

# Radiation and Risk

## *a hard look at the data*

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**R**adiation, and its effects on humans, may be the most studied, most regulated and most feared of the physical, chemical, and biological insults to which we are exposed. Ironically, it is also one of the most common. Every day, every minute of our lives, we are all subject to the constant bombardment of gamma rays, neutrons, and charged particles that are produced in our natural environment, even from radionuclides within our own bodies. This background environment of ionizing radiation is not a product of our modern world; rather, it has been present throughout human evolution.

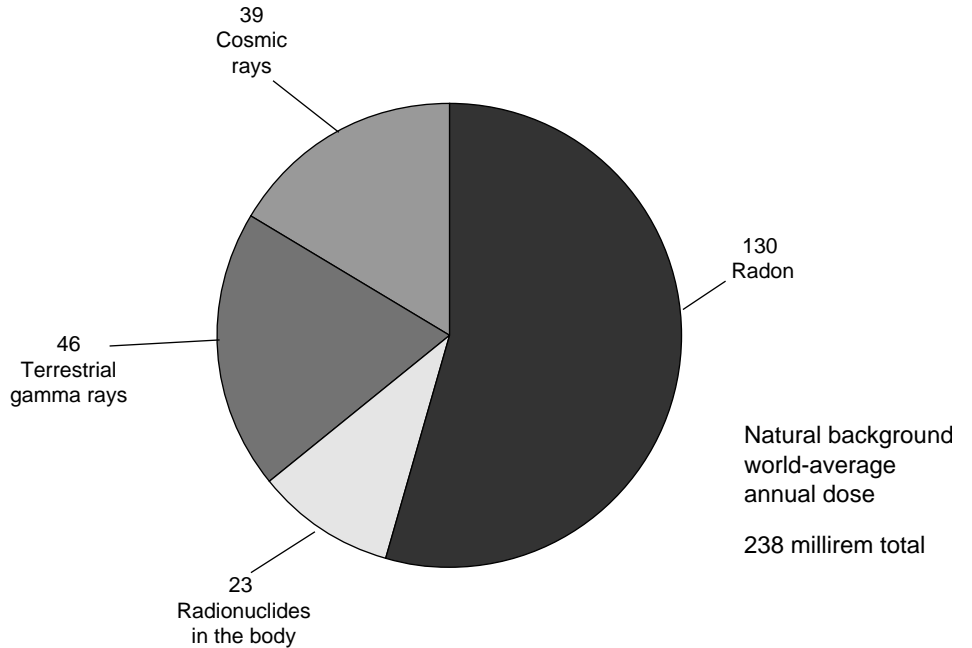
It has been conjectured by some that, because biological organisms evolved in the presence of low levels of ionizing radiation, we and other life forms must have developed effective mechanisms to repair the damage caused by this exposure. Others contend that even the lowest levels of radiation have the potential to cause serious biological effects, such as cancer or genetic disease. In fact, no one knows for sure if low doses of ionizing radiation can produce serious biological effects in humans. What we do know is that high doses of radiation can produce such effects, and the risks can be quantified. From these known risks at high doses, one may estimate the risks associated with low doses, based on some procedure of extrapolation. Disagreement about such a procedure for extrapolating from high doses to the low doses that are of practical concern to radiation workers and the general public lies at the heart of much of the controversy surrounding potential human radiation effects. In the end, such extrapolations from high doses to low doses are based on theoretical biophysical considerations and convenience of application but not on hard human data. This article examines some of the issues involved in estimating risks of exposure to low levels of ionizing radiation.

The red circles in the photo at left graphically portray the rate of cancer mortality in the United States. On average, one in five people die of cancer, and one in five people in the photo are labeled at random with a red circle. The purple circles represent excess cancer deaths above the normal rate. The job of the radiation epidemiologist is to determine the number of excess cancer deaths among a group that has been exposed to radiation and then determine whether that number is *statistically significant*.

Because the rate at which radiation causes cancer is quite low, it is very difficult to detect statistically significant increases in cancer mortality caused by radiation unless the population is very large and the radiation doses are also fairly large. Consequently, risk estimates for radiation-induced cancer are based primarily on data from the Japanese atomic-bomb survivors.

What is the level of background radiation, and is there any evidence that it is harmful? The world-wide average annual whole-body effective dose to humans from natural sources of ionizing radiation is 238 millirem (see “Radiation Units”). Figure 1 shows the average contributions to the world-average annual dose per person from each of the major natural sources of ionizing radiation. The components that vary greatly, depending on location, are cosmic rays, terrestrial gamma rays, and radon. Variations of up to a factor of two are common, and up to a factor of ten are not that rare. In contrast, the dose associated with internal radiation varies much less from person to person, regardless of location. This dose is due mainly to potassium-40, which is a naturally occurring isotope of potassium, an essential chemical element that is ingested whenever we eat foods containing it.

Is there a correlation between cancer incidence or mortality and exposure to background radiation? It is known, both from animal experiments and human exposures to high levels of radiation, that ionizing radiation can induce some cancers; however, epidemiological studies generally have failed to find a statistically significant correlation between cancer mortality and levels of background radiation (see “Epidemiology and Statistical Significance”). A few studies claim to find a negative correlation, which means that some areas with higher than average levels of background radiation have lower than average levels of cancer mortality. Some researchers have concluded from these studies, together with cellular studies, that small amounts of radiation may induce an adaptive response that serves to protect humans from diseases such as cancer (this effect is also known as radiation hormesis). However, such negative correlations of disease with radiation dose may be caused by confounding factors not properly accounted for in the epidemiological studies. Adaptive responses to low doses



**Figure 1. The Distribution of World-Average Annual Background Radiation**  
 The pie chart shows the estimated number of millirem per year from the four major sources of background radiation. These estimates for world-wide averages were made by the United Nations Committee on the Effects of Atomic Radiation (UNSCEAR93). They differ somewhat from those shown for the average U.S. citizen (made by the National Council on Radiation Protection and Measurements) in “Ionizing Radiation—It’s Everywhere!” page 29. Also, the total annual background dose quoted here, 238 millirem, does not include the average contribution of man-made sources to the public.

### Radiation Units

For ionizing radiation, the unit of absorbed dose, the rad, corresponds to the deposition, via ionization and excitation processes, of 100 ergs of energy per gram of tissue. Some radiations are more effective, per unit of energy deposited, at producing biological damage than others. To account for these differences, the absorbed dose (in rad) is multiplied by a quality factor to obtain the dose-equivalent, which is expressed in rem (roentgen-equivalent-man); one millirem (mrem) equals one-thousandth of a rem. The rad and the rem are being replaced internationally by a new pair of units, the gray (Gy) and the sievert (Sv). The unit of absorbed dose, the gray, corresponds to one joule of energy deposited per kilogram of tissue, so one Gy equals 100 rad. The sievert is the corresponding unit of dose-equivalent; one Sv equals 100 rem.

of radiation have definitely been observed in experiments with human cells *in vitro*; however, the jury is still out regarding the existence of adaptive responses in humans at the clinical level (UNSCEAR94, Annex B). In summary, no convincing evidence exists that

natural background radiation is harmful. Experiments at low doses using animals are useful. However, because the effects of radiation vary widely from one species to another, animal data alone cannot be reliably used to predict ef-

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## Epidemiology and Statistical Significance

Epidemiology, the statistical study of the occurrence of disease in populations, is the primary means of determining the relationship between radiation exposure and cancer risk. And yet such studies are no simple task. Their credibility is directly related to the strength of the numbers, or more technically, the statistical significance of the data. Using cancer as an example, we first explore the mathematical framework in which the significance of the data is evaluated.

### Sample size and statistical significance

One in five Americans dies of cancer. But because cancer is a mysterious disease with a very complicated origin, it is impossible to predict exactly who the one in five will be. Because its occurrence is so unpredictable, the epidemiologist may simply assume that cancer strikes at random and that each of us has the same 20 per cent probability of dying of it. Such an assumption implies that any possible confounding factors are negligible and that known familial (genetic) factors are ignored. It is as if everyone's fate were determined as they walked in line past a giant barrel containing marbles in which one in five of them are blue. Each person blindly picks a marble out at random. If at your turn, a blue marble is picked, cancer will be your fate, otherwise, not. Now suppose that there is a population of 1000 whose fate was determined in the random manner just described. Should we expect that *exactly* 20 per cent, or 200, of the 1000 people will die of cancer? No. Although 200 is the most likely outcome, it is also likely that the outcome will be close, but not equal, to 200. Theoretically, any number of cancer deaths between zero and 1000 (or percentage between zero and 100) is possible, but the further away from 200, the less likely the result.

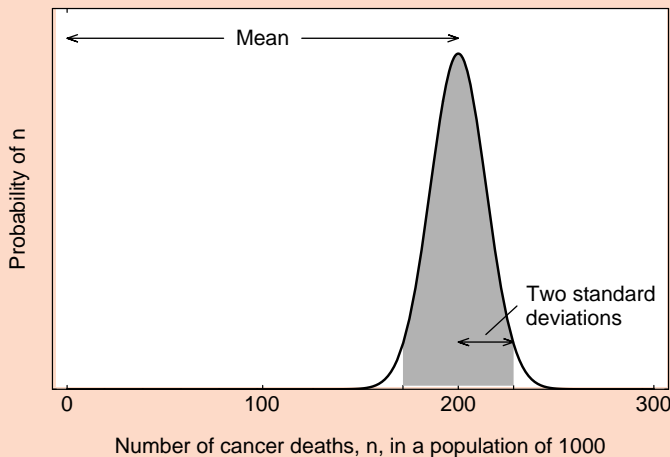
For a population of 1000, the probability of any given outcome lies on a bell-shaped curve, as shown in Figure 1. The curve is centered about 200, which is both the mean value ( $m$ ) and the most probable number of cancer deaths for a population of 1000 chosen at random. The width of the curve is indicative of the range of likely outcomes and is characterized by a quantity called the standard deviation,  $s$ . In these types of studies, a useful approximation of the standard deviation is simply the square root of the mean, which in this case is about 14. As you can see from the graph, the vast majority of the possible outcomes (about 95 per cent) falls within the range of 172 and 228, or two standard deviations ( $2s$ ), around the mean. Therefore, although 200 is the most probable result, we would be



**Epidemiologists treat cancer as a random event. It is as if everyone's fate regarding cancer were determined by whether or not he or she chose a blue marble from a giant barrel in which one out of five marbles were blue.**

wrong to expect to always get *exactly* 200. Instead, we expect that, 95 per cent of the time, the result will fall within a range of two standard deviations on either side of the mean.

In epidemiological studies of radiation effects, the number of cancer deaths in the exposed population generally must be greater than about two standard deviations above the mean in the unexposed population for the result to be considered statistically significant. If the observed number is greater than the mean by more than two standard deviations, then the epidemiologists say they have determined a positive correlation between cancer deaths and radiation exposure. Similarly, a negative correlation is inferred if the observed number of cancer deaths is less than the expected number by more than two standard deviations.



**Figure 1. Fluctuations in the Number of Cancer Deaths**

The probability of a certain number of random cancers occurring in a population of 1000 is represented by a bell curve centered about 200. The mean number and most probable number of cancer deaths is 200. The width of the curve is characterized by the standard deviation  $s$ , which is approximately equal to the square root of the mean, or 14. The shaded area under the curve between the values  $200 \pm 2s$  and  $200 \pm 2s$  is about 95 per cent of the total area, which means that in 95 out of 100 samples of 1000 people, the number of cancer deaths will fall between those two values. To find a statistically significant correlation between, say, radiation exposure and cancer, the number of cancer deaths would have to be greater than  $200 \pm 2s$ .

The ability to distinguish excess cancer deaths due to radiation exposure from the expected ones improves markedly as the sample size increases. That's because the relative size of the standard deviation,  $s/N$ , decreases as the sample size,  $N$ , increases.

$$s/N \propto 1/\sqrt{N}$$

Figure 2 illustrates this point. It shows the bell curve of Figure 1 for sample sizes of 1000 and 10,000, but this time the variable plotted on the horizontal axis is the fraction of the population that dies of cancer, rather than the absolute number of cancer deaths. Both curves are centered around the mean fraction of 0.20, but the widths of the curves, or the expected deviation from the mean, for

the larger population is much smaller than that for the smaller population. Therefore, one has a much greater chance of detecting a statistically significant number of excess cancer deaths in a very large sample than in a small one.

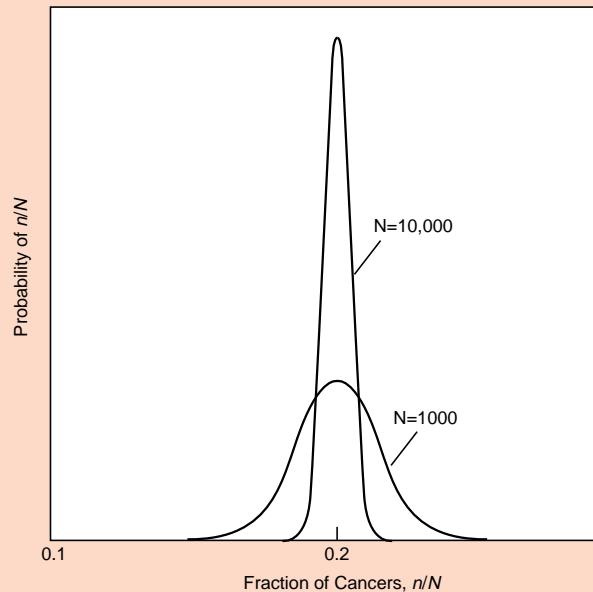
Now that the statistical framework is defined, what's the next step for the cancer epidemiologist? Statistics on the "normal" cancer incidence and mortality must be obtained by studying the general population. (Incidence refers to the number of new cancers in a defined population per year, and mortality refers to the number of cancer deaths in a defined population per year.) The statistician is typically limited to vital statistics obtained from birth and death certificates kept by health departments at the federal, state, or county level. Age at death, number of deaths, and causes of death are the most important data used in determining specific mortality rates such as cancer death rates. In principle, one would like to check medical records against death certificates, but this is possible only with permission of the next of kin, because medical records are totally confidential.

In radiation studies, the epidemiologist collects data on an exposed population to see whether or not they exhibit an excess number of cancers compared with the number expected based on the mortality rates of a similar, but unexposed, population. As we've pointed out, statistically reliable results require large populations as well as accurate records of individual radiation exposures. Only a few identified exposed groups meet these requirements: the atomic-bomb survivors, patients that have received radiation for the diagnosis or treatment of various diseases, and nuclear workers.

Certain populations exposed to relatively high natural-background levels have been compared to those living in areas with more normal radiation levels, but in this case, only the average population doses are known, not the individual doses. In occupational studies, and especially in nuclear-industry studies, it is often the case that both the exposed and the unexposed populations are chosen from within the industry. That choice helps to insure lifestyle similarity and minimizes the so-called "healthy-worker effect," which is the built-in bias among the working population of having fewer diseases and a lower mortality rate than the general population.

The interpretation of epidemiological studies is another challenge. In a perfect world, one would be able to compare the rates of cancer incidence and cancer mortality in two populations whose members have identical cancer risks except for the fact that, in one, the members are exposed to radiation above the background level, and, in the other, they are not. In practice, members of the population differ in many factors affecting cancer risk including age, genetic predisposition, exposure to chemical carcinogens, and perhaps certain lifestyle factors such as smoking and socioeconomic level. A study must take into account any significant differences in these factors between the exposed and unexposed group. Another complication is that, within the exposed population, the cancer risk varies depending on the age at which one is exposed, the size of the dose, and the time since exposure. Consequently, one must have information on these three factors for all the members of the exposed population to assess the cancer incidence or mortality data properly. Moreover, because the latency time from exposure to detection may be 30 to 40 years for most cancers, both populations should be followed for the lifetimes of the subjects.

In general, epidemiological studies do not prove causation, rather they determine the correlation between two or more variables. A positive correlation suggests a link or association of some kind, the significance of which must be evaluated. In the worst case, the correlation may be due to a systematic bias in the study or to so-called "confounding factors" that were not explicitly included in the study, yet had a profound impact on the results. (For example, if bars were the only public places in which one were allowed to smoke, it would be incorrect to attribute all excess lung cancer among frequenters of bars to the intake of alcohol.) It's easy to be fooled—there are many kinds of hidden variables in the selection of the population, the gathering of the data, and the analytic procedures for interpretation that may bias the results of the study. Sir Bradford Hill, a well-known epidemiologist, listed nine factors that must be taken into account in evaluating the significance of data. Among them are the strength of the numbers themselves (Is the observed excess large or just marginally elevated? Is there a correlation between the size of the dose and the size of the excess?), the agreement between biological data and theory, and the consistency of the result with other studies done using different methodologies and different study groups. The epidemiological studies that address as many of these factors as possible, and then clearly lay out the statistical basis of their work for others to critique, are the studies that should be most trusted, discussed, and used to support conclusions about the effects of radiation. ■



**Figure 2. The Advantage of Large Sample Sizes**

The two bell curves represent the probability for a given fraction of cancer deaths  $P(n/N)$  versus the fraction of cancer  $n/N$  deaths in a population of size  $N$ , where  $N$  equals 1000 and 10,000, respectively.

