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EDITORIAL

Healthy Worker and Healthy Survivor Effects in Relation to the Cancer Risks of Radiation Workers

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The cancer risk coefficients incorporated in radiation safety regulations are based on linear extrapolation of high dose effects [ICRP, 1977]. They therefore assume that, even above the threshold dose for marrow damage, there are no late effects of radiation other than cancer. According to the Radiation Effects Research Foundation (RERF), this assumption is consistent with the mortality experiences of A-bomb survivors [Beebe et al., 1977], and it is obvious that the survivor-based risk estimates of RERF are more highly esteemed by the International Commission on Radiological Protection (ICRP) and other standard setting committees than the worker-based estimates of Mancuso, Stewart, and Kneale (MSK).

The source of these authors' (MSK) risk estimates is a study of radiation workers at Hanford, which began by comparing the occupational exposures of men who died from cancer and other causes but eventually included all the badge-monitored workers in a relative risk analysis by the method of regression models in life tables [Mancuso et al., 1977; Kneale et al., 1981]. One excuse for ignoring this work is that other analyses of essentially the same data are consistent with there being few, if any, extra cancer deaths in the Hanford cohort [Darby and Reissland, 1981; Gilbert et al., 1989]. A further reason is that this cohort, as well as ones representing other branches of the nuclear industry, have Standard Mortality Ratios (SMRs) that are well below par [strong "healthy worker effect"; see Polednak and Frome, 1981; Checkoway et al., 1985; Smith and Douglas, 1986; Beral et al., 1988; Gilbert et al., 1989]. But much the strongest reason for the "official" rejections of the MSK estimates is because they are so different from a remarkably consistent set of RERF estimates [Beebe et al., 1977; Preston et al., 1986].

The RERF survivor cohort was assembled 5 years after the bombing of Hiroshima and Nagasaki, and comparisons between observed deaths after this date and expectations based either on national statistics (SMR analysis) or on a linear model of relative risk have constantly left an impression of no lasting effects of earlier events and no late effects of radiation apart from cancer. The choice of a risk model that had only one degree of freedom occasioned no surprise and was clearly the result of concluding that any selection for fitness during the period of acute heavy mortality had worn off by October 1950 [Beebe et al., 1978]. However, Stewart and Kneale,

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who had long suspected that chronic marrow damage was: 1) the reason why the exceptionally high death rates of 1945 and 1946 were not followed by a swing in the opposite direction; and 2) the reason why there has been a constant excess of rare blood diseases at high dose levels, have recently shown that there is a much better fit of RERF data with a linear quadratic model of relative risk than with a simple linear model [Stewart, 1982; Stewart and Kneale, 1984, 1988, 1989].

With limited access to RERF data, Stewart and Kneale have also shown that: 1) for all noncancer deaths (1950–82), the linear component of risk has a significant *negative* value and the quadratic component a significant *positive* value; and 2) the resulting U-shaped curvature of dose-response is enhanced by removal of cardiovascular diseases (i.e., removal of deaths that have only weak associations with immune system reactions). Therefore, since a steep linear trend for blood diseases as well as neoplasms is a feature of all the Beebe et al. analyses, it is probable that competition between early and late effects of the two nuclear explosions has never ceased and that both a "healthy survivor effect" and chronic marrow damage are still influencing the timing and frequency of noncancer deaths.

ICRP will probably require independent confirmation of the selection and marrow damage effects before recommending any changes in radiation safety regulations. However, it is becoming increasingly clear that, as a result of the unusual time frame of the Japanese survey, RERF data have been the source of many false impressions. In this follow-up of persons who were still alive several years after the bombing of Hiroshima and Nagasaki, there was no possibility of observing more than a small fraction of the deaths caused either by the tissue destructive effects of the radiation or blast or by the environmental effects of the blast and the general upheaval. This is important because the previous mortality experiences of any closed population will necessarily have a lasting effect on the remaining deaths. Therefore, a correct interpretation of RERF data requires recognition of the facts that, by October 1950, a huge number of premature deaths had already occurred that were dose related (via hypocenter distances) and that these early deaths were a special risk of persons whose weak holds on life were and were not a direct consequence of the bombing.

These biases made it inevitable that the death rates of survivors would be lower than normal (and inversely related to dose) *unless* chronic effects of the radiation or the blast were still causing premature deaths from causes other than cancer. Furthermore, acute marrow damage was responsible for thousands of the "not-observed" deaths and was often followed by anemia and other evidence of lasting damage to hemopoietic stem cells [Okhita, 1975]. Therefore, here was an obvious cause of later deaths from rare blood diseases such as aplastic anemia and myelofibrosis.

In these circumstances, it was clearly a mistake to try and account for extra cases of rare blood diseases in terms of leukemogenic effects of the radiation [Beebe et al., 1977, 1978] and equally misguided to apply the same pressures to the same causes of death in the ankylosing spondylitis survey [Court Brown and Doll, 1957].

