation of molecular/biochemical defense mechanisms.

Title & Researcher

1. Acquired Radioresistance in Low-Dose Irradiated Mice (M. Yonezawa, Research Center of Radioisotopes, Osaka Prefecture University)
2. Acquired Radioresistance and the Activated Defense Mechanisms (J. Matsubara, Faculty of Medicine, Tokyo University)
3. Examination of "Altruistic Cell Death Hypothesis" (Stimulation of Stem Cell Proliferation through Low-Dose Induced Apoptosis) (T. Yamada, School of Medicine, Toho University)
4. Action of Low-Dose to the Central Nervous System and Anti-stress Effects of Low-Dose Irradiation (T. Yamada, School of Medicine, Toho University)
5. Stress Protein and the Expression of Genes related to Active Oxygens (M. Inoue, Faculty of Medicine, Osaka City University)

Activation of Damage Recovery Mechanisms

Adaptive responses to radiation suggest that cells have intrinsic defense systems against circumstances that might cause irreversible damage. There are two groups: One group is looking at the activation of genes associated with DNA repair. In this study induced gene products and expression of genes related to DNA repair are examined using cultured CHO cells. The other group is looking at cellular changes in the adaptive response induced by

The current radiation literature will be interpreted to show that ~10^5 (or fewer) measurable DNA alterations occur per centigray of low-LET radiation per mammalian cell. Therefore every hour human and other mammalian cells undergo at least 50-100 times as much spontaneous or natural DNA damage as would result from exposure to 1 cGy of ionizing radiation. Since background radiation is usually less than 100-200 mrem (1-2 mSv)/y, it can be concluded, as discussed by Muller and Mott-Smith (15), that spontaneous DNA damage is due primarily to causes other than background radiation.

"Intrinsic" Or "Spontaneous" DNA Damage

DNA is not as structurally stable as once thought. On the contrary, there appears to be a natural background of chemical and physical lesions introduced into cellular DNA by thermal as well as oxidative insult. In addition, in the course of evolution, many cells have evolved biochemic mechanisms for repair or bypass of these lesions.

Some of the more common "natural" DNA changes include depurination, depyrimidination, deamination, single-strand breaks (SSBs), double-strand breaks (DSBs), base modification, and protein-DNA crosslinks. These are caused by thermodynamic decay processes as well as reactive molecules formed by metabolic processes leading to free radicals such as OH, peroxides, and reactive oxygen species.

Shapiro (14) has recently discussed and summarized the frequency at which various kinds of spontaneous DNA damage occur. Spontaneous DNA damage events per cell per hour are shown in Table I and were estimated from the data presented by Shapiro [Table 11(14)].

For single-stranded DNA of mammalian cells at least, 8×10^3 damage events occur/cell/hr, whereas for double-stranded DNA there were ~6×10^3 damage events per hour (Table I). While the ratio of single-stranded DNA to double-stranded DNA varies with phase of the cell cycle, it is reasonable to assume that double-stranded DNA is the usual configuration for most cellular DNA at any one time. From the data summarized in Table I it is not unreasonable to suggest that, at a minimum, the spontaneous DNA damage is of the order of $6\text{-}10 \times 10^3$ events/cell/h and to use 8×10^3 DNA damage events/cell/h as a reasonable average for the purpose of discussion. This allows a calculation of 1.9×10^5 spontaneous cellular DNA damaging events/cell/day or 7×10^7 per year in mammals including humans (Table II). The lifetime load of spontaneous DNA damage events per cell is then ~5×10^9 if an average life span of 75 years is allowed for humans.

DNA Damage Induced By Irradiation

Several recent reviews summarize the types and quantities of alteration of DNA in cells caused by exposure to low-LET radiation (16-18). The reader should refer to these for references to the original works from which the reviews were drawn.

The estimate of about 100 DNA events/cell/cGy used in this discussion is based on information contained in the reviews by Ward (16, 20) and assumes the molecular weight of the mammalian genomic DNA to be 6×10^{12} Da, constituting about 1% of the cell weight.

Ward [Table II (16)] lists the amount of energy deposited in various DNA constituents/cell/Gy. From this table a total of 15.5 DNA events/cGy is calculated. His estimate of damaged DNA sites/cell/cGy is 10-100. I chose the 100-lesion estimate to make as reasonable a conservative comparison with spontaneous DNA damage as possible (Table II). This number of damaged sites would include both direct and indirect DNA damage.

Spontaneous vs Induced DNA Modifications And Their Biological Consequences

Wallace has recently reviewed the nature of the DNA lesions caused by active oxidizing species produced both naturally and by low-LET radiation (17). Oxidizing radicals and especially OH radicals resulting from either cause produce similar types of DNA lesions (17-19). The enzymes involved in their repair are similar whether the DNA damage is produced spontaneously or by

Table I Estimated Spontaneous DNA Degradation Events (Cell/h)[a]

Reaction	Single-strand DNA	Double-strand DNA
Depurination	4000	1000
Depyrimidination	200	50
Deamination of cytosine	4000	15
Chain break resulting from depurination	—	1000
Direct chain break	—	4000

[a] Calculated from Shapiro (14)

radiation. However, radiation is known to induce an error-prone repair system in bacterial cells and perhaps in mammalian cells as well (21, 22).