The two curves are centered about the mean value of 0.2. Note that the width of the curve is much narrower for the larger population because, as  $N$  increases, the standard deviation of the fraction  $n/N$  decreases (approximately as  $1/\sqrt{N}$ ).

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fects in humans. Therefore, those responsible for making recommendations regarding dose limits rely on human data whenever possible. Human data generally come from four sources: Japanese atomic-bomb survivors, radiation accidents, occupational exposures, and medical exposures.

All of the observed effects of ionizing radiation in humans occur at relatively high doses (that is, greater than about 20 rem). At the low doses that are of interest to radiation workers and the general public (that is, below a few rem), the epidemiological data are generally inconclusive, mainly because the change (up or down) in cancer mortality that might occur at such low doses is less than the variations that occur for all other reasons, both known and unknown. Consequently, the risks associated with low-dose exposures must be *hypothesized*. The conventional choice, considered prudently conservative, is a linear extrapolation, all the way down to zero dose, of the risks determined from observed effects at high doses. This prescription is termed the linear-dose-response, no-threshold (LNT) hypothesis.

Is such an extrapolation reasonable? Down to what level of dose? A rem? A millirem? A microrem? All the way down to zero rem? The answers to these questions are important for risk assessment. They are also important because they help shape the public perception of the dangers of ionizing radiation. Public perception, in turn, is driving the ever-increasing number and variety of laws, regulations, and guidelines dealing with ionizing radiation, all of which add considerably to the cost of doing business at a facility that handles nuclear materials. This cost, ultimately, is paid by our society.

The recent re-examinations of human radiation experiments that were carried out in the 1940s and 1950s have focused new attention on the possible biological effects of radiation. Actually,

very little media attention focused on the health effects that resulted from these experiments, as this would have made very dull copy. In the interest of gaining a better perspective with which to evaluate the possible detrimental effects of those human radiation experiments, it is worthwhile to review what is known about the effects of ionizing radiation in humans, the dose levels at which these effects occur, and the risks deduced from these effects. The nature of the radiation protection standards derived from these high-dose risks by extrapolation to low doses is also of interest. More broadly, this review can help us to understand the significance of the levels of radiation that we ourselves might encounter and to evaluate the laws and standards that regulate our own exposures.

### Radiation Effects in Humans

What are the biological effects in humans that result from exposure to ionizing radiation, and at what dose levels are these effects observed? In this section, we attempt to answer these questions by reviewing some exposures, both historical and current, that have resulted in observed effects. All the studies reported in this section are at dose levels above 10 rem; below this level, results are not statistically significant.

Radiation effects fall into two broad categories: deterministic and stochastic. At the cellular level, high doses of ionizing radiation can result in severe dysfunction, even death, of cells. At the organ level, if a sufficient number of cells are so affected, the function of the organ is impaired. Such effects are called "deterministic." Deterministic effects have definite threshold doses, which means that the effect is not seen until the absorbed dose is greater than a certain level. Once above that threshold level, the severity of the effect increases with dose. Also, deterministic effects are usually manifested soon after exposure. Examples of such

effects include radiation skin burning, blood count effects, and cataracts.

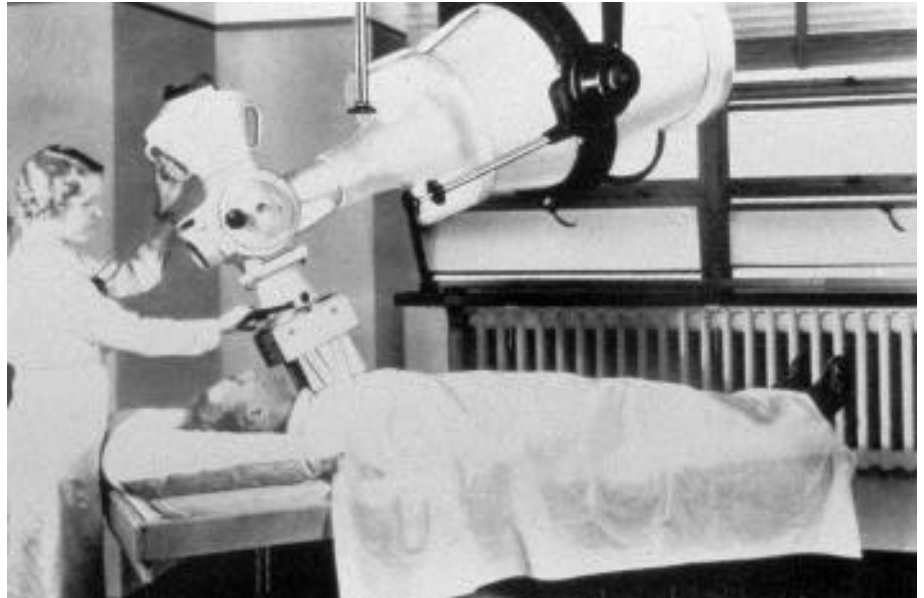
In contrast, stochastic effects are caused by more subtle radiation-induced cellular changes (usually DNA mutations) that are random in nature and have no threshold dose. The probability of such effects increases with dose, but the severity does not. Cancer is the only observed clinical manifestation of radiation-induced stochastic effects. Not only is the severity independent of dose, but also, there is a substantial delay between the time of exposure and the appearance of the cancer, ranging from several years for leukemia to decades for solid tumors. Cancer can result from some DNA changes in the somatic cells of the body, but radiation can also damage the germ cells (ova and sperm) to produce hereditary effects. These are also classified as stochastic; however, clinical manifestations of such effects have not been observed in humans at a statistically significant level.

**Nuclear Accidents.** During the first few decades of nuclear weapons development, several incidents occurred during which fissile material accidentally came together in a critical configuration that produced, just briefly, an uncontrolled nuclear chain reaction (see "The Cecil Kelley Criticality Accident" on page 250). During these so-called critical excursions, workers received very high, sometimes fatal, whole-body doses of neutron and gamma radiation. High dose levels also have resulted from industrial radiation accidents and accidents involving improperly discarded or lost high-level radioactive sources (for example, medical sources used in radiation therapy). The Chernobyl accident resulted in high dose levels, particularly to reactor personnel and firemen; the Three-Mile Island accident did not result in high dose levels to anyone. From these experiences, together with high-dose animal experiments, an understanding has emerged of the biological effects of high-dose acute whole-

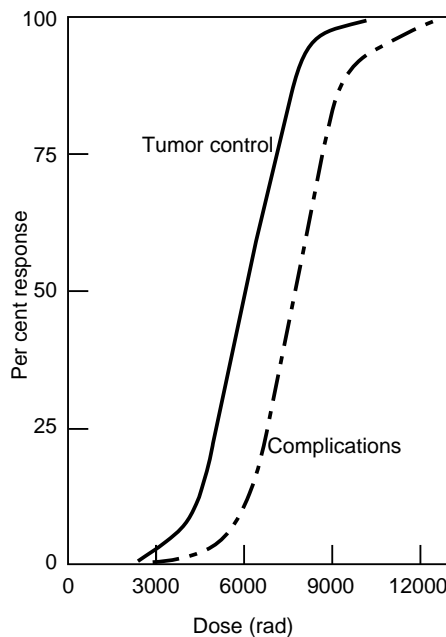
body exposure to ionizing radiation.

Acute radiation syndrome, the name given to the body's reaction to high-dose high-dose-rate exposures, involves three basic functional systems (the radiation-sensitive organ is given in parenthesis): the hematopoietic, or blood forming, system (bone marrow); the gastrointestinal system (epithelial lining of the small intestine); and the central nervous system (brain). Of the three, the hematopoietic system is the most sensitive to radiation, with syndrome and death thresholds of about 100 rad and 200 rad (whole-body effective dose), respectively. Irradiation causes the death of bone-marrow stem cells, which diminishes or stops the resupply of circulating red and white blood cells and other blood constituents. After about three weeks the reduction in blood supply causes immune deficiencies, infections and fever, bleeding, and even death unless the blood marrow has begun to regenerate. The earliest symptoms of fatigue, nausea, and vomiting probably involve all three functional systems. One measure of lethal dose is referred to as the LD50/60 dose, which is the acute dose that results in death within 60 days for 50 per cent of the exposed individuals. The LD50/60 in humans for hematopoietic syndrome is 300 to 350 rad (whole-body effective dose).

**Radiotherapy for Cancer.** Radiation therapy for the treatment of cancer is another context where both doses and dose rates are high, and the radiation effects are dramatic. The observable outcomes, both immediate and long-term, are an important source of information on radiation effects. The immediate effect at the cellular level is similar to that in acute radiation syndrome, namely the death of proliferating cells. The goal is to kill all of the malignant cells in a tumor, while sparing the surrounding healthy tissue. Dividing the total dose delivered into several smaller fractions preferentially spares normal tissues com-



X-ray machines of the type shown here (200-300 kilovolt) were the workhorses of radiation therapy from the 1930s through the 1960s. Damage to the patient's skin often limited the ability to treat deep lesions.



**Figure 2. Effects of Radiotherapy** This graph of tumor-control rate and complication rate versus dose illustrates the delicate balance between tumor control and complications arising from radiotherapy. Increasing the treatment dose to improve the tumor-control rate leads to a higher rate of complications, whereas decreasing the dose to reduce complications results in a lower tumor-control rate. (Reproduced with permission from M. R. Raju, 1980, *Heavy Particle Radiotherapy*, New York: Academic Press.)

pared to the tumor. A typical treatment may involve up to about 6000 rad, fractionated into doses of 200 rad per day, five days per week, for 4 to 6 weeks.

In terms of the goal of local tumor control, radiation therapy is successful for about two-thirds of the patients treated. However, it is estimated that approxi-

mately 5 per cent of second cancers that develop following radiation therapy are caused by the radiation delivered in therapy. As shown in Figure 2, there is a delicate trade-off between controlling the tumor and causing complications in nearby tissues. Although it is possible to reduce the rate of complications by lowering the treatment dose, this may be achievable only at the expense of decreasing the rate of control of the initial tumor.

Some individuals are particularly sus-



ceptible to radiation-induced cellular damage because they have inherited a deficiency in a mechanism that either signals or performs DNA repair. Individuals with such hereditary genetic disorders have an increased sensitivity to radiation. One of the best studied repair disorders is ataxia-telangiectasia (AT), a deficiency in cell-cycle checkpoint response to DNA damage (see "Radiation, Cell Cycle, and Cancer"). At the clinical level, patients with AT display progressive neurological and immune disorders. In addition, they are

statistically observable effects; they are not intended to be interpreted as threshold values for those effects.

statistically susceptible to radiation, but studies with cultured cells show only a small increase in radiation sensitivity. It is estimated that AT heterozygotes represent 1 to 3 per cent of the general population and 9 to 18 per cent of all breast cancers in young women.

**Historical Medical Exposures.** During the decades from 1930 to 1960, the widespread use of radiation for the diagnosis and treatment of disease led, in a number of cases, to the unexpected induction of primary cancers. Epidemi-

statistically observable effects; they are not intended to be interpreted as threshold values for those effects.

The following four studies all involve the use of large x-ray doses for diagnosis or treatment:

- More than 14,000 persons in Great Britain (1935-1954) were given x rays to treat ankylosing spondylitis, a disease of the spine. Cancers for which significant excess mortality was later found include: leukemia (380 rem), non-Hodgkin's lymphoma (380 rem), esophagus (400 rem), lung (180 rem), bone (300 rem), female breast (50 rem), and brain (140 rem).

- A study of about 19,000 female tuberculosis patients in Canada (1930-1952) who received multiple diagnostic chest-x-ray fluoroscopies found significant excess mortality for breast cancer (40 rem). A similar study of about 2600 female tuberculosis patients in Massachusetts (1925-1954) also found significant excess incidence of breast cancer (80 rem).

- About 11,000 children in Israel (1948-1960) and 2200 in New York (1940-1959) with tinea capitis (ringworm of the scalp) were treated by x-ray epilation, resulting in significant excess cancers of the brain (150 rem), thyroid (10 rem), and skin (non-melanoma) (450-680 rem).

- A study of more than 2600 persons in Rochester (1926-1957), who were exposed in infancy to x rays for the treatment of enlarged thymuses, showed a very significant increase in thyroid cancer (140 rem) and female breast cancer (80 rem).

From these studies, it would appear that the thyroid is a relatively radiosensitive organ, with a dose of the order of 10 rem sufficient to produce cancer in some cases. A similar conclusion applies to the female breast, for which a dose of the order of 40 rem seems sufficient to produce cancer in some cases.



**Mass chest screening for tuberculosis was common during much of the century. Full-sized films were often used, but here the fluorescent image was reduced to a 100 millimeter format. The "portable" apparatus shown was transported from site to site.**

much more susceptible to developing certain cancers and, also, can develop devastating necrosis of normal tissues as a result of radiation therapy. AT is a recessive disorder, which means that both copies of the relevant gene must be defective for the disease to be manifested. Cultured cells from AT patients are about 3 times as sensitive to x-ray-induced cell death as are control cells. This increased sensitivity to radiation may not be restricted to patients with a manifest disease. There has been some suspicion that AT heterozygotes (defect on only one copy of the gene) also are at increased risk of developing cancer, both with and without medical expo-

logical data have been collected from several of the exposed groups (UNSCEAR94, Annex A). Although the data are not sufficiently detailed to predict the quantitative increase of cancer risk with dose, they do demonstrate that doses in the hundreds, even tens, of rem have resulted in statistically significant increases in cancer mortality. The data also illustrate the many different types of cancer that can be induced by radiation exposure. For each study presented below, we show in parenthesis, if known, the *mean* organ dose for the group being discussed. We state these mean-dose figures to indicate the magnitudes of doses given that resulted in

### Measuring Risk

Several definitions of risk are commonly used in epidemiology. For example, let us suppose that we are interested in the cancer mortality risk associated with an exposure to some dose of radiation. The *relative risk (RR)* is defined as the ratio of the observed number of cancer deaths ( $O$ ) in the study population to the expected number ( $E$ ) for a similar, but unexposed, population ( $RR = O/E$ ). By similar, we mean similar in age and sex distributions, economic status, life style, and habits. The *excess relative risk (ERR)* is defined as the ratio of the excess number of cancer deaths ( $O-E$ ) to the expected number ( $E$ ):

$$ERR = (O - E)/E = (O/E) - 1 = RR - 1.$$

Note that the absolute excess *rate* of radiation-induced cancer mortality is obtained by multiplying *ERR* by the expected *rate* of cancer deaths for an unexposed population. Risk factors, or coefficients, are derived by dividing the risks defined above by the dose received.

We illustrate these concepts by a fictional example. Suppose a population of 1000 persons is exposed to an acute dose of 100 rem. And suppose that 220 are observed to die from various cancers, whereas the expected number is 200 (the expected rate is  $200/1000 = 0.2$ ). The relative risk and the excess relative risk are given by:

$$RR = 220/200 = 1.1,$$

$$ERR = 1.1 - 1 = 0.1.$$

The relative-risk factor and the excess-relative-risk factor are given by:

$$RR \text{ factor} = 1.1/(100 \text{ rem}) = 0.011 \text{ per rem, or } 1.1 \times 10^{-2} \text{ rem}^{-1}$$

$$ERR \text{ factor} = 0.1/(100 \text{ rem}) = 0.001 \text{ per rem, or } 10^{-3} \text{ rem}^{-1}.$$

Finally, the absolute excess cancer mortality rate is  $ERR \times (0.2) = (0.1)(0.2) = 0.02$ , and the corresponding factor is  $0.02/(100 \text{ rem}) = 0.0002 \text{ per rem, or } 2 \times 10^{-4} \text{ rem}^{-1}$ . An additional point to be made for this example is that, at the 95 per cent confidence level, the excess deaths are not statistically significant, because the expected number of cancer deaths lies in the range of 172 to 228 (see "Epidemiology and Statistical Significance"). ■

However, in both instances, the dose quoted is the mean dose per patient treated, not the mean dose per cancer induced; so the association of the doses quoted with cancer induction is more suggestive than definitive. Of particular concern is the trend for increased radiosensitivity among younger patients.