In relation to the twin subjects of the necessarily "slanted" observations of all epidemiological surveys and the need for accurate assessment of the initial health status of a study population, it is appropriate to mention that an early finding of the MSK analysis of Hanford data was an all-causes death rate that was *negatively* correlated with dose [Kneale et al., 1978]. This observation was contrary to normal expectations unless the workers who were most at risk of any radiation effects were making a larger contribution to the "healthy worker effect" than were the workers in

safer jobs (internal healthy worker bias). But, unfortunately, a straightforward test of this hypothesis—by comparing the death rates of occupational subgroups of the study cohort—was impossible partly because there was erratic coding of annual occupations and partly because there was no distinction between clean and contaminated workplaces.

MSK responded to this problem by allowing the frequency and results of urine examinations and other tests for internal radiation to be the basis of a score that measured danger levels and could be applied to job years or person years. Gilbert and her associates [1989] refused to follow suit. Instead, they recognized three levels of "main" occupation (i.e., white collar, other nuclear, and other manual) and observed the (negligible) effects of excluding from their relative risk analysis the 1% of male workers who had a recognizable body burden of plutonium. Therefore, it is possible that their quasinegative findings are the results of not making sufficient allowance for certain unusual components of the healthy worker effect. This is a reference to the fact that, in the nuclear industry, pressure on this effect could be coming from the health surveillance programs which are needed: 1) to keep annual doses of radiation "as low as is reasonably achievable" (ALARA principle); 2) to be sure that manual work requiring special respirators and coveralls is given to men who rate high on a respiratory fitness scale; and 3) to be sure that supervision of dangerous operations is the responsibility of health physicists who enjoy perfect health.

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REFERENCES

Beebe GW, Kato H, Land CE (1977): "Life Span Study Report 8 (1950–74)." Radiation Effects Research Foundation Technical Report, TR-1-77.

Beebe GW, Land CE, Kato H (1978): The hypothesis of radiation accelerated aging and the mortality of Japanese A-bomb victims. In "Late Biological Effects of Ionizing Radiation," Vol. 1. Vienna: International Atomic Energy Agency, pp 3–27.

Beral V, Fraser P, Carpenter L, Booth M, Brown A, Rose G (1988): Mortality of employees of the Atomic Weapons Establishment, 1951–82. Br Med J 297:757–770.

Checkoway H, Matthew RN, Shy CM, Watson JE, Jr., Tnakersley WG, Wolff SH, Smith JC, Fry SA (1985): Radiation, work experience and cause-specific mortality among workers at an energy research laboratory. Br J Ind Med 42:525–533.

Court Brown W, Doll R (1957): "Leukaemia and Aplastic Anaemia in Patients Irradiated for Ankylosing Spondylitis." London: Medical Research Council, MRC Special Report Series No. 295.

Darby S, Reissland J (1981): Low levels of ionising radiation and cancer—Are we understanding the risk? J R Stat Soc 144:298–331.

Gilbert ES, Petersen GR, Buchanan A (1989): Mortality of workers at the Hanford site: 1945–1981. Health Physics 56:11–25.

ICRP 26 (1977): "Radiation Protection: Recommendations of the International Commission on Radiological Protection." London: Pergamon Press.

Kneale GW, Mancuso TF, Stewart AM (1978): Hanford IIA: Re-analysis of data relating to the Hanford Study of the cancer risks of radiation workers. In "Late Biological Effects of Ionizing Radiation," Vol 1. Vienna: International Atomic Energy Agency, pp 387–410.

Kneale GW, Mancuso TF, Stewart AM (1981): Hanford Radiation Study III: A cohort study of the cancer

risks from radiation to workers at Hanford (1944–77 deaths) by the method of regression models in life-tables. Br J Ind Med 16:156–166.

Kneale GW, Mancuso TF, Stewart AM (1984): Job related mortality risks of Hanford workers and their relation to cancer effects of measured doses of external radiation. Br J Ind Med 41:9–14.

Mancuso TF, Stewart AM, Kneale GW (1977): Hanford I: Radiation exposures of Hanford workers dying from cancer and other causes. Health Physics 33:369–384.

Okhita T (1975): Review of thirty years study of Hiroshima and Nagasaki atomic bomb survivors. Acute effects. J Radiat Res (Tokyo) 16:49–66.

Polednak AP, Frome EL (1981): Mortality among men employed between 1943 and 1947 at a uranium processing plant. J Occup Med 23:169–178.

Preston DL, Kato H, Kopecky JK, Fujita S (1986): "Life Span Study Report 10 (1950–82)." Radiation Effects Research Foundation Technical Report TR1-86.

Smith PG, Douglas AJ (1986): Mortality of workers at the Sellafield plant of British Nuclear Fuels. Br Med J 293:845–854.

Stewart AM (1982): Delayed effects of A-bomb radiation: A review of five-year survivors. J Epidemiol Commun Health 36:80–86.

Stewart AM, Kneale GW (1984): Non-cancer effects of exposure to A-bomb radiation. J Epidemiol Commun Health 38:108–112.

Stewart AM, Kneale GW (1988): Late effects of A-bomb radiation: Risk problems unrelated to the new dosimetry. Health Physics 54:567–568.

Stewart AM, Kneale GW (1989): A-bomb survivors as a source of cancer risk estimates. Confirmation of suspected bias. In "Proceedings of the 14th L.H. Gray Conference," Oxford, England, September (in press).