United States Department of Energy (DOE) data and the records of A-bomb survivors that are the mainstay of radiation safety regulations in this country and elsewhere (A-bomb data). Also, analyses of the Hanford data show the variable nature of the relative risk model—that is, the one which measures the effect that the age when exposed has on the subsequent cancer risk, which should have a constant value whatever the source of the radiation—there is incompatibility not only between A-bomb data and DOE data but also between Hanford and Oak Ridge data and between Hanford data for different exposure periods.

When stating O'Donnell is not the number of times that Hanford data have been analysed (which is far fewer than the number of analyses on the A-bomb data) but the number of independent variables in the Kneale and Stewart relative risk model. Correct assessment of these variables is essential for future tests of important hypotheses, such as whether young people are more or less sensitive to cancer effects of radiation than old people and whether A-bomb survivors apart from their radiation dose are or are not representative human beings. So it is clearly important not to stint on verifying of recognising false elements in DOE and A-bomb data.

Finally, we have a special reason for making this point, as we hope shortly to publish a paper which shows that the A-bomb survivors who most closely resembled the non-survivors—that is, the survivors who had multiple acute injuries, such as burns, purpura and epilation—differ in several important respects from the much larger number of survivors who had no such injuries.

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Mesothelioma in a community in the north of England

Editor—Muir, who wrote a brief essay on the subject of bias in the field of occupational health in the final issue of the British Journal of Industrial Medicine, will find this paper useful for teaching purposes. He might take issue with the authors on the literary style and presentation of historical facts, and on their analysis of data. We are informed that the community was established in 1939 to produce gas mask filters. Reference to Defence of the Realm powers for initiating asbestos work might be misread by the reader as a plea in mitigation for the heavy harvest this disease reaps from post-war exposures. The introduction cites Bertram Mann as making some reference to problems resulting from asbestos exposure. DM. Kneale was commenting that there is a difficulty in routing out the text of his 1978 Royal College of Physicians Milroy lecture, will find that this chest physician had a lot to say about the amount of disease that he came across in this small part of his catchment area.

The discussion section states that: "In common with many asbestos factories, working conditions in respect of asbestos dust were poor, especially in the early years of its operation." This might be misread to imply that conditions in its latter days were acceptable. Sir Alan Marre's (The Ombudsman) report in 1976 of his inquiry into Acre Mill, although concerned solely with the question of maladministration, did find that the factory was a cause for concern. The authors' statement that; "The factory closed in 1970 and has since been demolished," is incomplete. After it was transferred to the manufacturer which owned it for several more years, in a not entirely decontaminated state.

In the discussion section we are informed that between 5000 and 3000 people worked at the factory, although the material and methods section is not explicit on this point. One may assume that the authors did not have access to the nominal roll of employees. Otherwise they would have used the Registrar General's facilities for tracing and flagging the total population. No researcher should be faulted when making the best of limited data, provided the necessary caveats are presented prominently.

In their calculations, the authors gave an average incidence of tumour in Calderdale over the period 1966-94 as "12.5/million persons/year" results from the overwhelming non-exposed population. When the factory population is studied separately, the rate works out not surprisingly as between 524 and 786 cases of mesothelioma per million person-years, depending on which extreme estimate of factory population is taken. For the non-exposed, the rate works out as 3-2 million person years, which is a higher rate than one would like to see.