For several of the studies, the excess relative risk was found to increase with decreasing age at exposure, especially for breast cancer and thyroid cancer (see "Measuring Risk").

The potential carcinogenic effects of prenatal exposure to radiation are of

importance because the developing fetus, who is experiencing rapid cell growth, may be more sensitive to radiation than are adults or children. Several studies have been made in the United States, the United Kingdom, and elsewhere of the possible association of childhood cancer with prenatal obstetric x-ray examinations. The relative risk estimate from all of these studies combined is about 1.4—that is, children irradiated *in utero* were found to have a 40 per cent higher incidence of cancer than unirradiated children. However, some researchers have expressed reservations about these results. One of the reservations is that the dose absorbed by the embryo or fetus is not very well known. Another is the surprising finding of the equality of relative risk for leukemia with that for solid tumors, which is not the case for postnatal exposures. Finally, among the Japanese atomic-bomb survivors, no association was found between childhood cancers and *in utero* exposures (mean uterine dose of 18 rad). As is often the case in epidemiology, these results seem to raise more questions than they resolve.

Another past medical practice that resulted in excess cancers was the injection of radium solutions for the treatment of various diseases. Radium is a naturally occurring radioactive element that was discovered by the Curies in 1898 and became widely taken for its alleged curative powers. When ingested or injected into the bloodstream, much of the radium is later deposited in the bone, where it and its radioactive daughter products bombard the surrounding bone tissues with radiation, most notably, alpha particles. Approximately 2000 persons in Germany (1944-1951) were treated for various diseases, including tuberculosis and ankylosing spondylitis, with multiple injections of radium-224 (physical half-life of 3.6 days) in the form of radium chloride. The resulting average skeletal dose was more than 400 rad, primarily from alpha particles, which are considered 20 times as damaging as x rays (1

rad absorbed dose of alpha radiation corresponds to 20 rem dose-equivalent). The subsequent incidence of bone sarcomas was found to be 280 times that expected from an unexposed population. Similar effects were observed in patients in the United States who were given radium-226 (1600-year half-life) and radium-228 (5.8-year half-life) before 1950.

Thorotrast, a colloidal solution of thorium dioxide, was used as an x-ray imaging contrast agent in several countries from the early 1930s to the early 1950s. It is deposited at several sites within the body, primarily in the liver and spleen.

**Occupational Exposures.** Before information about the potential dangers of radiation became well known and adequate measures were taken to control occupational exposures, high levels of exposure were fairly common and, in some cases, caused serious consequences for numerous workers. Perhaps, the most widespread serious biological effects from occupational exposure to radiation occurred among uranium miners. The miners inhaled radon and its decay products, most of which are alpha emitters, and suffered a greatly increased risk for lung cancer. Around the turn of the century, radon concentrations in the mines of central

sure results in a lung dose of almost 2700 rem, which corresponds to a whole-body effective dose of about 320 rem. This risk is not confined to uranium miners. For example, tin miners in China, who were also exposed to radon, suffered comparable excess lung cancer risk.

The occupational exposure that finally revealed the dangers of internal emitters was that of radium-dial painters, who were exposed to radium while painting luminous dials in the U.S. during the early decades of this century. The dial painters, most of whom were young women, would lick the ends of their paint brushes to get finer tips, thereby ingesting radium-226 and radium-228. Fatalities from severe anemia, resulting from exposure of blood-forming tissues to alpha particles, began to occur during the early 1920s among those with relatively large radium body burdens. Later, bone cancers began to appear among those with somewhat lower body burdens. A classic study of radium-induced cancers among the dial painters included more than 1500 females. Of the 154 subjects who received skeletal doses of greater than 20,000 rem, 62 subjects developed skeletal tumors (these 62 had a total of 65 head carcinomas and bone sarcomas combined). No skeletal tumors were observed in 1391 subjects who received skeletal doses less than 20,000 rem, which has been interpreted by some as evidence for a threshold—that is, a dose level below which no effect is observed.

This apparent threshold for radium-induced cancer seems to be contradicted by a study of a larger, but less homogeneous, population of more than 4000 subjects, including radium-dial painters, radium chemists, and patients who were therapeutically treated with radium in the U.S. before 1950. Of the more than 2400 persons for whom an estimate of skeletal dose was made, 66 bone sarcomas occurred, compared to fewer than 2 that would have occurred in an unex-

**Table 1. Whole-Body Doses for Mayak Nuclear Weapons Facility Workers**

	Worker Groups*			
	IA	IIA	IB	IIB
Average cumulative dose (rem)	122	49.2	245	71.6
Average annual dose (rem)	32.6	6.4	70.4	17.2
Per cent with greater than 100 rem per year	6.5	0.15	22.8	0.1

\*Groups are defined in the text.

Natural thorium consists entirely of thorium-232, which has a very long half-life (greater than  $10^{10}$  years), and many of its daughters are alpha emitters. It is estimated that an injection of 25 milliliters of Thorotrast delivered dose rates of alpha radiation of 1400 rem per year in the spleen, 500 rem per year in the liver, 320 rem per year in the endosteal layer of bone (inner surface surrounding the marrow), 260 rem per year in the bronchi, and 180 rem per year in the bone marrow. Not surprisingly, Thorotrast-treated patients suffered exceedingly high rates of liver cancer and leukemia, and statistically significant excess rates of several other types of cancer.

Europe were so high that about one-half of the miners died of lung cancer. A more recent comprehensive study of over 60,000 uranium miners from 11 locations throughout the world showed an 80 per cent increase in lung cancer deaths over what was expected, based on a comparison with over 7,000 unexposed miners. The uranium miners received an average exposure of 161.6 working-level-months.<sup>†</sup> Such an expo-

<sup>†</sup>A working-level is defined as a potential alpha-particle energy concentration of  $1.3 \times 10^8$  MeV per cubic meter, which corresponds to an activity concentration for radon-222 in equilibrium with its daughters of 100 picocuries per liter of air. A working-level-month is defined as an exposure to one working-level for 170 hours, or one working month.

posed population. In addition, 35 sarcomas of the paranasal sinuses and mastoid air cells occurred, compared to fewer than 1 that would be expected for an unexposed population. The median cumulative skeletal dose at the time of tumor diagnosis was about 120,000 rem for the bone sarcomas. Three head-sinus carcinomas and three bone sarcomas (including a British dial painter) have occurred in individuals with skeletal doses of less than 24,000 rem, whereas only 0.2 would be expected for an unexposed population. For each type of cancer, the smallest cumulative skeletal dose was about 2000 rem (one case each), which is a factor of ten lower than the threshold value suggested by the study of dial painters alone. These results would seem to contradict the indication of a possible threshold skeletal dose of 20,000 rem, but the small number of cancers do not make a very convincing case. This larger study has the advantage of a larger population, whereas the study of dial painters involves a more homogeneous population.

Exposures in the U.S. nuclear industry and weapons laboratories have been controlled from the beginnings of the nuclear era in the early 1940s, in part as a result of the experience of the radium dial painters and the subsequent adherence to radiation protection standards. Consequently, the average annual exposures have been kept to a few rem or less, and the health effects, if any, are very difficult to detect through epidemiological studies.

We now know that the situation in the former Soviet Union was rather different. A study of workers at the Mayak nuclear-weapons facility in Russia documents that average cumulative exposures were in the range of hundreds of rem and that significant increases in cancer mortality resulted from those exposures. The dose data given in Table 1 have been compiled through 1989 and are organized according to, first, whether the workers started in the

period 1948-1953 (I) or 1954-1958 (II), and second, whether they worked at the nuclear reactor (A) or the reprocessing plant (B). Statistically significant excess mortality risk for cancers of the hematopoietic and lymphatic systems, as well as all cancers combined, was found for group IB only. Apparently, during the early years of operation, chronic radiation sickness (chronic fatigue, depression, and an altered blood profile) was common, but rarely occurred in workers with less than 25 rem annual dose or 100 rem cumulative dose. Workers who exceeded both of these values had substantially higher



**X-ray fluoroscopy began around 1900. In this technique the x rays cause crystals on the screen of the instrument to fluoresce. The image is thus seen directly by the operator. Fluoroscopy was initially considered more effective than radiography because examinations could be conducted rapidly and without the use of expensive photographic plates. However, radiation damage to operators became well known even in the early years of the twentieth century.**

cancer mortality than those who did not. The cancer mortality for those workers who did not exceed these values was similar to that of the general population. After 1968 in plant A, and 1974 in plant B, annual doses averaged over all workers were kept below 5 rem, which was the internationally rec-

ognized annual limit for individual radiation workers at that time.

Studies on health effects of radiation on radiologists and radiology technicians go back to the early use of x rays in medicine. British radiologists who began their professional work before 1921 had a 75 per cent higher cancer death rate than other medical practitioners. Cancers of the pancreas, lung, skin, and leukemia were significantly elevated. Doses received by those early workers are not possible to estimate, but whole-body doses of the order of 100 to 500 rad might have been accumulated by those entering the profession between 1920 and 1945. The cancer death rate for British radiologists who started in the profession after 1920 was not significantly elevated.

Until about 1950, radiologists in the U.S. were also observed to have excess cancer mortality, especially leukemia, lymphoma, and multiple myeloma, when compared with internists or other medical specialists who have less potential for radiation exposures. Both the British and U.S. studies show that, since adoption of radiation protection practices, any hazard attributable to radiation can no longer be demonstrated. Medical x-ray personnel in China and Japan during study periods of two to three decades before 1985 had increased relative risks for cancers of the esophagus, liver, skin, large intestine, central nervous system, and leukemia. In all studies, a consistent finding for medical x-ray workers in earlier periods, when they accumulated higher doses, is an increased risk for all cancers combined. However, the lack of dose measurements is a serious deficiency and limits the value of those studies for estimating radiation risk.

This abbreviated survey of radiation effects in exposed populations suggests that acute radiation doses in the tens of rem range can result in an increased risk for some cancers, notably thyroid and female breast, and that the risk in-

creases with increasing dose for all cancers. The medical exposures were generally acute, whereas the occupational exposures were generally chronic. At high levels, both have been associated with elevated cancer incidence and mortality.

### Risk Estimates Based on Japanese Atomic-Bomb Survivors

What is the cancer mortality risk per unit dose that is derived from observed effects of radiation in humans? In this section, we obtain quantitative cancer mortality risk factors for high-dose high-dose-rate exposures from an analysis of the most recent data for the Japanese atomic-bomb survivors (UNSCEAR94, Annex A). In addition, we examine non-carcinogenic prenatal effects in this group (UNSCEAR93, Annex H).

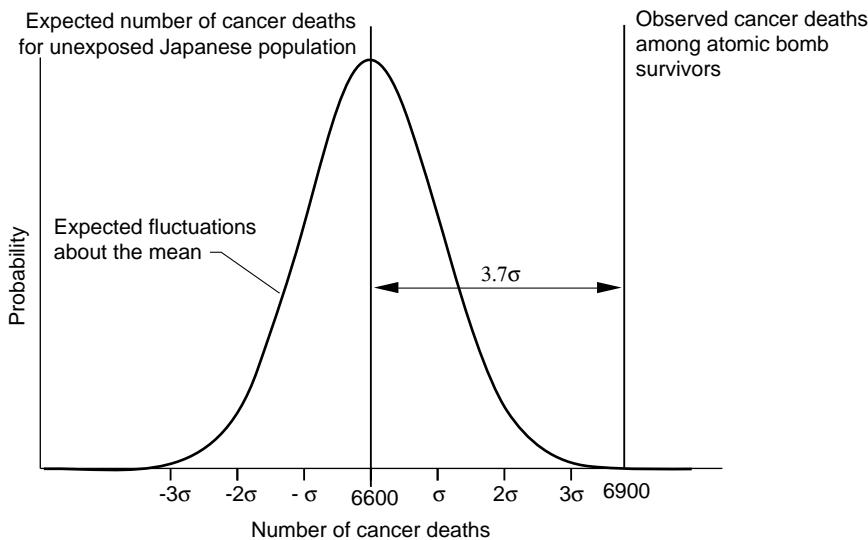
**Atomic-Bomb Survivors.** Perhaps, the best source of data on the radiation in-



duction of cancer in humans is the Life-Span Study of survivors of the atomic bombings of Hiroshima and Nagasaki. The study involves a large homogeneous population, the subjects have been followed with great care for decades, and they represent all ages at time of exposure, both sexes, and a wide range of doses. The data on solid-

tumor incidence cover the period from 1958 to 1987 and include about 80,000 individuals; the data on leukemia incidence and solid-tumor mortality cover the period from 1950 to 1987 and include about 86,000 individuals for each.

The 1985 total Japanese population is used as the basis for expected rates of mortality, cancer mortality, and cancer incidence, by age and sex, among an unexposed population. On the basis of these normal mortality rates in the atomic-bomb-survivor population, the number of solid-tumor deaths expected is about 6600, whereas the observed number is about 6900. As shown in Figure 3, this excess of 300 cancer deaths represents a statistically significant increase above the expected number, but the absolute number may seem surprisingly small to most members of the general public. Perhaps, this result, more than any other, provides a meaningful perspective for the public's anxieties regarding radiation, so it deserves emphasis. Of approximately 86,000 persons that survived exposure to atom-



**Figure 3. Excess Solid-Tumor Deaths among Atomic-Bomb Survivors** The observed number (6900) of solid-tumor deaths among Japanese atomic-bomb survivors (1950-1987) and the distribution of the expected number of such deaths, with a mean value of 6600. The observed number is 3.7 standard deviations from the mean, indicating that the number of excess cancer deaths is much greater than can be accounted for by fluctuations in the expected number. (Data from UNSCEAR94).

ic bombings in 1945, only 300, or 0.35 per cent, are estimated to have died later (1950-1987) from radiation-induced solid cancers. In the leukemia incidence cohort, 75 persons, or 0.087 per cent, are estimated to have developed radiation-induced leukemia.

Table 2 lists those cancers for which statistically significant (90 per cent confidence) effects were seen for cancer mortality and for cancer incidence. Also given are the excess-relative-risk factors. Statistically significant effects were not seen, in either the incidence or mortality data, for cancers of the esophagus, bone and connective tissue, and brain and central nervous system. Also, statistically significant effects were not seen in the incidence data for non-Hodgkin's lymphoma. Unfortunately, an earlier analysis, which assumed that neutrons and gamma rays were equally effective for carcinogenic effects, had to be used for the leukemia and multiple myeloma mortality data, as these were not available in the most recent analysis, which assumed that

**Table 2. Statistically Significant Radiation-Induced Cancers**

Cancer Site	Excess-Relative-Risk Factor for Mortality* (rem <sup>-1</sup> )	Mortality Rate per 100,000 person-years <sup>†</sup>	
		male	female
leukemia	0.052	8.5	5.0
multiple myeloma	0.023	3.4	2.2
breast	0.018	0.2	27.2
bladder	0.012	5.8	1.6
lung	0.0076	73.0	30.9
colon	0.0047	23.3	15.6
liver	0.0044	3.6	1.7
stomach	0.0022	6.3	2.8

Cancer Site	Excess-Relative-Risk Factor for Incidence* (rem <sup>-1</sup> )	Incidence Rate per 100,000 person-years <sup>†</sup>	
thyroid	0.015	2.5	6.4
skin (non-melanoma)	0.0088	—unavailable—	

\*Excess- relative-risk factors are calculated using a quality factor of 10 for neutrons, except for leukemia and multiple myeloma mortality, where a quality factor of unity is assumed.

<sup>†</sup>Normal age-adjusted cancer and incidence rates in the U.S. (1987-1991).

