Radiobiological effects of low-level radiation and cancer risks

Contrary to some perceptions, there is no unique association between radiation and cancer risk

by R. Mukherjee and J. Mircheva

Health risks from exposure to low levels of ionizing radiation, particularly those relating to cancer, invariably command considerable attention. Recent reports about radon levels in homes and buildings, the extensive fallout from the 1986 Chernobyl nuclear plant accident, and suspected cancer clusters around nuclear facilities have contributed to a heightened sense of concern.

Read from the popular press, such reports can create unnecessary fears and the distorted perception that radiation is somehow the sole, or dominant, cancer-causing agent in our environment. This is far from the case.

Unfortunately, such perceptions are not easily corrected. Although a virtual encyclopedia of scientific information is available about low-level radiation and health effects, most of it is published in specialized literature not easily accessible to the general public.

This scientific background includes basic concepts and studies that may help to place the issue of radiation and cancer risk into clearer perspective. This article briefly reviews some important points.

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Environmental and other factors

The turn of the 20th century saw the discovery of ionizing radiation and radioactivity. Pioneer radiation workers were at that time unaware of the associated health consequences. Many suffered heavily from radiation-induced neoplasms, primarily carcinomas of the epidermis.

Such tragic early incidents hurriedly caused an "era of ignorance", one that was later to be followed by an "era of progressive enlightenment", in radiation biology and radiation genetics. Over time, principles of radiation dose–effect relationships were established that helped characterize and quantitatively predict the potential carcinogenic incidence rates in animals and humans. Since then, data have progressively been obtained from epidemiological studies. In the late 1940s, one other significant source of direct studies of human exposures to high doses of ionizing radiation became available, namely those of Japanese atomic bomb survivors.

Yet early instances of radiation-induced human neoplasms, along with others that happened over the years, seem to have been instrumental in influencing the minds of people who think that there is a "unique association" between ionizing radiation and risk of cancer in humans. This perception arose even as there were advances of beneficial radiation applications in medicine, as well as the development of quantitative criteria and standards in the field of

radiological protection by bodies such as the International Commission on Radiological Protection (ICRP) and the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR).

An accurate assessment of natural background radiation also has become possible over the years. Anyone, whether belonging to a technologically advanced or a developing country, is known to unavoidably receive some low level of radiation exposure. Such natural sources of radiation include radon, cosmic rays, rocks, and soils, as well as potassium-40 in salt, for example. They account for the greatest share of human radiation exposure; an individual's average annual dose from natural sources of radiation amounts to about 2.4 millisievert (mSv).

Other sources of radiation exposure include medical diagnostic applications and the nuclear fuel cycle, which, under normal operations, is a minor source of human radiation exposure. An individual's average annual dose from the nuclear fuel cycle amounts to less than 1% of the 2.4 mSv received from natural background sources.

Apart from radiation, humans are exposed to numerous other environmental substances. They include chemical pollutants and noxious genotoxic agents, some of which are known carcinogens and suspected major causes of environmental degradation. They range from fossil-energy pollutants, such as polycyclic aromatic hydrocarbons, or benzo-a-pyrene; toxic heavy metals; tars and other organic products identical to carcinogens in cigarette smoke; noxious gases, such as sulphur dioxide and nitrous oxide linked to the "greenhouse effect" and the phenomenon of global warming. Other industrial pollutants, such as asbestos, vinyl chloride from the plastics industry, and dioxin, also are of concern.

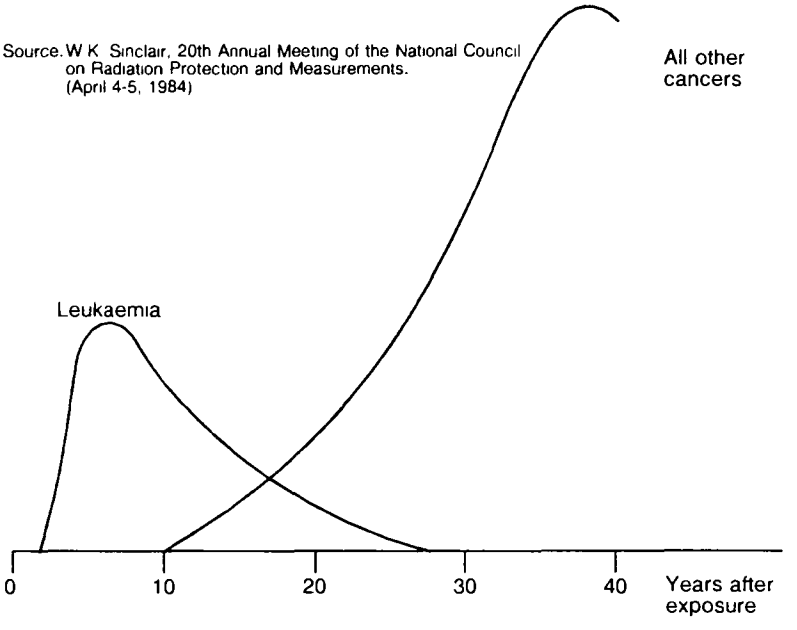
Such chemical agents, either singly or in interactions with environmental radiation, could synergistically increase the carcinogenic risk to humans. Consistent observations of higher cancer incidence co-efficients among urban populations, as compared to control populations in rural areas, seem to substantiate the claim that cancer is an ecological disease.

