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Risk of Cancer Subsequent to Low-Dose Radiation

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ABSTRACT: Prominent among media items related to the Three Mile Island episode were prophecies of future cancers. The credibility of some of these estimates are discussed. The average person has been exposed by the age of 50 to 2.5 rad (0.025 Gy) from natural background. We define low doses as under 25 rad (0.25 Gy). The most heavily exposed members of the general population during the Three Mile Island event received 83 mrad (0.83 mGy). Those exposed to 2500 mrad (25 mGy) would show no pathologically recognizable effects of radiation though there is evidence that chromosomal damage may occur with doses about 1 rad (0.01 Gy). An official stated among the consequences of the Three Mile Island accident that two additional cancer deaths would result. No epidemiologist could detect such an increase in the population at risk. It has been generally agreed that the linear hypothesis is useful for determining protection standards, not prognosis. Objective criteria for pathologic diagnosis of cause-effect relations are presented.

KEY WORDS: pathology and biology, cancer, radiation (nuclear)

Since the forensic sciences are broadly concerned with medicine, law, and human events, it is appropriate to discuss some aspects of the Three Mile Island nuclear plant accident, which involved all of these and a number of other disciplines. The accident, publicized intensively but not always with restraint or accuracy, proved to have major costs in plant damage and morale for the industry and the general public. The early reports, not always well informed, prompted some pronouncements on medical risks that added confusion to the already heated controversy over the actual and hypothetical dangers of low-dose radiation. The excellent and painstaking report of the Kemeny Commission to the President has done much to clarify what happened and why.

This paper discusses the credibility of a sample statement made by an official during the period of tense anxiety and tries to provide a factual basis for assessing potential risks from radioactivity from nuclear power plants. Typical of the early confusion was the statement to the press by the then-Secretary of Health, Education, and Welfare that two additional cancer deaths would result from the release of radioactivity incident to the Three Mile Island accident. Such a statement can never be proved or disproved because in the potentially exposed population of 2 000 000 the random natural variations in cancer mortality rates would entail a much larger number of deaths than two and because only with great difficulty, if at all, can a radiation-induced cancer death be specifically identified as such. His statement may have been based on the assumption that there exists a constant linear relationship between radiation dose and induction of cancer from high doses down to zero. This linear hypothesis is supported by some firm epidemiologic and experimental evidence, but

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there is some contradictory evidence. The hypothesis does provide effective guidance for protection standards as shown by its successful application to establishment of permissible dose levels of radiation, which have been proved by experience to be safe for exposed workers [1]. However, this experience has been confined to healthy adults. There is evidence that infants and embryos in utero are more susceptible to radiation damage than adults. To allow for this, a safety factor has been provided in selecting permissible dose levels for general populations.

Man has long been exposed to small amounts of radiation. It is impossible to escape from the natural background radiation to which all forms of life have been exposed since the beginning of life, and other radiation exposure must be related to it. This natural radiation, partly derived from the radioactive substances in the earth's crust, partly reaching earth from outer space, varies in different regions. Near sea level, as in most coastal regions, the terrestrial portion averages about 35 mrem (0.35 mSv) annually. The cosmic gamma radiation averages 38 mrem (0.38 mSv) per year [2], a total of 73 mrem (0.73 mSv) per year as contrasted with the 210 mrem (2.10 mSv) per year received by the inhabitants of the Colorado Plateau. If the doses from all of the medical X-rays taken annually are averaged out over the U.S. population, the dose per person is 103 mrem (1.03 mSv) [3]. The permissible occupational dose for atomic or other radiation workers is 5 rem/year, or 5000 mrem (50 mSv). In contrast to these dose levels the highest detected dose received by a member of the population adjacent to the Three Mile Island accident was 37 mrem (0.37 mSv), roughly the same amount of radiation that he would have received had he spent two months in western Colorado.

