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The Biologic Effects of Low-Level Radiation

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Few topics engender more vigorous debate than the biologic effects of low-level radiation and selection of a mathematical model to predict the incidence of cancer. A recent review on radiation risk stated (1):

> The A-bomb survivors represent the best source of data for risk estimates of radiation-induced cancer.
>
> It is clear that children are ten times more sensitive than adults to the induction of cancer.
>
> There are no assumptions, and no extrapolation indicated.

This chapter provides data that suggest that exactly the opposite of the above three statements applies; that is, I present a large amount of data indicating the linear no-threshold theory is erroneous. To that effect, this chapter discusses a review article (2) that scrutinized numerous scientific studies that arrived at drastically different conclusions. I present the information in four sections: the available experimental data, studies looking at the biologic effects of background radiation, the experimental evidence obtained from medical exposure to radiation, and in vitro studies.

First, let's look at the experimental data available on radiation risk. The only study that suggested a higher risk of cancer with low levels of radiation is the retrospective study by Ron and Modan (3) of 11,000 children treated for tinea capitis. The incidence of thyroid cancer was higher, especially in children less than 5 years old. Because the study was retrospective, the dose range was *estimated* to be 4.5 to 50 rem. But there are limitations of retrospective studies, as well as significant inaccuracies encountered in estimating radiation exposure. Also, a large proportion of the children received a dose (calculated to be) greater than 10 Rem. Therefore, it seems very inappropriate to draw any conclusion from this study, which was of dubious quality at best.

All the other studies, of much higher quality, done on the same topic have led to the opposite conclusions. A study of 14,624 infants less than

16 months of age treated for hemangioma did not reveal a higher incidence of cancer (4). Similarly, a Finland study of 1 million children, after the Chernobyl accident, did not reveal a higher incidence of cancer (5). Hjalmars et al. (6) reported no change in cancer incidence in a study of 1.6 million children in Sweden. The study by Rallison et al. (7), looking at the radiation fallout in Utah, reported similar results. Finally, a study of 35,074 patients who received diagnostic doses of iodine radioisotope ^{131}I did not find a higher incidence of cancer (8). Based on those studies of millions of children, it seems appropriate to conclude that low-level radiation does not increase the incidence of cancer, even in children.

We now review the conclusions stemming from studies about the biologic effects of background radiation. A Chinese study of 73,000 persons, comparing radiation doses of 96 mrem/yr versus 231 mrem/yr, found no difference in the incidence of cancer. Similarly, the study by Amsel et al. (9) comparing the incidence of cancer in a population of 825,000 patients living at an altitude of 1000 feet to the incidence in a population of 350,000 persons living at 3000 feet did not find a difference in the incidence of cancer between the two populations. One study comparing four groups living at different altitudes actually disclosed a negative dose-risk correlation (10). In the United States, a study looking at the radiation exposure of 1730 counties also found a negative dose-risk correlation (11). One more study of indoor radon exposure did not find any positive correlation (12).

As for the experimental evidence from medical exposure to radiation, a study by Saenger et al. (13) evaluated 33,888 Graves' disease patients treated with either surgery or with ^{131}I. The data revealed fewer complications in patient treated with ^{131}I. A study in 10,552 patients (8) and another study of 46,000 diagnostic doses of ^{131}I (14) did not disclose any higher incidence of cancer.

Looking at occupational exposure, data collected in approximately 200,000 persons (15–17) did not reveal an increase in cancer, notwithstanding that in one of those studies the mortality rate from cancer was lower in patients who were radiated! Also, the International Association for Research on Cancer study of 95,673 monitored radiation workers in the United States, the United Kingdom, and Canada found 3830 deaths for all cancers except leukemia but no deaths exceeding what was expected (18). No support for the linear no-threshold theory can be found here either. Finally, several studies have reported that workers who inhaled plutonium have lower lung cancer mortality rates than those not thus exposed (19–21). Contrary to impressions generated by the media, no record exists of cancer deaths resulting from human exposure to plutonium. Probably the most significant data on low-level radiation exposure in humans is still in the research stage, but preliminary results are interesting (22). In Taipei and other areas of Taiwan, 1700 apartment units were built using steel contaminated with cobalt 60, exposing 10,000 occupants for 16 years to an average, according to preliminary estimates, of 4.8 rem in the first year and 33 rem in total (23). From national

Taiwan statistics, 173 cancers and 4.5 leukemias would be expected from natural sources, and according to the linear no-threshold theory, there should have been 30 additional leukemias. However, a total of only five cancers and one leukemia have occurred among this group (23).