DNA glycosylases and endonucleases are involved in the repair of base damage. Other nucleases are available for sugar damage repair (17). Recognition of the damage site by the appropriate enzymes is dependent not on the initiating event but on the chemical nature of the end product. These end products appear to be similar whether induced by natural causes or radiation (17). It would seem reasonable to conclude that, due to common oxidizing radicals, many of the qualitative changes in DNA are quite similar for radiation-induced or spontaneous DNA damage.

The quantity and distribution of each class of lesion may, however, differ significantly. As indicated earlier there would appear to be relatively more DNA strand breaks than other lesions resulting from spontaneous causes as compared to radiation insult. A good portion of these may result from depurination (Table I) with production of 3' OH termini ("clean ends") as part of the repair process.

Many of the DNA strand breaks caused by low-LET radiation are incapable of serving as primer for DNA polymerase (23). However, endo- and exonucleases exist which can restore these blocking ends to clean ends and allow completion of the repair process (17).

A strong correlation exists between DNA DSBs and lethality in mammalian cells for low-LET radiation. While the quantity of DSBs produced by ionizing radiation is fairly well documented, this is not true for spontaneous DSB production in mammalian cells.

In spontaneous DNA decay, formation of a DSB is likely to be the result of single-strand events occurring in close proximity on each daughter strand and leading to cohesive ends which can be repaired easily by a ligation step.

A survey of the literature on the doubling dose for mutagenesis in eukaryotes exposed to low-LET radiation indicates a range of 4 to 300 cGy and for carcinogenesis a range of 100 to 400 cGy. Using the "ballpark" value of approximately 100 DNA events/cell/cGy, this would represent a range of 400 to 40,000 induced DNA damage events per doubling dose. Using 100 cGy as the approximate doubling dose, a total of 1×10^4 DNA damage events would be required to induce mutations in numbers equal to that observed in nature. This is approximately the number of DNA events (8.0×10^3) produced spontaneously in each cell/h (Table II).

The Negligible Dose Controversy

The comparison of low-LET radiation-induced DNA damage with that which occurs spontaneously indicates (Table II) that a relatively large number of DNA damage events can occur spontaneously during the lifetime of mammalian and other cells.

Dose protraction over a period of weeks or months would lead to an increasing ratio of spontaneous DNA damage events to those caused by irradiation. By extrapolation from high doses and high dose rate as discussed by Ward (16, 20), 1 cGy delivered in 1 s would cause 40-50 times as many DNA damaging events per cell as that caused spontaneously during the same time span (Table II). However, 1 cGy delivered evenly over 1 year would cause (on average) less than 1 DNA damaging event per cell/day. This can be compared to $\sim 2 \times 10^5$ natural events caused per cell/day.

From these numbers, it seems reasonable to suggest that there does exist a "negligible" dose in the range of our terrestrial background annual radiation dose of ~1 mSv (~10 DNA events/cell/year). This can be compared to the approximately 7×10^7 DNA events/cell/year produced by spontaneous causes.

Table II DNA Damage Events per Mammalian Cell

Character of event	Spontaneous DNA damage events: Per second	Per hour	Per year	DNA damage/cGy[a]
Single-strand breaks	1.4	~5 x 10^3	~4.4 x 10^7	10
Double-strand breaks				0.4
Depurination and/or base lesions	0.8	~1.5 x 10^3 ~1.25 x 10^3	~81.4 x 10^7 ~1.1 x 10^7	9.5
Total events	2.2	~8.0 x 10^3	~7 x 10^7	~20
cGy equivalents (1 cGy = 100 events)[b]	0.022	8.0 x 10^1	7 x 10^5	

a From Ward (20).

b Since other radiation-induced DNA damage such as DNA-protein crosslinking and base modifications (18) occur, 100 events/cGy is used as a "ballpark" value for ease of comparison with spontaneous events.

Adler and Weinberg (24) have proposed that the standard deviation of the background irradiation (~0.2 mSv) be used as an acceptable additional dose due to human activities. This would lead to ~2 additional induced DNA damaging events/cell/year as compared to ~ 7×10^7 spontaneous DNA damage events. Considering the magnitude of the spontaneously induced DNA changes in each human cell, it is not unreasonable to predict that 0.2 mSv delivered over a year would have negligible biological consequences.

When temporal considerations are factored in, it becomes clear that spontaneous DNA damage in mammalian cells may be many orders of magnitude greater than that caused by low and protracted radiation doses, especially in the terrestrial background range of 1-2 mSv (100-200 mrem) per year. It is important that further studies on the effects of both ionizing radiations and spontaneous events on DNA decay and repair be conducted to better understand the practical health consequences of low and protracted doses of radiation (2, 9, 25).

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