There are areas of the earth such as Kerala in India, portions of Madagascar, and portions of eastern Brazil where the level of terrestrial background radiation runs as high as ten times the usual. The populations of these areas are being studied. While final results will not be available for some time, none of the obvious radiation-induced abnormalities, either somatic or genetic, have been recognized to be present in excess of expected rates. Curiously, Guarapari in Brazil, a region of high radiation background, was in the past famed as a health resort.

From studies of humans and experimental animals exposed to radiation incident to medical diagnosis or treatment, of the survivors of the atomic explosions in Hiroshima and Nagasaki, and of the Marshallese accidentally exposed to fallout radiation in the 1950s, we have learned much about the effects (Table 1). Doses above 1000 rem (10 Sv) of localized radiation (the lethal dose of whole-body radiation for half of a human population is about 450 rem [4.50 Sv]) appreciably increase the likelihood of development years later of leukemia, cancer of the thyroid, cancer of bone, and a few other forms.

Localized radiation is less dangerous than that to the entire body. In a few instances radioactive elements present in nuclear wastes or fallout tend to be concentrated in certain organs and retained for various lengths of time. For example, the radioactive isotopes of iodine are concentrated in the thyroid gland, those of cesium or strontium in bone.

TABLE 1—Mean radiation dose rates per year in millirems.^a

Source	Terrestrial	Cosmic	Total
Background radiation			
Coastal	35	38	73 [4]
Colorado Plateau	140	70	210 [4]
Averaged medical X-rays	103 [4]
Permissible occupational dose	5000
Highest detected dose to members of population surrounding Three Mile Island	37 [3]

^a1 mrem = 0.01 mSv.

Radiation from fallout would be apt to affect the whole body, especially if the exposed population is outdoors, since many of the radioactive fission products are particulate, like dust, while others are gaseous and widely distributed.

In whole-body radiation the hematopoietic cells of the bone marrow are heavily at risk. Since they are largely confined to the marrow of the flat bones and the vertebrae, the risk of leukemia from radiation is virtually nonexistent when arms or legs alone are exposed.

Leukemia is the radiation-induced disease that has been most carefully studied. From the Japanese survivors of the atomic bombs and other groups exposed to considerable doses of radiation, we have learned that the peak incidence of the disease tends to develop 10 to 15 years after exposure and that the dose required for induction is ordinarily more than 100 rem (1.00 Sv), but in very rare instances smaller doses, perhaps as low as 1 rem (0.01 Sv), may induce the disease through abnormalities produced in chromosomes. The spontaneous incidence of childhood leukemia has been estimated to be about ten cases/10 000 for the first ten years of life. Exposure of the fetus to 1 rad (0.01 Gy) has been claimed on theoretical grounds to increase the incidence to 15 cases/10 000 by ten years of age [5]. This estimate is probably too high as shown by comparison with data from Hiroshima/Nagasaki survivors. More information exists on radiation-induced leukemogenesis in adults than in infants.

Data published in 1956 (Table 2) confirmed findings of earlier investigators who had indicated that U.S. radiologists occupationally exposed to radiation, some of whom had not protected themselves carefully, had at least three times as high an incidence of leukemia as would be expected. The survivors at Hiroshima and Nagasaki exposed to higher doses of acute radiation have shown to date seven times the incidence of leukemia expected (Table 2). A considerable amount of publicity has been given to a postulated increase of leukemia among those exposed as troops at the Smoky Test Shot in Nevada in 1957—eight cases of leukemia have been detected among them [12], whereas three would have been expected. Among the Marshallese exposed to fallout in 1954 there has been one case of leukemia, about what might be expected. The upper limit of their exposure was 1400 rem (14.00 Sv). In contrast to the doses to these exposed groups, the highest detected dose to a member of the public adjacent to the Three Mile Island accident was 37 mrem (0.37 mSv), quite insignificant.