**Table 3. Life-Span Study: Solid-Tumor Mortality (1950-1987)**

Absorbed Dose (rad)	Mean Weighted Dose-Equivalent (rem)	Person Years	Number of Subjects	Observed Deaths	Expected Deaths
, 1	0	1,385,374	46,176	3,435	3,433
1-10	4	693,935	23,147	1,868	1,837
10-20	14	171,130	5,713	472	444
20-50	33	188,444	6,283	582	508
50-100	74	93,116	3,111	312	234
100-200	142	46,891	1,543	178	108
. 200	252	9,984	336	40	18

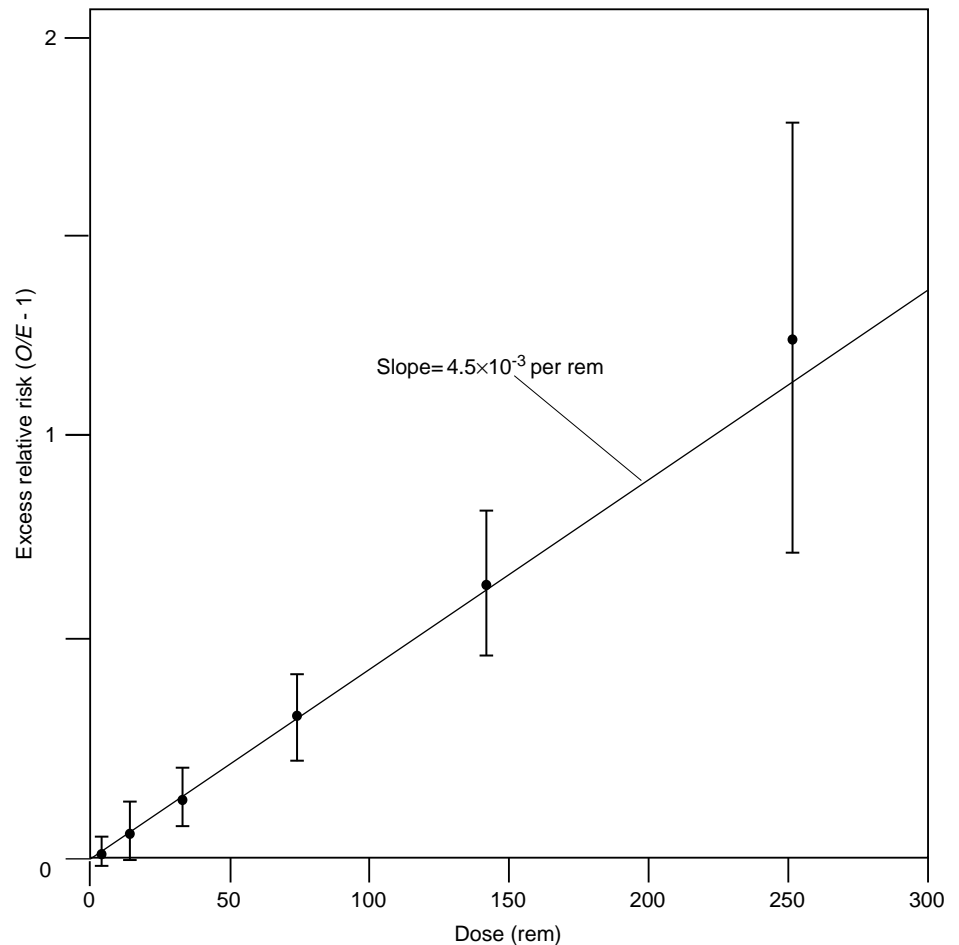
This table divides the exposed population into groups according to the dose received. The data in the first row, corresponding to absorbed doses of less than 1 rad, have been assigned a mean equivalent dose of zero rem. The first column gives the absorbed-dose intervals into which the data are organized, and these correlate with distance from the bomb blast. The second column gives the mean dose-equivalent (*D*) in rem received by each subpopulation. The third column gives the total number of person-years of follow-up (*PY*) for the subjects in each dose category. The fourth column gives the number of persons in each dose category. The next-to-last column gives the actual number of observed cancer deaths (*O*) in the time interval 1950-1987. The last column gives the number of cancer deaths expected (*E*) in each sub-population, based on a comparison of the age and sex distribution with an unexposed Japanese population.

neutrons were ten times as effective as gamma rays.

The solid-tumor mortality data for Japanese survivors are given in Table 3, grouped according to level of exposure, estimated from each subject's distance from the bomb blast. The data on doses are sufficiently consistent and the number of subjects in each dose interval is large enough to allow an estimate of the rate at which cancer mortality risk increases with radiation dose. This has been done by international bodies of experts in the fields of epidemiology and radiation protection.

With regard to hereditary health effects and prenatal carcinogenic effects, the numbers observed, even among this large cohort, are too small to be statistically significant. However, statistically significant noncarcinogenic prenatal deterministic effects have been observed. These effects include severe mental retardation, small head size, and low intelligence scores. For severe mental retardation, a sensitive period of 8 to 15 weeks after conception was identified. Radiation is thought to produce a dose-dependent loss of functional neuronal connections in the brain cortex, which is responsible for a downward shift of the bell-shaped Intelligence-Quotient (IQ) distribution. This downward shift is estimated to be about 30 IQ points per 100 rem, for exposures in the critical period of 8 to 15 weeks after conception. Severe mental retardation is clinically defined as more than two standard deviations (about 30 IQ points) below the average score of 100 IQ points, that is, below 70 IQ points. Based on these studies of the Japanese survivors, it is estimated that the radiation-induced shift in the IQ distribution, corresponding to a dose of 100 rem, would result in severe mental retardation in about 50 per cent of the prenatally exposed individuals. This effect is believed to have a threshold of about 10 rem.

#### Risk Estimates for High Doses and High Dose-Rates. How should the



**Figure 4. Excess Relative Risk for Solid-Tumor Mortality versus Dose for the Japanese Atomic-Bomb Survivors**

This graph is a plot of the data in Table 3. The error bars correspond to plus and minus one standard deviation. A straight-line fit to the data yields the high-dose, high-dose-rate relative risk factor of  $4.5 \pm 10^{-3}$  per rem. Note that the two data points below 20 rem, although lying on the straight line, are also consistent with zero risk. (Data from UNSCEAR94.)

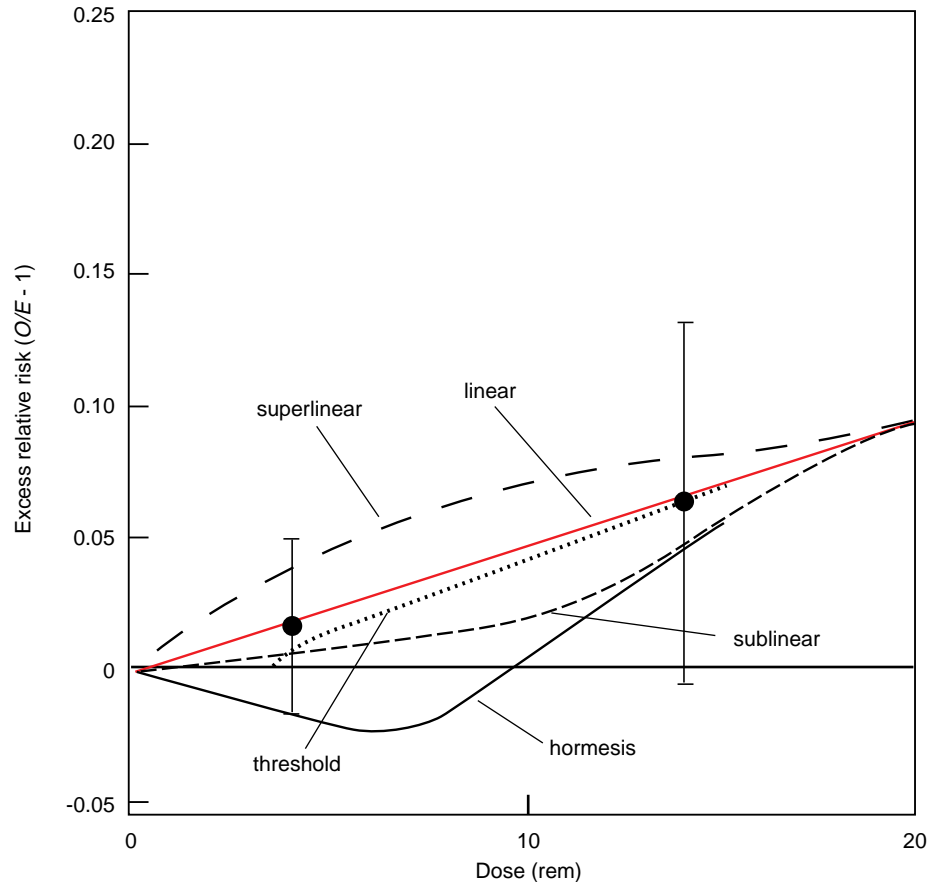
cancer data be analyzed to determine the risks associated with radiation exposure? Let us do a simple, straightforward analysis of the solid-tumor mortality data in Table 3 to determine a risk factor corresponding to the acute high-dose exposure experienced by the Japanese survivors. Following current practice, we shall use the *excess-relative-risk* model (see “Measuring Risk”). We plot in Figure 4 the *ERR* for solid-tumor mortality versus dose (*D*) for each of the seven dose groups listed in Table 3. The error bars reflect the statistical uncertainty of each data

point and are estimated assuming that the uncertainty in *O* (or *E*) is given by the square-root of *O* (or *E*); thus, they correspond to plus and minus one standard deviation (see “Statistical Significance”).

The data in Figure 4 are fit nicely by a straight line with a slope of  $4.5 \pm 10^{-3}$  per rem, which is the excess-relative-risk coefficient for solid-tumor cancer mortality. If we multiply this figure by the solid-tumor mortality rate in the general unexposed population, we can obtain the absolute rate of radiation-in-

duced cancer mortality per unit dose. In the Life-Span Study, the 1985 Japanese population and death rates are used as the unexposed population, from which is obtained the solid-tumor death rate of 24.3 per cent. Thus, we obtain the risk factor for radiation-induced solid-tumor mortality of 0.0011 per rem. If we include leukemia, the risk factor rises to 0.0012 per rem, which is the appropriate overall risk factor for high-dose high-dose-rate exposures. For example, if a population of 1000 persons is exposed to an acute whole-body radiation dose of 20 rem, we should expect, based on this analysis, 24 extra cancer deaths (1000  $\times$  0.0012 per rem  $\times$  20 rem) as a result of the exposure in addition to the 200 or so cancer deaths that might normally be expected. Stated differently, an individual exposed to an acute whole-body dose of 20 rem has about a 2.4 per cent chance of eventually dying from radiation-induced cancer. For comparison, an individual living in the U.S. has, on average, about a 1.5 per cent chance of dying in an automobile accident.

Referring to Figure 4, it will be noted that the solid-tumor data corresponding to doses below 20 rem (which is 84 times the average annual world-wide dose due to background radiation) are consistent with zero effect. If the error bars are extended to plus and minus two standard deviations, which corresponds to approximately a 95 per cent confidence interval, statistically significant effects are not seen below about 50 rem. Thus, the risk factor derived above may or may not apply to the low doses and low dose rates typically encountered by radiation workers and the general public. Nevertheless, an assumption of effects at low doses and low dose rates is prudent for establishing standards and guidelines for the protection of the health and safety of radiation workers and the general public.



**Figure 5. Extrapolation of High-Dose Data to Doses below 20 Rem**

The low-dose data from Figure 4 with a straight-line extrapolation from the high-dose data, as well as other possible fits to the data, including (a) threshold/linear, (b) sub-linear, (c) superlinear, and (d) adaptive, or hormetic, response.

### Extrapolating Risk Estimates to Low Doses of Radiation

Since the 1920s, when the risk of exposure to both internal and external radiation sources became apparent, official organizations have been established to recommend radiation protection standards. The most influential international organizations are the International Commission on Radiological Protection (ICRP) and the United Nations Committee on the Effects of Atomic Radiation (UNSCEAR), and in the U.S., the National Council on Radiation Protection and Measurements (NCRP). These organizations are charged with estimating the risks associated with exposure to low levels of radiation and recommending

dose limits for radiation workers and the general public.

**Risk Estimates for Low Doses.** In the absence of convincing human data at the low doses and low dose rates that are of interest to radiation workers and the general public, the above-mentioned organizations have estimated the low-dose low-dose-rate risk principally by extrapolation of the risks obtained from the high-dose high-dose-rate atomic-bomb survivor data and other radiation effects studies. But what type of extrapolation is appropriate? The easiest choice (Figure 5) is to extrapolate the straight line drawn through the high-dose data in Figure 4 all the way down to zero. This choice, known as the linear-dose-response, no-



threshold (LNT) hypothesis, implies that the risk is proportional to dose all the way down to zero dose. This hypothesis further implies that the same number of excess cancers would arise from exposing 100 persons to 100 rem, or 10 thousand persons to 1 rem, or 10 million persons to 1 millirem (all doses are in addition to natural background). In the latter two cases, the predicted excess is well within the normal fluctuation of the expected number of cancer deaths for an unexposed population and, therefore, not identifiable as due to radiation exposure.

Figure 5 also shows some other possible choices for extrapolation from the high-dose data, namely: (a) threshold, where there is some value of dose below which there is no effect; (b) sublinear (dose exponent greater than 1), where the effect per unit dose at low doses is less than at high doses; (c) superlinear (dose exponent less than 1), where the effect per unit dose at low doses is greater than at high doses; and (d) adaptive response (radiation hormesis), where very low doses have a protective effect. The body of human exposure data, together with experimental animal data, do not allow the definite exclusion of any of the above possibilities; however, the results of most animal and cellular experiments favor either the LNT or sublinear hypotheses. Theoretical considerations involving the random nature of the fundamental damage processes in cellular DNA, as well as the fallibility of cellular repair mechanisms, also favor the LNT and sublinear hypotheses over the others. For the LNT hypothesis, the cell's repair effectiveness is assumed to be independent of dose. For many cellular experiments, the cell's repair effectiveness is seen to increase with decreasing dose, which is consistent with the sublinear hypothesis. In other words, the radiation becomes less effective per unit dose at low doses. Also, the cell's repair effectiveness is seen to increase with increasing time between doses, and with lower dose rates.

The radiation-protection community has adopted the LNT hypothesis as a conservative basis for estimating risk. However, they have chosen to modify risk estimates based on this hypothesis to take into account results from animal and cellular experiments indicating that low doses and low dose rates are less effective at causing biological damage. In particular, the risk factor for low doses (less than 20 rem) or low dose rates (less than 0.6 rem per hour) is set equal to one-half the risk factor for high doses ( $1.2 \times 10^{-3}$  per rem) (see UNSCEAR 94). The risk factor for radiation-induced cancer mortality then becomes  $6 \times 10^{-4}$  per rem for the general population, which is within the range of uncertainty of the official NCRP and ICRP-recommended risk factor of  $5 \times 10^{-4}$  per rem. Because the working population does not include children, the risk factor for workers is set somewhat lower, at  $4 \times 10^{-4}$  per rem.

Thus, the risk factors for low-dose (less than 20 rem) or low-dose-rate (less than 0.6 rem per hour) radiation exposure that are generally used throughout the world today are  $5 \times 10^{-4}$  per rem for the general public and  $4 \times 10^{-4}$  per rem for workers. These factors are to be applied to exposures in excess of natural background levels. For example, a person living on the East Coast, with a natural background level of 200 millirem per year, who is occupationally exposed to a dose rate of 100 millirem per year for 40 years, has incurred an excess risk for cancer mortality of 0.16 per cent ( $4 \times 10^{-4}$  per rem  $\times$  0.1 rem per year  $\times$  40 years = 0.0016). Another person, living in Denver, with a natural background level of about 340 millirem per year, who receives no additional exposures, incurs no additional risk for cancer mortality. Thus, the person on the East Coast incurs a greater risk than the person in Denver, despite the fact that the person in Denver is receiving a higher total dose per year than the person on the East Coast. If this seems strange to the reader, you are not alone.

It should also be noted that radiation received from medical exposures is not included in records of occupational exposures.

What is the risk factor for radiation-induced hereditary effects? It is known that radiation can cause mutations in the DNA of germ cells (ova and sperm), and those changes can be propagated from one generation to the next. These radiation-induced mutations are similar to those that occur spontaneously. Are there clinical manifestations arising from radiation-induced mutations? Epidemiology has not detected statistically significant hereditary health effects of ionizing radiation in humans. Based on cellular and animal studies, statistically significant hereditary health effects in human populations at the dose levels usually experienced are not expected. Even among the Japanese atomic-bomb survivors, predicted hereditary health effects of their exposure to radiation would not appreciably increase the normal incidence of such effects that are due to all other causes.

Risk estimates, therefore, must be based largely on genetic studies of organisms and on cellular studies with radiation. Using two different methodologies, UNSCEAR estimates the risk in the reproductive segment of the population for serious effects in the two succeeding generations following exposure to be about  $3 \times 10^{-5}$  per rem. (Serious effects include stillbirths, major congenital defects, and cancer incidence before the age of twenty.) A risk value of  $1.2 \times 10^{-4}$  per rem is given for all generations after exposure.

Population studies show that diseases with an important genetic component occur in five to six per cent of live-born individuals. If all congenital anomalies are considered part of the genetic load, the percentage rises to about eight per cent. Thus, the additional genetic risk from low radiation doses is trivial compared with the genetic load carried in the general population.