Epidemiological studies and risk models

There is extensive data on cancer induction by high levels of radiation, mostly because of comprehensive surveys of the Japanese survivors of the atomic bombings in Hiroshima and Nagasaki in 1945. Additionally, epidemiological studies have been carried out on patients exposed during radiation treatments of ankylosing spondylitics, cervical cancer, and other diseases, as well as on occupationally exposed populations. Results of such studies are documented in the specialized joint Japanese/United States reports of the Radiation Effects Research Foundation (RERF), which are based on life-span studies of the atomic bomb survivors and their offsprings. Results also are reported in studies by UNSCEAR, the US National Research Council's Committee on Biological Effects of Ionizing Radiation (BEIR), and others of significance to radiation protection.

Studies of the atomic bomb survivors, generally speaking, have so far shown that various cancer types have been causes of increased mortality in this population. The appearance of malignancies, in terms of time after exposure to radiation, has been observed to follow a specified pattern. *(See graph.)* Leukaemia appears first, after an approximate short latent period of about 2 to 3 years, reaching peak frequency at around 6 to 8 years, then declining and tending to almost disappear after about 25 years after exposure. Cancers other than leukaemia, however, tend to exhibit a different behaviour.

Cancer and time

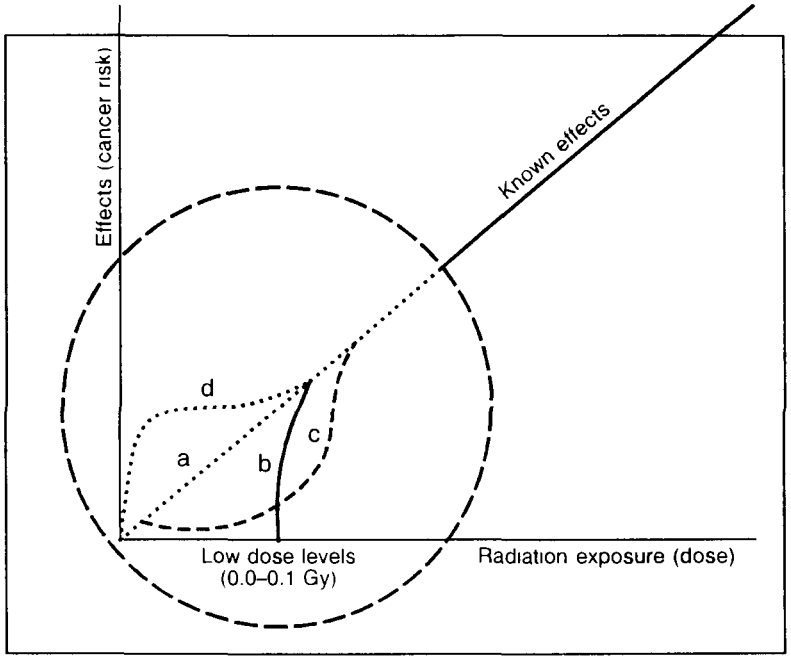


Source. W K Sinclair, 20th Annual Meeting of the National Council on Radiation Protection and Measurements. (April 4-5, 1984)

Leaving aside some differences in the details among the different cancer types, in general they tend to appear after a latent period of about 10 years after exposure. They show a progressive increase, bearing a relation to the radiation dose received and age-dependent parameters.

ICRP and UNSCEAR estimates of the cancer risk per unit of absorbed dose — when delivered at high doses and dose rates for an average member of the general population — range from 4.5 to 7.1% per sievert (Sv), depending upon the projection model used.

Some proposed models of how radiation effects vary with doses at low levels



However, for low levels of radiation (generally speaking, those below 0.2 gray) available data do not unequivocally document cancer risks from exposure to low levels of radiation. The radiobiological assumption, however, is conservative. It is based on a linear dose-response relationship which presumes that any exposure to radiation, no matter how small the dose is, could in principle produce some health effects, whose extent should be in proportion to the total radiation dose absorbed. This hypothesis is the foundation for national and international standards in the field of radiation protection.

