Correspondence

Risk factors for radiogenic cancer: a comparison of factors derived from the Hanford survey with those recommended by the ICRP

Sir,—In their recent letter (1985;42:647) Stewart and Kneale claim that our comparison of risk estimates derived from their model for risks from exposure to low doses of ionising radiation (the MSK model) with those recommended by ICRP (1985;42:341–5) is misleading. They draw attention to the large standard errors associated with risk estimates derived from their model and point out that our comparison is too precise. They describe the doubling dose of 0·15 Gy that we used as “a point estimate” and draw our attention to the substantial confidence limits on this value.

Our interest in this matter was originally stimulated by Dr Stewart’s repeated claim that the risk estimates used by ICRP are underestimated by a factor of 10–15 times. The basis for this claim is the MSK model for cancer induction by low doses of radiation constructed from an interpretation of the results of the Hanford survey.1 This detailed model specifies a dose response relation, has factors to allow for changing sensitivity with age and latency after exposure, and relies on the assumption that radiation acts multiplicatively on spontaneously occurring disease. Since we have available the results of a survey of people exposed to moderately low doses of ionising radiation, we decided to test the MSK model at its face value using the value for doubling dose that Dr Stewart has herself advocated when criticising present standards. We were comparing like with like since although ICRP recommends a single value for risk, there are large confidence limits on that value.

In fact we have shown that when using the MSK model the doubling dose (D) that best predicts the observed results of the luminiser survey is between 13·0 and 14·0 Gy and taking the 95% Poisson confidence limits for observing 27 deaths we conclude that D should lie between 0·30 Gy and infinity.

Stewart and Kneale questioned the relevance of the luminiser survey for this test because of the deficit in observed non-cancer deaths compared with expectation and concluded that it is unlikely that more than two thirds of the deaths in our survey were traced. We have no evidence to conclude that there is a substantial under-ascertainment of deaths in our survey and neither have Stewart and Kneale. We are currently investigating the reasons for the deficit we observe and will be reporting on this in due course.

We do not understand the mechanistic basis for the cells of older individuals being more sensitive to neoplastic transformation by radiation than those of young individuals. One interpretation of the age dependence for cancer is that the disease is a multi-stage process with a stochastic dependence on time. A possible mechanism which would give a sharply increasing sensitivity with age would be that radiation acted as a promoter of cancer in the final stages of this process. There is no evidence for radiation as a promoter; however, rather it seems more probable that it acts at an early stage as an initiator of the disease.

Finally, we would like to comment on the plight of workers wishing to challenge the MSK hypothesis. A complex model with four independent variables has been derived and much of the basis for the analysis is obscured from the reader by the nature of the statistical treatment. For example, the significance of differences in log likelihood between different sets of parameters or indeed the dependence of log likelihood on minor variations in each parameter are not accessible without access to the data. It is because of the difficulty of challenging this model without such access that we chose to test the model on the same grounds that Dr Stewart has applied it. If by so doing we have been misleading then we can only conclude that Dr Stewart’s own claims for the difference between her model and risk estimates derived from ICRP recommendations are also misleading.

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Reference


Dr Kneale and Dr Stewart reply:

The original finding of Baverstock et al was that in a cohort of 1110 radium luminisers the standardised mortality ratio for breast cancer was higher (1·56) than the ratio for other causes of death (0·99) and also showed signs of being dose related since the ratio was 1·44 for four women with estimated gamma radiation exposures of less than 0·2 Gy, and 1·60 for 12 women with higher doses.1 Baverstock and Papworth then included four cancer sites (lung, stomach, breast, and leukaemia) in certain statistical tests of the luminiser cohorts and came to the following conclusions2: (1) “all the excess cancer may be accounted for by the excess of breast cancer among women aged under 30

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at exposure” and (2) the tests provided conclusive rejection of a recent (Hanford based) model for cancer induction by small doses of ionising radiations.³

Meanwhile Sorahan had discovered that the mortality experience of the luminiser cohort was internally inconsistent and suggested that this might be due to unrecognised selection effects.⁴ Therefore, it only remained for us to point out that the Hanford model “is a source of risk estimates whose standard errors are large because they were of necessity based on a relatively small number of Hanford deaths.”⁵

In reply Dr Baverstock has shown that there is genuine incompatibility between the Hanford model and the luminiser cohort. In so doing, however, he has shown other problems that strongly support the Sorahan hypothesis. For example, the luminiser based estimate of the doubling dose for gamma radiation (13·0 to 14·0 Gy) is not only far larger than the Hanford based estimate (0·15 Gy) but is three times as large as the A bomb based estimate (3·0 to 4·0 Gy) which is the main stay of ICRP recommendations for radiation workers.

For this reason we have carried out a Mantel-Haenszel analysis of the luminiser data—similar to the Hutchinson et al analysis of Hanford data.⁶ According to this test of dose related effects there is not only no evidence of any radiogenic breast cancers there is actually a deficit of these cases at high dose levels compared with other cancer and non-cancer deaths. There would, therefore, appear to be genuine flaws in the luminiser cohort which prevent any valid comparisons with the Hanford cohort.

References

Book reviews


Control of environmental hazards and monitoring to confirm that control measures are working is a central aspect of the World Health Organisation’s environmental health programme. It is hoped that countries involved in the programme will eventually formulate and develop national policies for health protection. The guidelines are intended as a source of practical information on the design and conduct of genetic study on populations exposed or suspected of being exposed to mutagens. The report contains the collective views of an international group of experts. As they are guidelines they do not include comprehensive protocols for studies; however, attention is directed to important details that must be included as well as the limitations of the methods. The guidelines encompass methods that are practicable at present for studying somatic and germlinal genetic effects in human populations.

Increases in the frequency of somatic effects may contribute to an increase in the frequency of, for example, cancer, whereas increases in germlinal effects are likely to contribute to inherited defects in the offspring. The general principles for detecting these effects are the same for all countries and comparability can be achieved through standardisation of the procedures. Certain general principles influence the design of studies for genetic effects: there should be a means of identifying the exposed population which should have a similar unexposed group; there should be some knowledge of the perceived mutagen and where possible some separation into different exposure levels and a means of observing the time course of the exposure; when long term follow up is concerned attention should be paid to the identification of individuals so that starting and end point data will be unambiguously matched; confounding variables such as smoking, radioactivity, etc, must be taken into account. In relation to somatic effects the report describes how to detect chromosome damage, sister chromatid exchange, and gene mutations in human peripheral lymphocytes. The chromosome methods are now well established but the gene mutation methods less so. Some of the findings described—for instance, sex differences and age effects—have been challenged by recent work on sister chromatid exchanges. The methods for detecting germlinal effects are used less commonly than those for