### Population Requirements of Low-Dose Studies

Statistically significant results showing a definite correlation (either positive or negative) between low-level exposures and excess cancers are very difficult to obtain, primarily because the risk factor for excess cancer mortality per unit dose is so small. Thus, for low doses, one needs to follow a very large population for several years for there to be a chance of detecting any correlation at all.

As an illustrative example of the statistical difficulties encountered at low doses, consider the problem of trying to correlate variations in cancer mortality with variations in doses from natural background radiation. Background doses vary by more than a factor of two, depending on location. Let us suppose that the actual number of radiation-induced cancer deaths varies as predicted by the linear-dose-response no-threshold hypothesis. Then, for a population of  $N$  persons, the number of excess cancer deaths is given by  $(5 \times 10^{-4})DN$ , where  $5 \times 10^{-4} \text{ rem}^{-1}$  is the hypothetical cancer mortality risk factor for the general public and  $D$  is the dose in rem (above normal background). The expected number of cancers for an unirradiated population is  $0.20 N$ , where 0.20 is the cancer mortality rate for the general population. The expected fluctuation in the number of expected cancer deaths is given by the standard deviation,  $(0.20 N)^{1/2}$ . In order to be confident of the result, the number of excess cancer deaths should be more than two standard deviations; let us say three standard deviations. Thus, for the number of radiation-induced excess cancer deaths to be at least three times as great as the expected fluctuation in the number of cancer deaths in an unirradiated population, the following inequality must be satisfied:

$$(5 \times 10^{-4})DN \geq 3(0.20 N)^{1/2},$$

which yields  $N \geq 7.2 \times 10^6/D^2$ . Therefore, to observe a change in cancer mortality due to an extra dose (from an elevated background level) of, say, 0.24 rem per year over a lifetime of 75 years, or 18 rem, requires a study population of more than 20,000 persons. A similar population is required for a control group, and both populations must be stable (that is, individuals remaining in the area). This simplified example assumes that everyone in the population receives a similar background dose, and it takes no account of possible confounding factors involving diet, habits (for example, smoking), physical activity, and so forth. Including all of these additional considerations may well double or triple the populations required, resulting in a very large, very expensive project that must last for several years. It is, therefore, not too surprising that few such studies are undertaken. ■

Another measure of the effectiveness of ionizing radiation in producing hereditary health effects is the dose required to double the normal incidence of the observed effect, which is estimated to

be about 200 rem for the Japanese atomic-bomb survivors. The overall uncertainty in this estimate is considerable, but the figure is thought to be conservative. Applying a low-dose-rate

factor of two for chronic exposures results in a minimal estimate of the doubling dose of 400 rem, which is about 1700 times the average annual dose from background radiation (UNSCEAR93).

### Radiation Protection Standards.

Both the ICRP and the NCRP have recommended upper limits on radiation exposure that are intended to prevent the occurrence of deterministic effects and to ensure acceptably low levels of risk for stochastic effects. Both organizations use the conservative LNT hypothesis to estimate risks for doses below the level of statistically significant data. This hypothesis is equivalent to a stochastic model of radiation effects. It should be emphasized that the cancer mortality risk factors ( $5 \times 10^{-4}$  per rem for the general public,  $4 \times 10^{-4}$  per rem for workers) are often applied, especially for public exposures, at dose levels that are orders of magnitude smaller (that is, a few millirem) than those at which effects of ionizing radiation are actually observed in humans.

The annual dose limits recommended by the NCRP in 1993 (NCRP116) include, for occupational exposures, 5 rem for stochastic effects, and for non-stochastic effects, 15 rem for the lens of the eye, and 50 rem for all other organs. Also, the NCRP recommends that a worker's lifetime effective dose not exceed 1 rem multiplied by the worker's age in years. Thus, for example, a worker who retires at an age of 65 years with a cumulative whole-body dose of 65 rem (which is relatively rare) has a hypothetical probability of 2.6 per cent ( $4 \times 10^{-4}$  per rem  $\times 65$   $\times 0.026$ ) of dying from radiation-induced cancer. The probability of cancer mortality for the general population is about 20 per cent. For the general public, the NCRP recommends an annual limit of 0.1 rem for continuous or frequent exposure and 0.5 rem for infrequent exposure. Thus, a person exposed to 0.1 rem per year for 75 years has a hypothetical probability of about

0.4 per cent ( $5.3 \times 10^{-4}$  per rem  $\times 0.1$  rem per year  $\times 3.75$  years  $\times 0.00375$ ) of dying from radiation-induced cancer. All exposures are considered to be in addition to background levels.

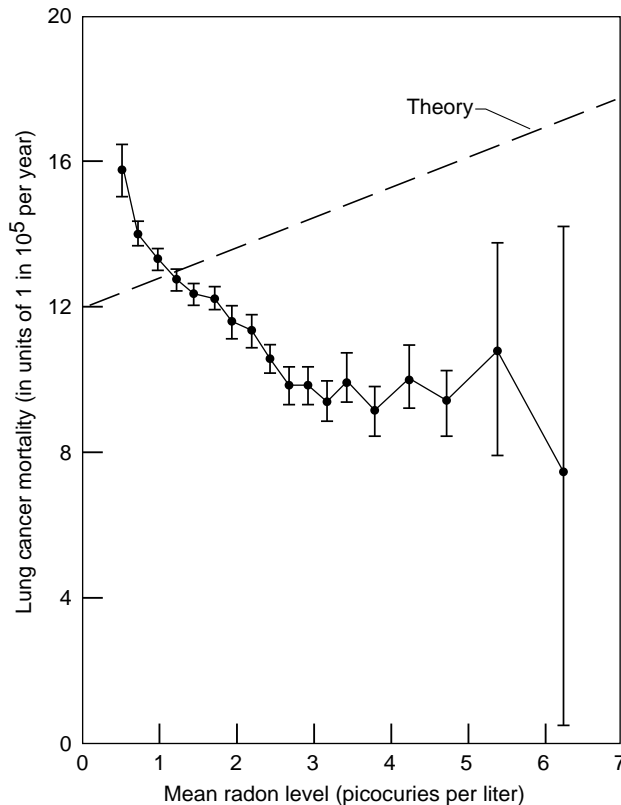
A more complete listing of the standards, together with the events and the philosophy that has guided their development, can be found in the article "A Brief History of Radiation Protection Standards."

### Human Exposures to Low Doses of Radiation

In previous sections of this article, we described human exposures to radiation that resulted in observed effects, particularly cancer. Generally, the doses received in these cases were high. Most of these exposures occurred in the first half of this century, before the risks associated with radiation were well understood. What levels of radiation exposure are radiation workers and members of the public experiencing today, and what effects, if any, are observed? What are the risks associated with these exposures?

In this section, we attempt to answer these questions by reviewing the dose data and epidemiological studies for environmental and diagnostic medical exposures of the general public and the occupational exposures for nuclear workers. We shall also apply the risk factors derived in the previous sections to determine the hypothetical risks for cancer mortality associated with these low-level exposures and compare the results with epidemiological data, where possible.

**Environmental Exposures.** As stated earlier, the world average annual effective



**Figure 6. Is this Hormesis?**

The graph shows lung cancer mortality versus mean radon concentration in lowest level of homes for 1,601 U.S. counties. Data are for females, and error bars correspond to plus and minus one standard deviation (the data for males are similar). The theory line is obtained by applying the linear-no threshold (LNT) hypothesis to higher-dose data for miners. The theoretical risk increases at a rate of 7.3 per cent per picocurie per liter, whereas the data show a decreasing risk with increasing radon concentration. Thus, the LNT hypothesis is contradicted by this study. (Reproduced from B. Cohen, 1995, *Health Physics* 68: 157-174.)

dose from natural sources is about 240 millirem, with a little more than half due to radon and its decay products and 23 millirem from radionuclides within the body, particularly potassium-40. Cosmic rays and terrestrial gamma rays account for the remainder. No one knows what percentage of observed cancer deaths, if any, is due to exposure to background radiation. However, it is of some interest to determine the percentage obtained from a straightforward application of the risk factors for radiation-induced cancer mortality, even though the risk factors are meant to be

applied to exposures in excess of natural background. This exposure (240 millirem per year), taken over a 75-year life span, would result, hypothetically, in an increased risk of cancer mortality of 0.9 per cent ( $5.3 \times 10^{-4}$  per rem  $\times 0.240$  rem per year  $\times 3.75$  yrs  $\times 0.009$ ). Thus, according to the risk estimates extrapolated from high doses, background radiation may account for less than 5 per cent (0.009/0.20) of all cancer deaths.

If background radiation is responsible for some cancer deaths, then the considerable variability in background levels with location and altitude might result in observable variations in cancer mortality from one region to another. The magnitude of the variability of this natural background radiation is noteworthy. While cosmic radiation accounts for about 25 millirem per year at sea level, this rate is approximately doubled for the "mile-high" cities of Albuquerque and Denver, and approximately quadrupled for Quito, Ecuador, at 9350 feet, because of the decreased atmospheric shielding at higher altitudes.

Gamma rays resulting from the decay of radioactive nuclides in the soil and rocks accounts for 46 millirem of the world average annual dose. In the U.S., this contribution varies in the range of 15 to 150 millirem per year, with the East Coast and Gulf Coast regions generally at the lower end of the range, and the Central Rockies (Denver area) near the upper end of the range. In several locations of the world where deposits of thorium-rich monazite sands occur, notably the Ker-

ala Coast of India, dose rates of several hundred millirem per year are found for the terrestrial contribution.

Indoor radon represents the largest contribution to the average annual background dose, and it can vary by a factor of ten or more. Studies of U.S. homes have found a mean activity concentration in the ground floor (lowest livable area) of 1.25 picocuries per liter, which would correspond to an annual whole-body effective dose equivalent of about 400 millirem, if these areas were occupied 100 per cent of the time (or 40 millirem for 10 per cent occupancy). The activity concentration in approximately 6 per cent of U.S. homes exceeds 4 picocuries per liter, the level at which the U.S. Environmental Protection Agency recommends corrective action be taken.

Because background radiation levels vary so widely around the world, epidemiologists have looked for correlations between cancer rates and background dose. The effect of exposures to widely varying levels of background radiation are more likely to be observed with leukemia than most other cancers. This is because the radiosensitivity for leukemia is greater, the time interval between exposure and the onset of disease is less than for most other cancers, and the natural incidence of leukemia is extremely low. Also, the influence of other environmental risk factors is thought to be less for leukemia. Studies in the United States, Canada, France, Sweden, and China have failed to find a significant correlation between leukemia incidence and background radiation levels (see "Population Requirements of Low-Dose Studies").

The Chinese study (1970-1985) in Yanjiang County, Guangdong Province, represents the most extensive study on the health effects of natural background radiation. This study, involving some 70,000 persons, took place in two neighboring regions in which a difference in annual dose of 200 to 300 mil-

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**Table 4. Medical Diagnostic Procedures**

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**X-ray Examinations\***

(1985-90) average annual total number of examinations	1200 per 1000 persons
(1985-90) average annual number of dental examinations	400 per 1000 persons
(1980) average annual effective dose per patient	50 millirem
(1980) annual collective effective dose	$9.2 \times 10^6$ person-rem

**Effective Doses from Diagnostic X-Ray Procedures†**

lower GI tract	720 millirem
upper GI tract	410 millirem
angiography	680 millirem
urography	310 millirem
computed tomography	430 millirem
dental examinations	a few millirem

**Nuclear Medicine Procedures\***

(1985-90) average annual number of procedures	26 per 1000 persons
(1982) average annual effective dose per patient	500 millirem
(1982) annual collective dose	$3.2 \times 10^6$ person-rem

**Effective Doses from Diagnostic Nuclear-Medicine Procedures†**

cardiovascular	1400 millirem
brain	870 millirem
bone	630 millirem
thyroid scan	380 millirem
thyroid uptake	250 millirem

\*Data for the US.

†Data for a group of nations for which there is at least one physician per 1000 persons.

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lirem was associated with nearby deposits of monazite sands. Based on estimates from the Japanese Life-Span Study (omitting the dose-rate reduction factor), an excess risk for leukemia incidence of 27 per cent by age 50 years would be expected for the group with the higher annual dose. However, the

leukemia mortality rate in this group was lower than in the control group (26 versus 33 deaths), though the difference was not statistically significant. One would conclude from this result that the risk factor based on extrapolation from the high-dose Japanese data overestimates the leukemia risk. However, an

increase in chromosome aberrations was seen in cells taken from the group receiving the higher annual dose compared to the control group.

Another possible correlation to look for is one between radon exposure and lung cancer. Figure 6 shows the results of a study of lung cancer mortality per county versus mean radon concentration per county for more than 1600 U.S. counties, representing almost 90 per cent of the U.S. population. The data show a *negative* correlation up to concentrations of at least 7 picocuries per liter. This result would seem to imply that up to dose-rate levels of 200 to 300 millirem per year (assuming 10 per cent occupancy) radon exposure has a hormetic effect, that is, radon exposure *decreases* the chance of lung cancer mortality. The LNT hypothesis, of course, predicts an *increasing* lung cancer mortality with increasing radon exposure. Of ten other studies in countries world-wide, two (Norway and Sweden) showed a significant positive correlation between lung cancer and radon concentration, two (France and United Kingdom) showed a significant negative correlation, five (Canada, China, Finland, Italy, and Japan) showed no significant correlation, and Denmark was found to have a higher lung-cancer rate than Sweden despite a lower mean radon concentration.

**Diagnostic Medical Exposures.** Medical diagnostic examinations represent the largest exposure of the general public to man-made radiation. Table 4 lists frequency and dose information for x-ray examinations and nuclear-medicine diagnostic procedures. Although individual doses are relatively small, the total annual collective dose equivalent from diagnostic x-ray and nuclear-medicine procedures in the U.S. is  $1.24 \times 10^7$  person-rem, which is rather large. How many excess cancer deaths might be attributed to this collective medical exposure? Simply multiplying the collective dose by the risk factor for cancer mortality ( $5 \times 10^{-4}$  per rem) yields



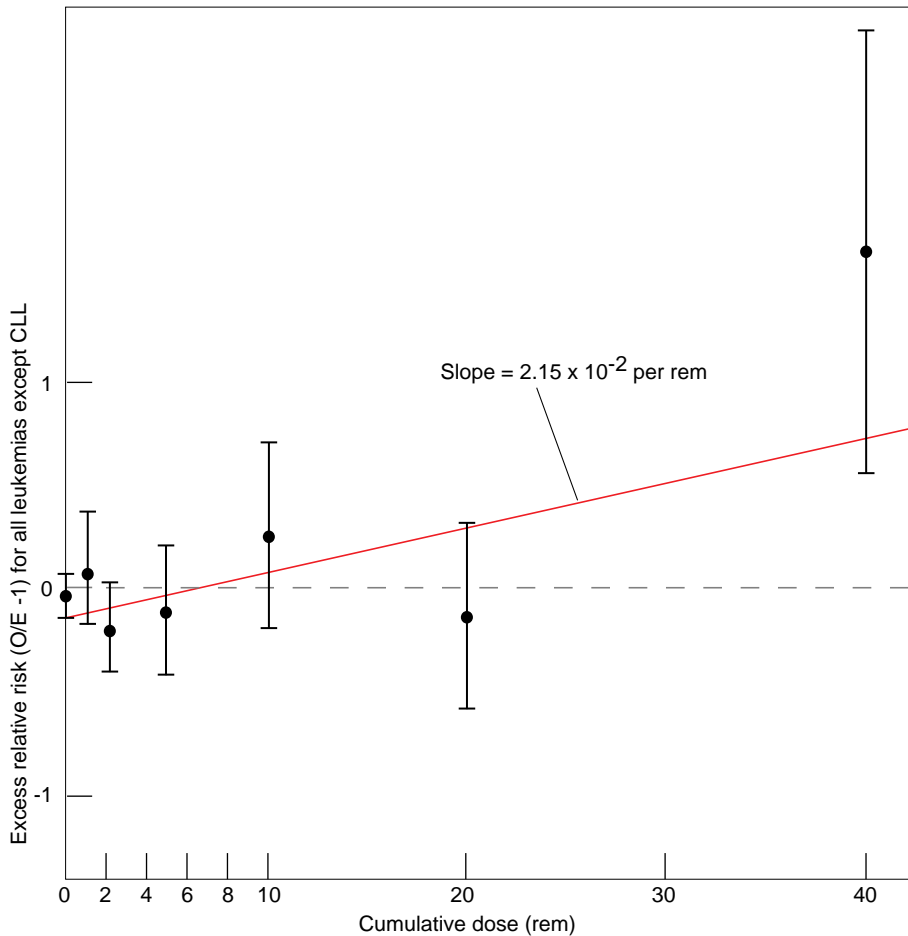
**Table 5. Distribution of Cumulative Doses in IARC Study of Nuclear Workers**

Dose Range (rem)	Fraction of Workers
0	0.11
0 - 1	0.49
1 - 5	0.20
5 - 50	0.19
50 - 100	0.009
.100	0.001

6200 hypothetical excess cancer deaths per year for the U.S., which is about 1 per cent of the total annual number (547,000) of cancer deaths and about 8 times the standard deviation (740) of this number. This crude estimate would seem to suggest that the number of hypothetical radiation-induced cancer deaths associated with diagnostic x-ray and nuclear-medicine procedures in the U.S. should be observable, if real. Interpretation of these data would be complicated by a number of confounding factors—for example, many persons exposed in diagnostic procedures have pre-existing disease, and up to one-half of the procedures take place in the last year of life. These confounding factors would diminish the significance of ob-

served mortality statistics.