There are no statistically sound, well-designed studies that have validated the applicability of the linear no-threshold model at low doses (2). On the contrary, there is a suggestion that low-level exposure may be beneficial. This has been dubbed *hormesis,* and there are myriad of studies that suggest the beneficial effects of radiation. A study in human lymphocytes showed a protective effect of exposure from low-dose ^3H to subsequent exposure to 150 rem of x-rays (24). Shadley and Dai (25) found that preexposure of human lymphocytes to 5 rem reduces the number of DNA aberrations induced by 400 rem. Sanderson and Morely (26) found a decrease in mutagenesis. Kelsey et al. (27) found fewer mutations from 300 rem if human lymphocytes are preexposed to 1 rem of radiation. Shadley and Wolff (28) found a decrease in the number of DNA breaks if cells are irradiated with less than 20 rem. Fritz-Niggli and Schaeppi-Buechi (29) found lower embryonic mortality when *Drosophila melanogaster* eggs are exposed to 200 rem. Finally, ingenious experimental techniques have been developed for observing the effects of a single alpha particle hitting a single cell. Miller et al. (30) found that the probability for transformation to malignancy from N particle hits on a cell is much greater than N times the probability for transformation to malignancy from a single hit. This is a direct violation of the linear no-threshold theory, indicating that the estimated effects based on extrapolating the risk from high exposure, represented by N hits, greatly exaggerate the risk from low-level exposure as represented by a single hit.

The aforementioned data indicate that the linear nonthreshold model is unable to predict the biologic effects of low-level radiation, and consequently grossly overestimates the incidence of those effects. We shall demonstrate that this viewpoint that has exaggerated the risk from low-level exposure unduly poses a burden that is detrimental to the general welfare.

After a review of studies on natural, occupational, and medical exposure to radiation, health risk from low-level dose could not be detected above the "noise" of adverse events of everyday life (2). No available data confirm the hypothesis that children are more radiosensitive than adults (2). The evidence is consistent with the statement from the Health Physics Society that the health risk from the exposure to up to 10 rem is "either too small to be observed or nonexistent" (31). A sentiment has recently developed in the community of radiation health scientists to regard the risk estimates in the low-dose region that are based on the linear no-threshold theory as being grossly exaggerated or completely negligible (22). The data regarding leukemia among atomic bomb survivors (32) strongly suggest a threshold greater than 20 centisievert (cSv) (22). The evidence presented in that review leads to the conclusion that the linear nonthreshold theory fails badly in the low-dose region because it grossly overestimates the risk from low-level radiation (22).

A controversial analysis and interpretation by Pierce et al. (32) of some of the A bomb survivor data from Japan suggested that a linear model is valid at exposures as low as 50 millisievert (mSv) and that this is the lowest dose linked to a statistically significant radiogenic risk. In other independent analyses of the same data, a curvilinear dose-response also provided a satisfactory fit to the Japanese data (33). Heindenreich et al. (34), using the same data and applying different analytical methods, did not find any evidence for increased tumor rates below 200 mSv. Finally, if error bars are ignored (22), the points suggest a linear relationship with the intercept at a near-zero dose. The data themselves give no statistically significant indication of increased incidence of cancer for doses of less than 25 cSv. In fact, considering only the three lowest dose points, the slope of the dose-response curve has a 20% probability of being negative (risk decreases with increasing dose) (22).

The data largely comes from observation at relatively high doses and dose rate and do not suffice to define the shape of the dose-response curve in the millisievert dose range; however, it is noteworthy that "the dose-response curve for the overall frequency of solid cancers in the atomic-bomb survivors is not inconsistent with a linear function" (35). It is important to note that the rate of cancer in most populations exposed to low-level radiation has not been found to be detectably increased, and that in most cases the rate has appeared to decrease (35). The same report asserts that low-dose epidemiologic studies are of limited value in assessing dose-response relationship and have produced results with sufficiently wide confidence limits to be consistent with an increased effect, a decreased effect, or no effect. For some types of tumors there is actually a decrease in cancer frequency with exposure to radiation (35).

Finally, let us consider a legal interpretation in this country of the current scientific data. Recently, a U.S. federal court dismissed all 2100 lawsuits against GPU Nuclear Corporation that claimed radiation injury from the 1979 Three Mile Island accident because of lack of evidence that anyone had received doses greater than 100 mGy (36). The court determined that there is consensus within the scientific community that "at doses below 10 rems [100 mGy], the casual link between radiation exposure and cancer induction is entirely speculative." The Health Physics Society recommends against quantitative risk assessment of radiogenic health effects below an individual dose of 50 mGy in 1 year (36).

The former vice chancellor of Oxford University (37) stated that risk perception is intricate, as it involves fear and dread. However, an oversimplified algorithm is likely to prevent useful empirical application of radiation for the health benefit of children. In addition to the large number of studies we have reviewed, numerous scientific groups believe the linear no threshold model grossly overestimates the incidence of biologic effects, if any, of low-level radiation (38–49).

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