The rate at which radiation is received is also important, as the body can repair the damaged tissue to some degree. Radiation received over days or longer, as may be the case with fallout, is about four or more times less effective than is the same dose received in minutes or hours. This difference holds for germinal as well as somatic cells.

Radiation is one of the most powerful mutagenic agents. However, excess congenital abnormalities have not been found in children of the survivors of Hiroshima and Nagasaki [13], nor in the next generation. Based on the Hiroshima/Nagasaki data the dose of radiation required to double the incidence of significant mutations lies between 20 and 200 rem (0.20 and 2.00 Sv) to the gonads of the patients [14]. One may assume from this that any added dose of radiation below background levels would entail additional consequences, if any, less than those experienced by the human race during its evolutionary history [15].

Plutonium, the first man-made transuranic element, is a significant hazard because it emits densely ionizing though poorly penetrating radiation made up of alpha particles. An important ingredient of some atomic weapons and produced by some atomic fuel cycles, it is highly carcinogenic, on the basis of experimental animal evidence, and one of the most hazardous substances known to man. Plutonium may be an occupational hazard to those working directly with it or, rarely, a possible environmental hazard, for example as a result of the fire in the Colorado Rocky Flats plant. The method of exposure is usually through inhalation of minute particles. The carcinogenicity of plutonium appears to be less in man than in animals. For example, 26 workers with plutonium had received during World War II and shortly thereafter exposures to airborne plutonium particles resulting in body burdens ranging from 7 to 230 nCi (260 to 1610 Bq) [16]. None of these exposed persons has had

TABLE 2—Incidence of leukemia in some irradiated populations.^a

Location	Type of Radiation	Total Dose, rem	Patient Years	Observed Cases, <i>n</i>	Expected Cases, <i>n</i>	References
U.S. radiologists 1950-1954	X-ray	5 to >2000 (chronic radiation)	20 190	3	1	6
Hiroshima and Nagasaki	n, γ	1 to >500 (acute radiation)	950 000	81	12	4, 7, 8
Nevada Smoky Shot	γ	? <10 (acute radiation)	63 000	8	3	9
Marshall Islands	β , γ	700 to 1400	3 832	1	1	10
Near Harrisburg, Pa.	γ	<0.04	2 000 000	?	?	11

^a1 rem = 0.01 Sv.

adverse health effects as a result of the 32 years of body burden. This suggests that the hazard may not be as great as is sometimes estimated. However, the data on the high toxicity of plutonium in animals are so striking they warrant extremely careful methods of containment of this substance.

Currently, there is some discussion as to the effect of occupational levels of radiation on the health of workers at atomic plants. Their health is clearly better than that of the general population based on studies done at plants in the United States and the United Kingdom. However, it has been claimed [17] that exposure to radiation within permissible occupational levels has resulted in increase of a certain few types of cancer in workers at Hanford, Wash. A study with supporting conclusions has been made by Gofman [18]. The validity of these claims has been disputed by others [19-21] whose opinions I share.

In view of the data reviewed above, moderation rather than exaggeration in projection of possible carcinogenic effects of acute or chronic low-dose radiation is desirable to avoid needless alarm to survivors and to permit fair judgment by the public of the desirability of use of nuclear energy as a source of power.