**Nuclear Industry Exposures.** The nuclear industry provides a setting in which the average exposures are above background, but are still relatively low, because of the adherence to radiation protection standards. Nuclear workers make an ideal group for studying the effects of low-level exposures in the few-rem range, because they are monitored regularly and records are easily available. In fact, several studies have been made of workers in nuclear energy and weapons facilities in the United Kingdom, United States, and Canada. Averages of individual cumulative doses for workers at these facilities were in the range of 0.8 to 12.4 rem, which, when



**Figure 7. Nuclear Worker Data for Leukemia Risk**

Excess relative risk for mortality for all leukemias, excluding chronic lymphocytic leukemia, versus cumulative dose for 96,000 nuclear industry workers in the United Kingdom, the United States, and Canada. The error bars correspond to plus and minus one standard deviation. Forcing a straight-line fit to all of the data yields a relative risk factor of  $2.15 \pm 10^{-22}$  per rem. However, if the highest-dose data point is excluded, the remaining data show no increase of risk with increasing dose. (Data from E. Cardis, et al., 1995, *Radiation Research* 142: 117-132.)

multiplied by the risk factor for workers of  $4 \pm 10^4$  per rem, yield a hypothetical average risk range for radiation-induced cancer mortality of 0.03 per cent to 0.50 per cent. For all cancers taken together, there were no statistically significant excess risks of radiation-induced cancer found in any of the studies.

Looking at specific cancers, a significant excess risk (about 27 per cent) was found for lung cancer in workers at Oak Ridge plants, with the average individual cumulative dose a very low 1.7

rem. This dose yields a hypothetical risk for cancer mortality of 0.07 per cent. However, there is some indication that smoking may be a confounding factor in these results. At the Sellafield plant in the United Kingdom, the average individual cumulative dose was 12.4 rem, which yields a hypothetical cancer mortality risk of 0.5 per cent. A “significant trend” was reported for excess leukemia risk when exposures were lagged by 15 years to better align them in time with the appearance of the disease. However, it should be noted

that there were 10 leukemia deaths overall at Sellafield, whereas 12 would have been expected if the radiation exposures posed no risk.

The International Agency for Research on Cancer (IARC) Study Group on Cancer Risk among Nuclear Industry Workers performed an independent study of the combined data, mentioned above, from the United Kingdom, United States, and Canada. This study, involving more than 95,000 individuals, is the most extensive study to date for cancer mortality risk associated with protracted exposure to low levels of radiation. The distribution of cumulative doses received by the study population, listed in Table 5, was rather skewed in that 60 per cent of the cohort received doses of 1 rem or less and only about 1 per cent received doses of 50 rem or more. All doses are assumed to be at low dose rates. Excluded from the study were 19 workers who received greater than 25 rem in a single year.

The excess relative risk (ERR) for all cancers, excluding leukemia, was reported to be negative at  $-7 \pm 10^{-4}$  per rem, with a 90-per-cent confidence interval from  $-39 \pm 10^{-4}$  to  $+30 \pm 10^{-4}$  per rem, which is consistent with zero risk. For leukemia, excluding chronic lymphocytic (CL) leukemia, which is thought not to be induced by radiation, the excess relative risk (ERR) was reported to be positive at  $2.2 \pm 10^{-2}$  per rem, with a 90-per-cent confidence interval from  $0.1 \pm 10^{-2}$  to  $5.7 \pm 10^{-2}$  per rem, which is barely significant (the 95-per-cent confidence interval overlaps zero risk). Taking into account the range of uncertainties, the quoted results for non-CL leukemia are consistent with those obtained from a linear extrapolation of the high-dose, high-dose-rate data from the atomic-bomb survivors, and with a low-dose, low-dose-rate effectiveness multiplier of one-half, though the range of uncertainty of this multiplier is quite large (0.027-1.7).

**Table 6. Plutonium Experiments in Humans (1945-1947)**

Subject	Isotope	Intake (nCi)	Time (yrs)	Dose (rem)	LNT Probability (per cent)
CAL-I	Pu-238	3500	20.7	6400	, 100.
	Pu-239	46			
CAL-II	Pu-239	169	0.698	13	0.65
CAL-III	Pu-238	51	45.0	155	7.7
CHI-I	Pu-239	400	0.438	19	1.0
CHI-II	Pu-239	5900	0.0465	29	1.5
CHI-III	Pu-239	5900	0.465	300	15.
HP-1	Pu-239	280	14.2	380	19.
HP-2	Pu-239	310	2.45	80	4.0
HP-3	Pu-239	300	37.2	880	44.
HP-4	Pu-239	300	1.42	46	2.3
HP-5	Pu-239	310	0.411	14	0.7
HP-6	Pu-239	330	38.3	990	50.
HP-7	Pu-239	390	0.715	30	1.5
HP-8	Pu-239	400	29.7	1000	50.
HP-9	Pu-239	390	1.25	52	2.6
HP-10	Pu-239	380	10.9	410	20.
HP-11	Pu-239	400	0.0164	0.6	0.03
HP-12	Pu-239	290	8.01	230	12.

The authors of this study give the relative risk (*RR*) for all leukemias except CL leukemia for 10-rem exposure as 1.22, which means that a person exposed to 10 rem of low-LET radiation over a working lifespan is 22 per cent more likely to die from non-CL leukemia than a similar, but unexposed worker. This statement would lead the casual reader to infer that the data at dose levels around 10 rem actually show an effect. However, an examination of the data presented for all non-CL leukemia mortality in 7 dose intervals, the last being greater than 40 rem, shows that for only the last dose interval

is a positive effect observed (Figure 7). The risk factors quoted above are found by forcing a linear fit to all of the data; however, if the one data point for doses above 40 rem is excluded, the remaining 6 data points for doses below 40 rem show a flat response with dose (that is, no increasing risk with dose). The range of uncertainties in the final results would also seem to allow either a sub-linear or superlinear dose response at low doses, in addition to the assumed linear response. This very large and careful study of nuclear workers does not provide a definitive resolution of the problem of determining the dose re-

sponse at low doses (less than 20 rem). However, this study does provide valuable new information at low dose rates.

### Human Radiation Experiments

Recently, a great deal of attention has been focused (for the third time) on human radiation experiments that were carried out in the United States during the 1940s and 1950s. Most of the experiments in which Los Alamos were involved are discussed in part III of this volume. Here, we wish to examine the

doses received and the hypothetical risks associated with those experiments. The experiments include the plutonium-injection experiments and three series of tracer studies done at Los Alamos.

**Plutonium Injections.** Starting in April 1945 and continuing for a period of about two years, 16 persons were injected with plutonium-239, one person with plutonium-238, and one person with a plutonium-238/239 mixture (see Table 6). The subjects in the studies were patients at the following hospitals: Manhattan Engineer District Hospital in Oak Ridge (subject designated HP-12); Billings Hospital of the University of Chicago (CHI-I to III); University Hospital of the University of California, San Francisco (CAL-I to III); and Strong Memorial Hospital of the University of Rochester (HP-1 to 11). Both plutonium-238 and plutonium-239 are alpha emitters and are retained in the body for several decades. The amounts injected ranged from 100 to 5900 nanocuries. The purpose of these investigations was to determine the excretion rate of plutonium over time for known intakes. These data, together with extensive animal data, were critical for constructing models that were used to determine the plutonium intakes and consequent body burdens, based on excretion data, for workers in the nation's nuclear-weapons complex. It was not the purpose of the studies to observe radiation effects, as none were expected; nor were any observed. The subjects in the studies were chosen partly on the basis of expected short remaining life spans (less than 10 years), although about one-third lived much longer than expected. Whether the subjects were informed of the nature of the experiment and the potential hazards is a matter of some controversy. What is known is that at least one subject was not informed and at least one subject was informed. The issue of informed consent is an important one and is treated elsewhere (see "Ethical Harm" on page 280). Here, we wish to examine the doses received and the associated

hypothetical risks of cancer mortality, based on the current risk factor ( $5.3 \times 10^{-4}$  per rem) derived from the LNT hypothesis and the subsequent lifetimes of the subjects. It should be noted that the recommended limit for plutonium-239 in the body during most of the Manhattan Project was 5 micrograms (310 nanocuries). Around the time the injections were begun, a provisional limit of 1 microgram (62 nanocuries) was adopted. In 1950, the official limit was lowered to 0.5 microgram (31 nanocuries).

Let us derive the risks associated with the radiation exposures resulting from these plutonium injections by naively applying the hypothetical risk factor recommended for radiation protection applications. In Table 6, we give the relevant data for each of the subjects; the fourth column is the remaining lifetime from time of injection for each subject. The current radiation risk factor for cancer mortality is applied to the cumulative whole-body effective dose equivalent, which is given in the fifth column of Table 6. The hypothetical LNT probability that this dose could have induced death from cancer, given sufficient time, is given in the last column of Table 6. It should be pointed out that this procedure is meant to apply for relatively small probabilities, and it overestimates relatively large probabilities. Excess mortality probabilities of greater than 100 per cent are, therefore, excluded, as in the case of CAL-I. Most of the subjects did not live long enough for any possible plutonium-induced cancers to develop. For four of the subjects, who lived 20 years or more, the hypothetical probability for radiation-induced cancer mortality exceeded 40 per cent. However, none of the subjects died of causes that could be related to the plutonium injections. From these results, one might conclude that the risk factor overestimates the cancer mortality risk for internal exposures to plutonium. Although the number of cases is too small to be significant, this conclusion is consistent with

the observed results for the radium-dial painters. In both cases, the doses were due to internal alpha emitters that deposit their radiation in bone. In general, the uncertainties associated with plutonium dosimetry are rather large. Even in these cases, in which the activities injected are known precisely, substantial uncertainties in the resulting doses remain, primarily related to the activity distribution in the body and to the subsequent biological damage produced.

**Tracer Studies: Radioiodine.** During a period of almost two decades following World War II, 42 persons, including 8 children (under 10 yrs) and 6 teenagers, ingested iodine-131 and iodine-125 in studies at Los Alamos with the dual objectives of improving diagnostic techniques to detect thyroid disease and estimating doses due to ingestion of food containing radioiodine that came from the fallout of atmospheric nuclear-weapons tests. The volunteers in these studies comprised the researchers themselves, their children and their colleagues. The activities of the radioisotopes ingested by the adults were in the microcurie range, resulting in doses to the thyroid of a few rem and whole-body effective doses of about 100 millirem or less. The children ingested about 10 nanocuries of radioiodine, resulting in thyroid doses of 80 to 160 millirem, depending on age, and whole-body effective doses of about 5 millirem or less. For both adults and children, the whole-body dose was a small fraction of the annual background dose in Los Alamos. As a result of these studies, the doses received by patients diagnosed for thyroid disease using radioiodine were significantly reduced. Also, these studies enabled researchers to determine the doses associated with radioiodine in fallout from nuclear weapons tests.

**Tritium.** During the 1950s, three volunteers from Los Alamos ingested tritium in the activity range of 2.5 to 14 microcuries, resulting in whole-body ef-



fective doses of about 200 to 900 millirem, which corresponds to a maximum of about three times the annual background dose in Los Alamos. The volunteers were the researchers themselves. The tritium was ingested as HTO, which is distributed in the body in the same way as water. The biological half-life of HTO in the body is about 10 days. The purpose of these experiments was to study body water kinetics and to improve radiation dosimetry for tritium exposures.

**Other Radionuclides.** During the 1960s, several metabolic studies and studies with nuclear-medicine applications were carried out with volunteers at Los Alamos using a variety of radionuclides, including sodium-22, potassium-42, zinc-65, rubidium-86, cesium-134, and cesium-137. The activities administered were in the range of 0.1 to 1.4 microcuries, resulting in whole-body effective doses of 0.1 to 100 millirem, which correspond to small fractions of the annual background dose in Los Alamos.

## Discussion and Conclusions

We have seen that biological effects in humans resulting from exposure to ionizing radiation have been observed with statistical significance in a large variety of situations. Very high doses lead to cell killing, which is an intended effect in radiation therapy in the treatment of cancer, and which has been seen in several accidental exposures, leading to acute radiation syndrome. Lower, but still high, doses were received in many medical and occupational exposures, mostly during the first half of this century, leading to the induction of several types of cancer. The Life-Span Study of the Japanese atomic-bomb survivors represents the most complete source of information on human exposure to ionizing radiation, with doses spanning the range from low to very high, and with several types of cancer induced. From these experiences, we know that radia-

tion is relatively effective at inducing cancers of the thyroid and breast, as well as leukemia, and relatively ineffective for bone cancer and cancers of the brain and central nervous system. Our knowledge of clinically observable hereditary effects, on the other hand, is gained mostly from cellular and animal experiments, as no such effects have been observed in humans.

Based on the cancer-induction and mortality data obtained in the Life-Span Study of the Japanese atomic-bomb survivors, as well as data obtained from other studies, a linear dose-response relationship for ionizing radiation at doses above about 20 rem, delivered at a high dose rate, is well established. Quantitative risk factors are readily derived from these high-dose, high-dose-rate data. For the low-dose, low-dose-rate regime that is pertinent to radiation workers and the general public, the conservative *hypothesis* is made that these same risk factors apply all the way down to zero dose. The acknowledged diminished effect of ionizing radiation at low doses (less than 20 rem) or low dose rates (less than 0.6 rem/hr) is approximated by multiplying the risk factors obtained at high doses and high dose rates by one-half, resulting in a cancer mortality risk factor for the general public of  $5.3 \times 10^{-4}$  per rem (or 1 chance in 2000 per rem), and for occupational workers of  $4.3 \times 10^{-4}$  per rem (or 1 chance in 2500 per rem).

Below about 20 to 40 rem, most data on cancer induction and mortality in humans are inconclusive because of inadequate statistics. One human study at low doses reported here that seems to involve sufficient numbers for good statistics is the U.S. study that found a *decreasing* mean lung-cancer incidence rate with *increasing* mean indoor radon concentration on a county-by-county basis. However, when all studies of radon-induced lung cancer are considered together, the results are inconclusive. A second such study is the one dealing with background radiation due

to monazite sands in Guangdong Province, China, which failed to find an increased leukemia risk, as predicted by the LNT hypothesis. A third study with the potential for good statistics is the study of nuclear workers in the United Kingdom, the United States, and Canada, which failed to find an increased risk for all cancers combined, excluding leukemia. A positive risk was reported for non-CL leukemia; however, an examination of the data shows that, below 40 rem, the data are consistent with no excess risk.

Epidemiological studies of cancer induction in humans exposed to low-LET radiation at low doses and low dose rates generally have low statistical power, and consequently, have been interpreted by some as being consistent with a linear extrapolation from the high-dose, high-dose-rate data, and by others as indicating no additional risk at low doses compared with the observed cancer incidence in the general population. Taking all of the studies together, one is forced to conclude that, at present, the low-dose response for cancer induction in humans cannot be determined with any reasonable degree of confidence.

Unless more studies with high statistical power become available to settle the question (see "Population Requirements of Low-Dose Studies"), the linear-dose-response, no-threshold hypothesis must be viewed as a prudent choice for estimating effects at doses below 20 rem. This is not to say that it is reasonable to regulate public exposures all the way down to zero dose. The hypothetical risk associated with the dose received by everyone from natural background radiation represents a small fraction of the sum of the real risks that all of us face in our daily lives. These real risks are associated with our jobs, our automobile use, our personal habits and tastes, and our leisure activities. The number of fatalities per year related to specific occupations, miles driven, smoking, alcohol consumption, bicycle

riding, hang-gliding, and so forth, are measured quantities; they are not hypothesized. It seems reasonable to this author to cut off our concern with the risks accompanying exposure to man-made radiation at some sensible fraction of the dose due to natural background radiation, since we all seem to accept with alacrity large variations in the natural background as we move from place to place. Within the context of the linear-dose-response, no-threshold hypothesis for extrapolating risks to low doses, there is no difference in collective cancer mortality risk between 1000 persons receiving 10 millirem and one person receiving 10 rem (assuming that all 1001 persons are “similar”). To this author, such a conclusion seems absurd.