At lower doses and rates, the majority of radiation biologists believe that the potential health risks are relatively small, in line with the linear model. Some researchers, however, postulate a threshold below which the risk is effectively zero; others contend that the risks are disproportionately lower or higher than those predicted by the linear model. *(See graph.)*

Radiobiological considerations

In the absence of conclusive data, this theoretical basis governs evaluations of the health effects from exposure to low levels of ionizing radiation. The dose rates of interest are many times lower than the lowest rates at which effects (including carcinogenic risk) have been documented unequivocally.

Common cancers, such as cancer of the female breast, lung, gastrointestinal system, and leukaemia can be induced by a number of agents. Those that are induced by chemical agents are clinically indistinguishable in character from those induced by ionizing radiation. This fact has emerged from research in cell biology and genetics, particularly studies of cell functions and deoxyribonucleic acid (DNA), which is the chemical and molecular basis of heredity. *(See figure.)* There is similarity between molecular damage (lesions) to DNA inflicted by radiation and /or chemicals. In either case, affected cells have the ability to repair damage either fully or partially, or they may die off, depending on the extent of exposure and damage. Cells that survive with lesions can serve as "proliferative stimuli" and initiate carcinogenic transformation. The process could be further promoted by external and/or genetic factors such as substances in food or viral genes called oncogenes. The statistical probability of this multi-step cancer process occurring in a given cell line is a function of all such factors and events. At low doses and dose rates of radiation, the risk of cancer initiation is believed to be small because of the effectiveness of the inherent repair capacity of cells. Ongoing studies in molecular radiobiology are expected to further advance scientific understanding of the dose–response relationship in more quantitative terms, thereby strengthening the analytical basis of cancer risk assessments.

In perspective

Given the relatively high incidence of cancer in the general population, the identification of the extra effect of low-level radiation has proved to be difficult and controversial. Health effects are masked by the normal occurrence of disorders, which may or may not be due to radiation exposure. Any analysis is further complicated by the fact that it is not possible to isolate a control population which is not exposed to radiation.

Below a level of 0.05 to 0.1 gray, which invariably and frequently happens to be the case for issues of radiation protection, attempts to estimate any additional cancers induced by exposure to low-level radiation are subject to a range of uncertainties and assumptions. It is generally agreed that the *probable* effect of the exposure of a large number of people to low-level radiation may be the induction of relatively few cancers in addition to the thousands which occur naturally, years or even decades after the exposure has been incurred.

Societies have been and will continue to be unavoidably exposed to minute doses of ionizing radiation from natural sources. In some geographical locations in India, China, Brazil, and other countries, people live in areas where natural radiation levels are, in fact, three to four times higher than the normal average amount. So far, there have been no unequivocal observations of an increased incidence of cancer among these populations.

Following the Chernobyl accident in 1986, some reports included claims of as many as 10 000 to 20 000 projected excess cancers over the next 70 years in an affected population of about 10 million people. Even if this does happen to be the case, will these cancers be statistically detectable from the natural spontaneous incidences of cancer in this large population? In net terms, the chance may be that no more than one or two additional cases of a certain cancer type occur that could be attributed to Chernobyl-related radiation. There is no certainty to the validity of either the high or the low prediction.

There have also been recent claims of apparently elevated childhood leukaemia cases among the progeny of some male workers at the Sellafield nuclear reprocessing plant. The mechanism of increased leukaemia risk has been attributed to some "cryptic" genetic changes in the paternal germ cells of the leukaemic cases under consideration. However, this inference made on an extremely small sample size stands in sharp contradiction to that of a comparable Japanese study, and seems to violate all plausible biological mechanisms of reproductive biology and genetic transmission. In Hiroshima, there were only 13 cancers, including five leukaemia cases, detected among 10 903 children (20 years of age and younger) whose fathers had been exposed to the atomic bomb fallout (their average dose was 466 mSv). In a parallel case-control study of 41 066 children, there were 49 cancers, including seven leukaemia cases. These studies show no noticeable effect of paternal radiation exposure on the incidence risk of childhood leukaemia.

The risks of radiation exposure to low-level radiation should not be disregarded, and they have been exhaustively under review for nearly a century. During that same time, it has been increasingly recognized that the risks to health posed by many other collateral non-radiation agents are often assessed to be much greater. Many more still remain unknown.

The fact that the effects of low-level radiation are still not certain has served to fuel both the controversy and the publicity surrounding this issue. However, it also demonstrates that if there are effects, they are small, and extremely difficult to conclusively document.

Under the circumstances, the armamentarium of radiation protection standards, which are conservatively based, seem to lie on a sound scientific basis. Future developments in molecular radiobiology should provide more quantitative data that could throw additional light on carcinogenic mechanisms, and the understanding of dose-response relationships.

Schematic mechanisms of cancer induction