UNIVERSITY of OTAGO

Te Whare Wānanga o Otāgo

Review of the study "New Zealand Nuclear Test Veterans' Study – a pilot project (sister chromatid exchange)

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A report presented to the New Zealand War Pensions Medical Research Trust Board, 2005

This study describes a case-cohort study of New Zealand War Veterans who were involved in nuclear test detonations in the Pacific during the 1950s. The study seeks to examine evidence for chromosomal damage in these individuals compared to a matched cohort of similarly aged individuals who were not in the vicinity of the test sites at the time of the detonations. The measure that is chosen to gauge whether or not chromosomal damage has been sustained is a laboratory measure of sister chromatid exchange. This is a naturally occurring process that occurs at a basal level in all humans that becomes elevated in conditions in which chromosome breakage is increased. It measures one form of damage, but is not a comprehensive measure of genetic damage *in toto*.

The authors should be commended for their thorough and thoughtful approach to what is a difficult problem – measuring a biological effect to an exposure which was sustained in the distant past. I think the matching of the exposed and control groups was very good, although in retrospect one would have controlled from cigarette smoke exposure which is a potentially confounding variable.

The scientific design and methodology employed to measure sister chromatid exchange is excellent and I do not believe can be faulted. As the authors note there is variability in how different labs perform this test – the critical thing here is that they must be consistent between case and cohort groups (which they have been). The results of the study indicate that the exposed and control groups exhibit a *statistically* significantly different degree of sister chromatid exchange, with the exposed group demonstrating more elevated levels. The authors reasonably conclude that this is indicative of statistically significant elevations in chromosomal breakage, a known consequence of exposure to ionizing radiation.

The authors have endeavoured to account for their findings as artefactual in an honest and genuine fashion but failed to locate a confounding factor that in their mind explains their experimental findings. One such factor (cigarette smoking) is discounted since previous studies have shown that its effect on elevating SCE is not measurable a comparatively short time affect smoking cessation. At another point in this report, however, the authors quote evidence that

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indicates that elevated SCE induced by exposure to ionizing radiation can persist for decades, not only because the radionuclides persist in the body, but also because affected blood lymphocytes can exhibit pronounced longevity. Although definitive proof is lacking either way, this reviewer is left wondering if the smoking has been definitively discounted as a confounding factor.

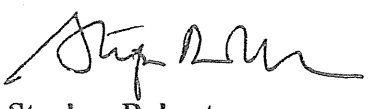
This observation aside, if the elevated level of SCE is presumed to be associated with radiation exposure in excess of 40 years prior to study, then what would the implications be? The first thing to note is that although the distribution of SCE is *statistically* different between the two groups studied (and this is examined in a reasonably rigorous statistical fashion), the magnitude of elevation of rate of SCE in the exposed group is still very modest and its meaning biologically is hard to guage. To my knowledge there is little in the literature that ascribes the size of this change to potential health outcomes. This would, therefore, imply that although a biological difference between these two groups has been detected, its magnitude may be of insufficient size to have any untoward affect on the health of the exposed group.

At one point in this report the authors also suggest that the offspring of the exposed group be monitored on account of their fathers' radiation exposure. For the same reasons above there is no evidence to suggest that this magnitude of change will impact adversely upon the health of the offspring of the exposed group. It must be conceded however that what is being measured here is the vestige of a long-gone event. It is entirely plausible that the degree of SCE may have been distinctly abnormal immediately after the exposure.

In summary, I think that these authors have demonstrated a biological difference between these two study groups. There is no way of knowing whether this difference would have been far greater and clearer if it had been studied at a time nearer to the exposure in the late 1950s. Confounders may explain this difference but they are hard to identify. I am unconvinced that cigarette smoking has been formerly excluded as a confounder in this study, although I must concur with the authors that the weight of evidence lies against it being the explanation for the effect observed.

There are other genetic measures of genomic damage that have been used in the wake of other radiation releases into the atmosphere, most notably micro-satellite instability. I would think that a case could be made to study these cohorts further using another technique such as this to further support their findings if a causal link was to be strengthened.

Although cautious conservative practice may advocate increased medical monitoring of the exposed veterans, there is no evidence that any adverse effect of this magnitude is conferred transgenerationally and, therefore, I think any recommendation for enhanced medical surveillance of the offspring of the exposed group is not sustainable at this time.



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