We must choose, as a society, to begin to treat the risks associated with man-made radiation rationally or to continue to deal with these risks emotionally. Treating these risks rationally means placing them in perspective with all of the other risks that we willingly, perhaps reluctantly, accept. Continuing to deal with these risks emotionally rather than rationally means that we shall continue to waste societal resources that might be spent more constructively, and in some cases, continue to choose a greater risk over a lesser risk. Nowhere is this choice framed more sharply than in the issue of nuclear-power generation. We can continue to oppose nuclear generation in the hope of getting environmentally “friendly” non-nuclear options, such as solar, geothermal, or wind-driven power; but such a choice is, in reality, a choice for fossil-fuel generation, which is definitely not environmentally “friendly” (for example, smog, respiratory illnesses, and global warming all result from fossil-fuel generation). We can continue to insist that we be protected from every last “particle” of man-made radiation, in the expectation that the very high cost of such protection will be borne by someone else; but in fact, that cost is borne by our society and, ultimately, affects us

all. We have the freedom to base our choices on reason or on emotion, but we are not immune from the consequences of our choices. ■

### Further Readings

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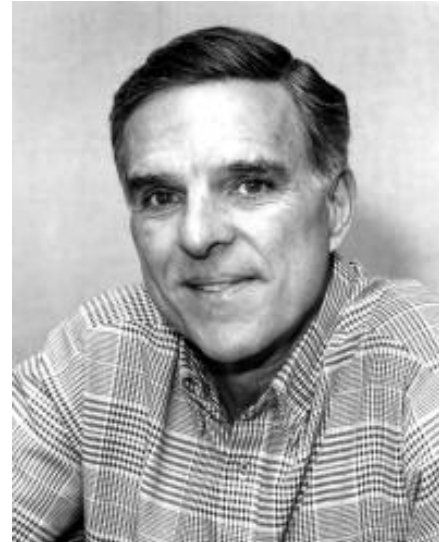
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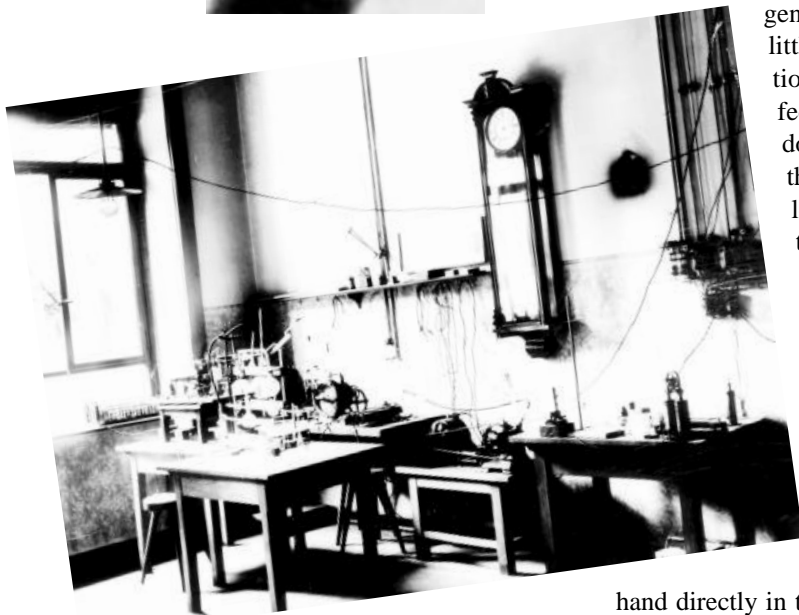


**Mario E. Schillaci** came to the Laboratory in 1967 as a postdoctoral fellow in the Theory Division. In 1970, he joined the Medium-Energy Physics Division where his principal interests included non-nuclear research applications of LAMPF beams. During his tenure with LAMPF, Mario completed investigations in several diverse fields including: radioisotope production, muon chemistry, muon spin rotation, pion channeling, the neutrino oscillation experiment (LSND), and pion radiotherapy, for which he helped develop codes for determining energy deposition in tissue from pion beams. In 1982, as an outgrowth of this collaboration, he joined a radiobiology research project headed by M. R. Raju, of Life Sciences Division, that studied mechanisms of biological damage in mammalian cells using ultrasoft x rays. Mario's interest in biological effects of radiation led him in 1993 to join the Dose Assessment Team (ESH-12) of the Environment, Safety, and Health Division. Mario was a member of the Human Studies Project Team that investigated the Laboratory's involvement in human radiation experiments. He received his B.S. in physics from Drexel University and earned his Ph.D. from Brandeis University in theoretical elementary particle physics.

# A Brief History of Radiation

**H**ealth physics is concerned with protecting people from the harmful effects of ionizing radiation while allowing its beneficial use in medicine, science, and industry. Since the discovery of radiation and radioactivity 100 years ago, radiation protection standards and the philosophy governing those standards

have evolved in somewhat discrete intervals. The changes have been driven by two factors—new information on the effects of radiation on biological systems and changing attitudes toward acceptable risk. The earliest limits were based on preventing the onset of such obvious effects as skin ulcerations that appeared after intense exposure to radiation fields. Later limits were based on preventing delayed effects such as cancer that had been observed in populations of people receiving high doses, particularly from medical exposures and from the atomic-bomb exposures in Hiroshima and Nagasaki.



**Wilhelm Conrad Roentgen (above) discovered x rays in 1895 in Wurzburg, Germany. Also shown is his laboratory and a radiograph of a hand that he made in 1896 after his only public lecture on the discovery of x rays.**

During the evolution of standards, the general approach has been to rely on risk estimates that have little chance of underestimating the consequences of radiation exposure. It is important to realize that most of the effects observed in human populations have occurred at high doses and high dose rates. The information gathered from those populations must be scaled down to low doses and low dose rates to estimate the risks that occur in occupational settings.

Immediately after the discoveries of x rays in 1895 and radioactivity in 1896, x-ray devices and radioactive materials were applied in physics, chemistry, and medicine. In the very early days, the users of x rays were unaware that large radiation doses could cause serious biological effects. They also had no instruments to measure the strength of the radiation fields. Instead, the calibration of x-ray tubes were based on the amount of skin reddening (erythema) produced when the operator placed a

hand directly in the x-ray beam. The doses needed to produce erythema are very high indeed—if the skin is exposed to 200-kilovolt x rays at a high dose rate of 30 rad per minute, then erythema appears after about 20 minutes (or 600 rad) of exposure, and moist desquamation (equivalent to a third-degree burn) occurs after about 110 minutes (or about 2000 rad) of exposure. (For comparison, recall from the primer “Ionizing Radiation—It’s Everywhere!” that for x rays and gamma rays the rad, the unit of absorbed dose, is equal to the rem, the unit of dose-equivalent, and that the average annual background dose in the U.S. from natural and man-made sources is about 0.36 rem per year.)

# Protection Standards

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Early ignorance of the hazards of radiation resulted in numerous unexpected injuries to patients, physicians, and scientists, and as a result, some researchers took steps to publicize the hazards and set limits on exposure. In July 1896, only one month after the discovery of x rays, a severe case of x-ray-induced dermatitis was published, and in 1902, the first dose limit of about 10 rad per day (or 3000 rad per year), was recommended. The 10 rad-per-day limit was based not on biological data but rather on the lowest amount that could be easily detected, namely, the amount required to produce an observable exposure, or fogging, on a photographic plate. By 1903, animal studies had shown that x rays could produce cancer and kill living tissue and that the organs most vulnerable to radiation damage were the skin, the blood-forming organs, and the reproductive organs. Table 1 contains estimates of dose rates encountered by radiation workers in the early part of the 20th century.

In September 1924 at a meeting of the American Roentgen Ray Society, Arthur Mutscheller was the first person to recommend a “tolerance” dose rate for radiation workers, a dose rate that in his judgement could be tolerated indefinitely. He based his recommendation on observations of physicians and technicians who worked in shielded work areas. He estimated that the workers had received about one-tenth of an erythema dose per month (or about 60 rem per month) as measured by the x-ray-tube current and voltage, the filtration of the beam, the distance of the workers from the

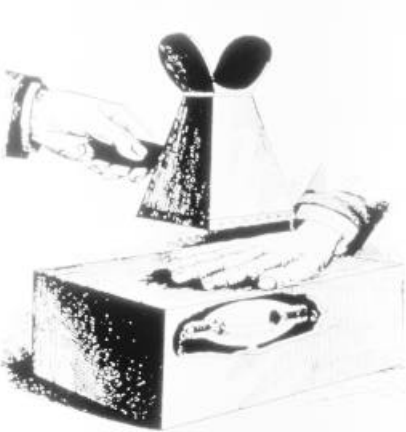
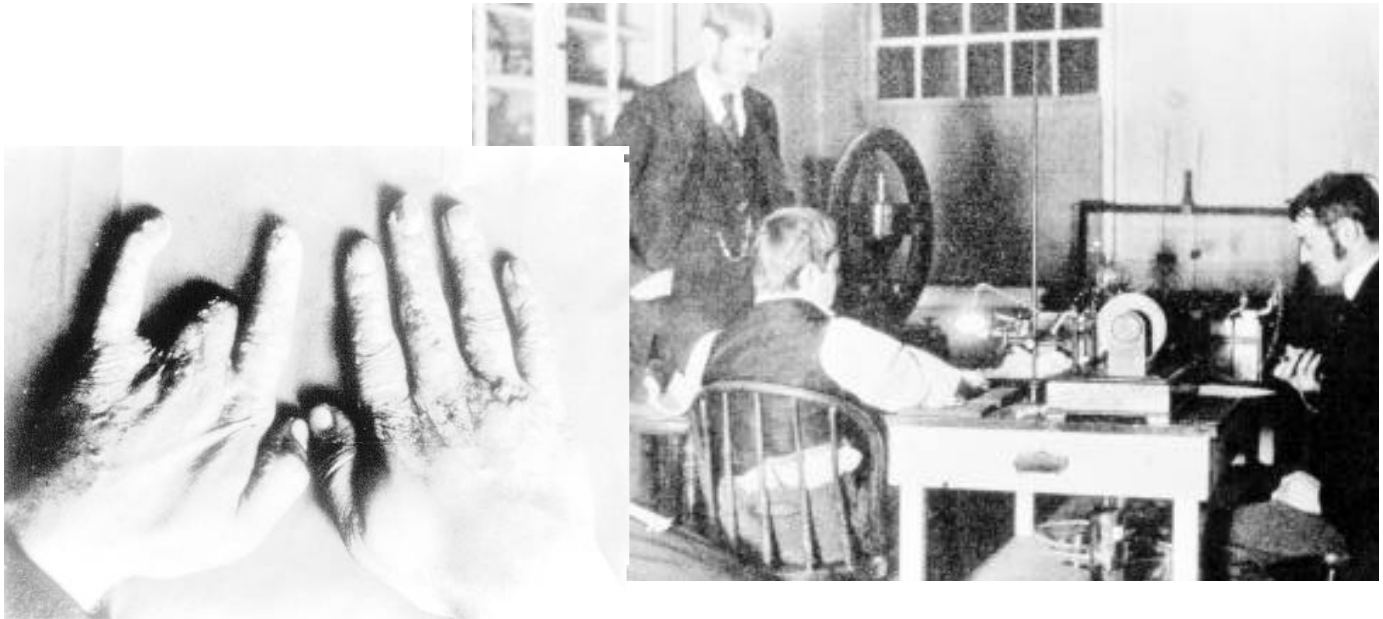


**Antoine Henri Becquerel discovered radioactivity in 1896 in Paris. He is shown here in his laboratory.**

**Table 1. Dose Rates for Radiation Workers in the Early Part of the 20th Century**

Occupation	Approximate Dose Rate (rad min <sup>-1</sup> )
fluoroscopist	0.6 - 6 (hands) 0.006 - 0.06 (body)
x-ray therapy technician	0.006 (body)
radium therapist or technician	0.006 - 0.06 (body)

x-ray tube, and the exposure time. He also observed that none of the individuals had shown any signs of radiation injury. He concluded that the dose-rate levels in the shielded rooms were acceptable, but in proposing a tolerance dose, he applied a safety factor of ten and recommended that the tolerance limit be set at one-hun-



**It was common for the hands of the early radiologists to receive exceptionally high radiation doses. The loss of fingers, as shown in the photograph above, was sometimes the result. Such conditions are ultimately caused by outright killing of many cells. In the case above, dermal basal cells and blood vessels were critically injured in the fingers, scar tissue probably plugged the blood vessels and stopped the flow of blood. The loss of blood supply ultimately led to the death of tissue in the fingers and the loss of those extremities.**

dredth of an erythema dose per month (equivalent to about 70 rem per year). A tolerance dose was "assumed to be a radiation dose to which the body can be subjected without production of harmful effects." Mutscheller presented his recommendation in a paper entitled, "Physical Standards of Protection Against Roentgen Ray Dangers," which was published in 1925. Quite fortuitously, F. M. Sievert arrived at about the same limits using a similar approach.

In 1934, the U.S. Advisory Committee on X-ray and Radium Protection proposed the first formal standard for protecting people from radiation sources. By then the quantitative measurement of ionizing radiation had become standardized in units of roentgens,\* and therefore, the recommended limit on dose rate was expressed as 0.1 roentgen per day. That value was in line with Mutscheller's recommendation of one-hundredth of an erythema dose per month, and in fact, the two tolerance limits differed only by a factor of two. Whether that difference was due to a rounding factor or a technical difference in the way the roentgen was measured in the U.S. versus Europe is open to interpretation.

It is worth emphasizing that those early limits on exposure to x rays were not arrived at through quantitative observation of biological changes but rather through a judgement call based on the absence of observed biological harm.

The dose limits for radiation sources outside of the body (external sources) were augmented in 1941 by a limit on the amount of radium a person could tolerate inside the body (radium tends to be retained by the body, and because of its long radioactive half-life, it thereby becomes a relatively constant internal source of radiation). The devastating experiences of the radium-dial painters and the origin of the radium standard are described in "Radium—The Benchmark for Internal Alpha Emitters" (see page 224). Decade-long clinical observations of twenty-seven persons who were exposed internally to radium, in combination with quantitative

\*The roentgen, the first formal radiation unit, was adopted in 1928 and specifies the quantity of ionizing radiation in terms of the amount of electrostatic charge it produces passing through a volume of air. In particular, the Roentgen is defined as that amount of ionizing radiation that produces 1 electrostatic unit of negative charge in 0.00129 gram of air (1 cubic centimeter of air at standard temperature and pressure). For x rays, 1 rad = 1 rem = 0.96 roentgen.

measurements of their radium body burdens, were the basis for the radium standard. In particular, it appeared that the retention of 1.0 microgram or more was required to produce deleterious effects. Applying a safety factor of ten to that result, the committee members responsible for recommending a standard (many of whom had performed the clinical research on the radium patients) suggested that 0.1 microgram (or 0.1 microcurie) of radium would be an appropriate tolerance limit. Again, the ultimate criteria used was a judgement call: They all agreed that they would feel comfortable even if their own children had that amount in their bodies. That initial standard has essentially remained in effect up to the present.

In 1944, the radium standard was used as a basis for setting the first tolerance limit for internal retention of plutonium. A working-lifetime limit of 5 micrograms (0.3 microcuries) was proposed on the basis that plutonium was long-lived and would be a boneseeker like radium and that the alpha-particle emissions from 5 micrograms of plutonium would deposit ionizing energy at the same rate as the alpha emissions from the allowed 0.1 microgram of radium. In 1945, as a result of animals studies on the relative toxicity of plutonium and radium and on their relative distribution in the body, the Manhattan Engineer District reduced the plutonium limit a factor of 5 to 0.06 microcuries. The Hanford Site, where plutonium was being produced in reactors, reduced the limit even further to 0.03 microcuries. Although today's standards are expressed in terms of an annual inhalation limit rather than a maximum permissible body burden, the current limit recommended by the International Commission on Radiation Protection (ICRP) translates to a body burden that is about the same as the working-lifetime limit set at Hanford during World War II. The concern for limiting and monitoring intakes of radium and plutonium were the beginnings of the field of internal radiation dosimetry.

