Notes and miscellaneous

Tetrachlorodibenzodioxin

I would like to take issue with some of the conclusions in May's paper, "Tetrachlorodibenzodioxin: a survey of subjects ten years after exposure" (May 1982). Since 90 people were originally exposed sufficiently to develop chloracne but only 46 remained employed 10 years later, of whom 41 were studied, it is probably misleading to conclude that "there has been no death from neoplasm in the relevant population." Since the "relevant population" constitutes active (surviving) workers and about half were lost to follow-up, lack of deaths should not be surprising, even ignoring 10 years as an inadequate latent period for most tumours to become clinically apparent.

The scattergrams which show greater gamma-glutamyltransferase in the exposed groups are not accompanied by any calculations of statistical significance, but judging from the scatter, the difference may be significant. Further, the author assumes that this must be an artifact and that changes induced by dioxin must be transient once exposure was ceased. No evidence in support of this conclusion is given, merely an analogy with phenobarbitol enzyme induction. His conclusion may or may not be correct: the evidence is not convincing.

The differences in fetal outcomes also have no calculations of statistical significance, although they may well be borderline. Again, they are dismissed without adequate evidence.

In short, the study is not designed to evaluate carcinogenesis, the numbers are probably inadequate to evaluate fetal outcomes, and there is a difference in enzyme induction between exposed and unexposed groups, which may be but is not necessarily related to exposure.

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Dr May replies:
In answer to Ziem's first paragraph I must point out that the text of my article includes the phrase "the whereabouts of all living cases (89 out of 90) being known" and means exactly what it says. Though I was precluded from incorporating in my study those employees who had left the company, I was given every assistance in locating their current whereabouts. The death which did occur was due to cardiac failure in a retiree. I am at a loss to understand, therefore, how it can be misleading to say there has been no death from neoplasm.

The comment about the scattergrams does not dispute, indeed, appears to support, my own findings. It would have been easy to say, "there are significant variations in some of the biochemical results, and I attribute these to dioxin exposure albeit that exposure was ten years ago" (14 years now). Such an assumption would probably not have been disputed and for years to come reference would have been made to it by other authors. A case in point is the fact that a passing reference to cholesterol concentrations in my 1973 paper is quoted widely and regularly and out of context. I believe, however, that the biochemical variations are unlikely to be due to dioxin exposure. I have therefore considered it necessary to offer an alternate and more acceptable proposition, not a statement of fact.

I do not see how, with such very small numbers and in the absence of national statistics, it would be possible to make significant calculations on fetal outcomes.

I accept Ziem's last paragraph. The study was undertaken for the benefit of the employees as a purely internal matter without thought of publication. The results were considered to be so interesting, however, that wider distribution was urged from the highest levels. I make no claims to be either an epidemiologist or a statistician but have endeavoured to acquaint the medical community with my findings, being careful to avoid deductions which the small sample was incapable of sustaining. The continued re-assuring passage of time reinforces the tenor of my article and increasingly defies the overreaction with which some greeted the original measurements.

References