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References

- [1] Warren, S., "Effects of Low Levels of Radiation on Rodents and Potential Effects in Man," *Health Physics*, Vol. 29, No. 2, Aug. 1975, pp. 251-255.
- [2] "Natural Background Radiation in the United States," Report 45, National Council on Radiation Protection and Measurements, Washington, D.C., 1975.
- [3] Ad Hoc Population Dose Assessment Group, "Population Dose and Health Impact of the Accident at the Three Mile Island Nuclear Station (A Preliminary Assessment for the Period March 28 Through April 7, 1979)," U.S. Government Printing Office, Washington, D.C., 10 May 1979.
- [4] Advisory Committee on the Biological Effects of Ionizing Radiations, "The Effects on Populations of Exposure to Low Levels of Ionizing Radiation," National Academy of Sciences—National Research Council, Washington, D.C., 1972, p. 12.
- [5] Hall, E. J., *Radiobiology for the Radiologist*, 2nd ed., Harper and Row, Hagerstown, Md., 1978.
- [6] Warren, S., "Longevity and Causes of Death from Irradiation in Physicians," *Journal of the American Medical Association*, Vol. 162, No. 5, Sept. 1956, pp. 464-468.
- [7] Atomic Bomb Casualty Commission, "Bibliography of Published Papers of the Atomic Bomb Casualty Commission 1947-75," in *The Atomic Bomb Casualty Commission 1947-1975. A General Report on the ABCC-JNIH Joint Research Program*, Radiation Effects Research Foundation, Hiroshima and Nagasaki, Japan, 1978.
- [8] Segi, M., "Graphic Presentation of Cancer Incidence by Site and by Area and Population. Compiled from the Data Published in Cancer Incidence in Five Continents, Vol. III," Segi Institute of Cancer Epidemiology, Nagoya, Japan, 1977.
- [9] Committee on Literature Survey of Risks Associated with Nuclear Power, "Risks Associated with Nuclear Power: A Critical Review of the Literature. Summary and Synthesis Chapter," National Academy of Sciences, Washington, D.C., April 1979.
- [10] "Brookhaven Highlights July 1976-September 1978," BNL 51000, Brookhaven National Laboratory, Upton, N.Y., Nov. 1979.
- [11] Kemeny, J. G. (Chairman), "Report of the President's Commission on The Accident at Three Mile Island. The Need for Change: The Legacy of TMI," U.S. Government Printing Office, Washington, D.C., Oct. 1979.
- [12] "1978-1979 Report of the Assembly of Life Sciences," National Research Council, National Academy of Sciences, Washington, D.C., 1979.
- [13] Neel, J. V. and Schull, W. J., *The Effect of Exposure to the Atomic Bombs on Pregnancy Termination in Hiroshima and Nagasaki*, Publication 461, National Academy of Sciences—National Research Council, Washington, D.C., 1956.
- [14] Advisory Committee on the Biological Effects of Ionizing Radiations, *The Effects on Populations of Exposure to Low Levels of Ionizing Radiation*, National Academy of Sciences—National Research Council, Washington, D.C., 1972, p. 115.

- [15] Advisory Committee on the Biological Effects of Ionizing Radiations, *The Effects on Populations of Exposure to Low Levels of Ionizing Radiation*, National Academy of Sciences—National Research Council, Washington, D.C., 1972, p. 129.
- [16] Voelz, G. L., Hempelmann, L. H., Lawrence, J. N. P., and Moss, W. D., "A 32-Year Medical Follow-up of Manhattan Project Plutonium Workers," *Health Physics*, Vol. 37, No. 4, Oct. 1979, pp. 445-485.
- [17] Mancuso, T. F., Stewart, A., and Kneale, G., "Radiation Exposures of Hanford Workers Dying from Cancer and Other Causes," *Health Physics*, Vol. 33, No. 5, Nov. 1977, pp. 369-385.
- [18] Gofman, J. W., "The Question of Radiation Causation of Cancer in Hanford Workers," *Health Physics*, Vol. 37, No. 5, Nov. 1979, pp. 617-639.
- [19] Sanders, B. S., "Low-Level Radiation and Cancer Deaths," *Health Physics*, Vol. 34, No. 6, June 1978, pp. 521-538.
- [20] Gilbert, E. S. and Marks, S., "An Analysis of the Mortality of Workers in a Nuclear Facility," *Radiation Research*, Vol. 79, No. 1, July 1979, pp. 122-148.
- [21] Gilbert, E. and Marks, S., "Comment on 'Radiation Exposures of Hanford Workers Dying from Cancer and Other Causes,'" *Health Physics*, Vol. 37, No. 6, Dec. 1979, pp. 791-792.

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