A great deal of research, particularly animal studies, on the biological effects of radiation were carried out during and immediately after World War II. In 1949 the United States, Canada, and Great Britain held a conference at Chalk River, Ontario, on permissible doses and then published the Tripartite report in which all radiation protection information that had been gathered was discussed and collated. A number of new concepts concerning the measurement of dose had been developed through animal studies. These included *absorbed dose* (measured in rad), *dose-equivalent* (measured in rem), *relative biological effectiveness* (RBE), which relates the rad to the rem for different types of radiations, the absorbed dose as a function of photon energy and depth in tissue (depth dose), the radiotoxicity of plutonium, and the concept of a reference anatomical human. The Tripartite report also recommended standards for internal and external radiation protection, including a plutonium body-burden limit of 0.03 microcuries, a limit on the bone-marrow dose of 300 millirem per week (about 15 rem per year), and a limit on the skin dose of 600 millirem per week (a factor of 2 lower than the value initially recommended by Mutscheller in his 1925 publication). With the exception of the plutonium limit, those values were adopted by the ICRP and the National Council on Radiation Protection and Measurements (NCRP, the new name for the old U.S. Advisory Committee) in 1953 and 1954, respectively. (The plutonium limit recommended by the ICRP was somewhat higher at 0.04 microcuries for the maximum permissible amount of plutonium-239 fixed in the body.)

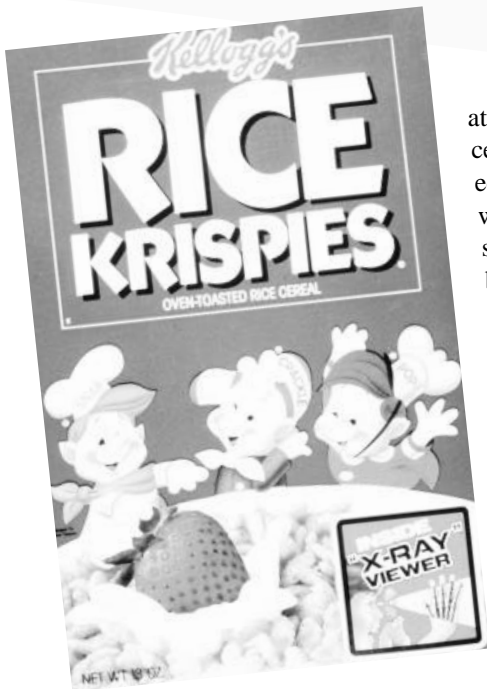
During the 1950s, further reductions in the standards for external radiation were made as a result of studies on the survivors of the two nuclear weapons dropped on Japan and studies of survivors of high-dose medical procedures. In particular, an early analysis of data from the Japanese atomic-bomb survivors indicated an apparent change in the ratio of the number of males to females among infants born



**In the 1930s, Robley D. Evans developed the first quantitative technique for making *in vivo* measurements of radium body burdens. Those measurements were the basis for the radium standard set in 1941.**

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Radiation had a big impact on the popular imagination in the 1950s.

to survivors. At the same time, data from experiments on mammals and fruit flies demonstrated that genetic changes could be induced from very high radiation exposures. Thus, radiation-induced genetic effects became a dominant concern in the early 1950s and led to the first recommended standards for annual dose limits to the public. Later analyses indicated that the early assessment of the atomic-bomb survivors was incorrect, and to this day, radiation-induced genetic changes in humans have *never been observed*. Nevertheless, the fear of future genetic effects lingered on and probably inspired the creation of such science fiction characters as Godzilla, the Incredible Shrinking Man, Spiderman, the Incredible Hulk, and many others. The concern also led to a reduction in radiation protection standards.

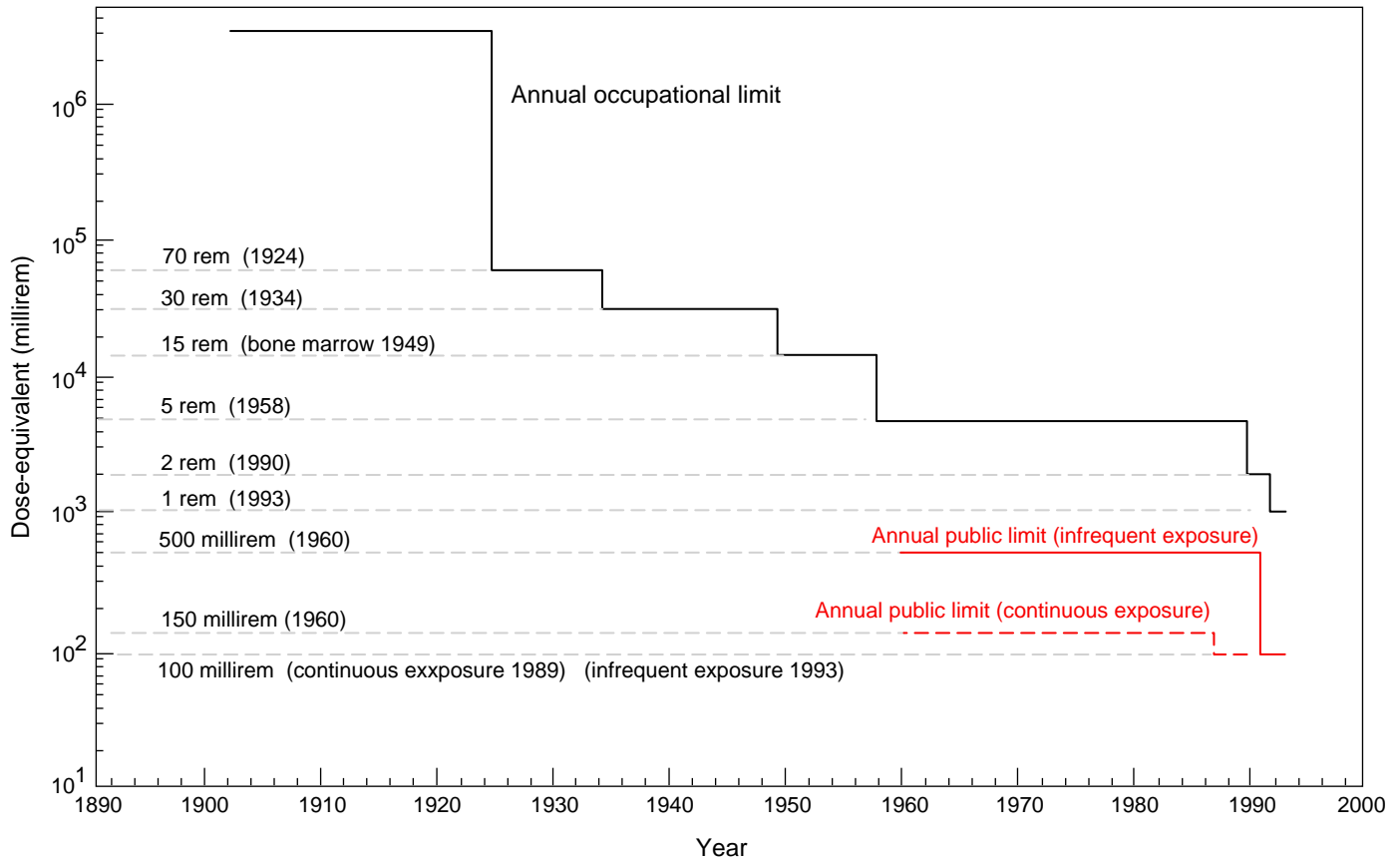
In 1957, the ICRP recommended an annual occupational dose limit of 5 rem per year, and in 1958 the NCRP recommended a life-time occupational dose limit of [(age in years 2 18) 3 5] rem, or a limit of 235 rem for someone who works from ages 18 to 65. The NCRP also recommended an annual limit to the public of 500 millirem per year. In 1960, the Federal Radiation Council recommended an annual limit of 500 millirem per year for an individual in the general public and a limit of 170 millirem per year as the average annual dose to a population group.

By 1961, it was generally understood that the risk of genetic effects had been overestimated in studies of the atomic-bomb survivors, but another risk was becoming apparent—studies of cancer incidence and mortality among the survivors were beginning to show elevated rates for leukemia. As time passed, elevated rates for solid-tumor cancers were also observed. Those findings as well as other studies led to the understanding that different cancers have different latency periods, or elapsed times, between irradiation of the individual and clinical observation of a malignancy. Solid tumors have latency periods of 25 to 40 years, and leukemia has a latency period of 2 to 25 years. The latency periods generally hold true irrespective of the particular agent that serves as the carcinogen.

The unmistakable appearance of an increased rate of cancer among the atomic-bomb survivors had a profound impact on the radiation protection community—it brought into focus the possibility that even low levels of exposure might induce cancers. Of course, the data regarding malignancies were obtained from populations receiving high doses at high dose rates. Risks estimates for low doses could only be made by extrapolating the high-dose data, and that procedure suggested that the cancer risks from low doses were small. Nevertheless, there were no data to suggest the existence of a threshold dose for radiogenic cancers, so the small risk per person at low doses had to be considered in relation to the large number of workers who were receiving those doses.

Those considerations resulted in a philosophical shift from mere compliance with dose limits and the avoidance of deterministic effects (such as cataracts and per-

manent damage to organs) to an emphasis on reducing overall cancer risks to working populations. The ICRP defined a system of dose control consisting of three parts: justification, optimization, and limitation. Justification requires that no new practice involving radiation shall be allowed unless its introduction produces a positive net benefit. Optimization requires that all doses shall be kept *as*



*low as reasonably achievable* (ALARA) taking into account the relevant economic and social factors. Limitation requires that any individual dose not exceed limits set for appropriate circumstances. In today's applications of the dose-control concept, justification and optimization dominate. (More to the point, subjective judgments of regulators rather than the mathematics of optimization often drive the dose limits to lower and lower levels; economic factors are often ignored; and the net result is to make operations involving radiation and radioactive materials extremely expensive.)

In 1977, the ICRP adopted a more formal risk-based approach to setting standards. That approach required that the average incremental risk of death from radiation exposure to workers in radiation industries be no larger than the average incremental risk of death from traumatic injuries to workers in "safe" industries. The incremental risk of death in safe industries is one in ten-thousand, or  $10^{-4}$ , per year. Studies of the atomic-bomb survivors had shown that the risk coefficient for radiation-induced cancer mortality was about  $10^{-4}$  per rem. Based on that risk coefficient, the ICRP recommended a maximum annual dose limit to a radiation worker of 5 rem per year. The 5-rem annual limit was set under the assumption that the

### Figure 1. Radiation Dose Limits over the Past Century

This logarithmic plot of the recommended limits on annual exposures to radiation shows a continual decrease from the beginning of the century to the present. The 1993 NCRP recommendation for occupational dose limits allows for an average of about 1.5 rem per year over a working life from age 18 to age 65 (that is, a lifetime limit for an individual 65 years old is 65 rem; this dose distributed over a 47 year period yields about 1.5 rem per year). The ICRP does not recommend a lifetime dose limit; rather, an annual limit of 2 rem per year averaged over any 5-year period is recommended.



average dose would be less than 1 rem per year, and, thus, the average risk of death would be the same as for safe industries. Thus, the new 1977 limit was unchanged from the 1957 limit, but it was now justified in terms of a risk-based philosophy.

During the 1980s, estimates of the doses received by the atomic-bomb survivors were adjusted downward based on new estimates of the ratio of neutrons to gamma rays in the radiation produced by the bomb. Also, new data on cancer incidence and mortality among the survivors indicated higher rates for some cancers than previously thought. That meant the risk per unit dose, or the risk coefficient, was higher, and in fact, it was calculated to be  $4.3 \times 10^{-4}$  per rem. Based on that increase, the ICRP released a new set of international recommendations in 1990. They recommended limiting radiation exposure to 10 rem over any 5-year period and 5 rem in any one year. The public limit was set at a 100 millirem per year averaged over any 5-year period.

**The 1993 NCRP limits on annual radiation doses relate both to stochastic effects, such as cancer and genetic effects, and to deterministic effects, such as cataracts or permanent damage to an organ. Stochastic effects, by definition, arise from random processes. The probability of their occurrence increases with increasing dose, but their severity does not. Moreover, there is no threshold dose below which the risk is zero. In contrast, there is a threshold dose for deterministic effects. That is, doses below the threshold will not kill enough cells to cause dysfunction in a tissue or organ.**

The NCRP released its own new set of national recommendations in 1993. Those limits and the associated risks are listed in Table 2. They relate both to stochastic effects, such as cancer and genetic effects, and to deterministic effects. The present limits for deterministic effects are not much different than the first recommendations: 50 rem per year to any tissue or organ and 15 rem to the lens of the eye to avoid cataract formation. The recommended limits on whole-body doses for stochastic effects, first set at 5 rem per year in 1958, are now set at no more than 5 rem in any one year and a lifetime average of no more than 1.5 rem per year.

**Table 2. Current Standards and Associated Estimates of Risk (NCRP Report Number 116, 1993)**

Category	Annual Limit	Recommended Risk Coefficient	Estimated Risk at the Annual Limit
Occupational annual whole-body limit for stochastic effects	5 rem (stochastic)	$4.3 \times 10^{-4} \text{ rem}^{-1}$ (for fatal cancer)	2 in 1,000 per year
		$8.3 \times 10^{-5} \text{ rem}^{-1}$ (for severe genetic effects)	4 in 10,000 per year
Occupational lifetime limit	1 rem $\div$ 3 age (years)	—	3 in 100 at age 70
Occupational annual limit for deterministic effects	15 rem to lens of eye 50 rem to any other organ or tissue system	—	no risk if limits not exceeded
Public annual whole body limit for continuous exposure	100 mrem	$5.3 \times 10^{-4} \text{ rem}^{-1}$ (for fatal cancer)	1 in 10,000 per year
		$1.3 \times 10^{-4} \text{ rem}^{-1}$ (for severe genetic effects)	1 in 100,000 per year
Public annual whole-body limit for infrequent exposure	500 mrem	$1.3 \times 10^{-4} \text{ rem}^{-1}$	1 in 10,000 per year
Negligible individual dose (annual whole-body dose per source or practice)	1 mrem	—	no discernable effects (5 in 10,000,000)

The current limits represent a culmination of intensive epidemiology and radiobiological research. However, there are still many open questions regarding the detailed mechanisms that cause biological effects. What are the relative risks of different types of radiations, acute versus chronic exposures, age of exposure, and chronic exposure to low doses? Those concerns dominate discussions on the future evolution of radiation protection standards. ■



**Charles B. Meinhold** has been the President of the National Council on Radiation Protection (NCRP) since 1991. He is also a Senior Scientist and Deputy Division Head of the Radiological Sciences Division at Brookhaven National Laboratory. Charles's field of expertise is the application of radiological physics and radiobiological data to radiation protection. He served as Chairman of NCRP Scientific Committee I on Basic Radiation Protection Criteria from 1988 to 1992 and was a co-author of the basic recommendations of the NCRP and ICRP. Charles has been a member of the International Commission of Radiological Protection (ICRP) Main Commission since 1978 and is presently its Vice Chairman. He was Chairman of Committee 2 on Basic Standards of the NCRP from 1985 to 1992. Charles is President of the International Radiation Protection Association (IRPA) and has been a member of the IRPA Executive Council since 1984. He has served on the oversight committees for Rocky Flats and for the Indian Point, Shorham, and Pilgrim nuclear power stations, and was appointed by the NRC to serve on the Blue Ribbon panel for Three Mile Island Unit 2. Charles has a B.S. in physics from Providence College and studied radiological physics at the University of Rochester under an AEC Fellowship. He is certified by the American Board of Health Physics, and is an Honorary Professor of the China Institute of Atomic Energy.



**John C. Taschner** joined the Laboratory in 1992 as a technical staff member in the Environment, Safety and Health Division (ESH-10) and is involved in radiological transportation accident exercise planning. In 1994, he joined the Laboratory's Human Studies Project Team, and was the Project Leader for the RaLa/Bayo Canyon Project. Prior to coming to Los Alamos, John was Deputy Director of the Navy's Radiological Controls Program Office in Washington, D.C., and has held numerous key health physics management positions with the U.S. Navy and the U. S. Air Force. Over the past thirty years, John has served on several Radiation Protection Standards Committees. Since 1992, John has been the Vice Chairman of the American National Standards Institute's N43 Committee, which writes radiation safety standards for non-medical radiation producing equipment. He has been a member of the Health Physics Society since 1958 and is a member of the American Academy of Health Physics. John earned his M.S. in radiation biophysics from the University of Kansas in 1966 and, in 1973, received his certification in Health Physics by the American Board of Health Physics.

**William C. Inkret** See biography at the end of "On the Front Lines."