The authors state that there were no neighbourhood cases of asbestos related disease. Yet of the 17 cases of malignant mesothelioma reported in the population not exposed to asbestos, eight had excessive amounts of amphibole in their lung tissues. We are not informed of how this might have been acquired. It is possible that despite the Pennine geography and meteorology exposure conditions lying further inland, the Healthier were less sensitive to mesothelioma than in the "dust bowls" of Barking and North Western Cape province. Apoposis of lung fibre counts in the lungs (which commonly means the parenchyma, rarely the pleura, and even more rarely the bronchus), toxicologists look at the science of xenobiotic disease differently from pathologists, mineralogists, statisticians, and physicians. Physicians looking at disease in the pleura or peritoneum are content to relate it to the amount and type of fibre in the lung parenchyma rather than the type and quantity that has penetrated to the critical tissues. (Yet it is chrysotile rather than the amphiboles that is more often reported by pathologists to be found juxta-pleurally.) Again, although physicians are agnostic about the high level of chrysotile fibre because of its rate of clearance from the body, toxicology requires a better understanding of the toxicokinetics and mode of action of amphiboles, which have not been conducted on the various asbestos species to relate their carcinogenic effects, dose for dose, fibre for fibre when equal dimensional are involved. This crude studies have in fact pointed that they can share similar carcinogenic power. The courts are led to think that one can differentiate between the tumour caused by asbestos and the tumour not so caused, on an estimation of parenchymal fibre content. This is despite the width confidence limits that need to be placed around an estimate involving uncertainties in sampling and in counting, and despite the overlap in the distribution curves for lung fibre content between people with a history of asbestos exposure and those with no ascertainable exposure.

As for the authors' more sanguine attitude to chrysotile, the reader would be well advised to turn to the authoritative account of chrysotile in the Environmental Health Criteria series published as part of the International Programme on Chemical Safety. This has had a stormy passage but is due out soon. Murriss Greenberg's repeated concern that parts of our article might be misread is touching but likely to understate the magnitude of your fears. It is difficult to imagine how the factual statement that Acre Mill was "commandeered by the Home Office in 1939" could be construed as a "plea in mitigation for the heavy harvest of asbestos disease". Likewise his concern that our observations about working conditions might be misread to "imply that conditions in the latter days were acceptable". We wrote this article not with the purpose of apportioning blame but to set the medical scientific record straight about the number of cases of mesothelioma found in Calderdale. Even after rereading the article we do not recognise any suggestion that the working conditions at Acre Mill were any better or worse than any other asbestos factory working at that time. Perhaps David Muir might find this letter by Greenberg an interesting example of bias for teaching purposes.

Two of the authors (ATE and DW) worked alongside Bertram Mann for many years and his paper is well known to us. He referred to his claim (in papers or in writings) about asbestos linked disease arising from asbestos pollution from the factory a detailed analysis of tissue seen mosaiecium failed to detect any such case in a person living within two to four square miles of the factory who had not been employed at Acre Mill. Furthermore ATE performed most of the postmortem examinations in the district from 1960 to 1994 and he examined the reports of those not performed personally and he is not aware of any case of asbestos related disease occurring as a result of atmospheric pollution from the factory. The paper contains a high proportion of asbestos related disease among the medical profession and in the community whereby suspected cases were readily referred to the local coroner.

We had very good access not only to senior ex-management of the mill but to many other ex-employees who are still alive and who had worked during wartime and later periods leading up to the 1930s. It is difficult to measure. DW carried out personal interviews with many to gather information about the type of asbestos used and the working conditions. Several of DW's colleagues had worked at Acre Mill from the 1940s to
ng/mL creatinine, depending on whether log to the base 10 or natural log is used, respectively. This number seems to be very low compared with that given in many studies which are usually in the range of 1000 ng/mL creatinine. It will be helpful if Ong et al could provide an explanation for this apparent discrepancy.

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Author's reply—The overall objective of our article was to evaluate the usefulness of five common biomarkers of benzene exposure (0-25 ppm) to benzene and as stipulated in the conclusion all the biomarkers were unable to provide sufficient specificity for biomonitoring at the low concentration range. All data reported that these biomarkers are not to be used for estimation of exposure to low level environmental exposure to benzene, particularly <0.25 ppm. Our earlier data showed that trans,trans-muconic acid could be useful for environmental exposure to benzene >0.5 ppm; with a calculated exposure to 1 ppm benzene, about 0.9-1.7 mg/g creatinine would be expected at the end of eight hours of exposure.

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4 McDonald JC, McDonald AD. Chrysotile, tremolite and mesothelioma. Science 1995;269:368-70.

Biomarkers of exposure to low concentrations of benzene: a field assessment

Editor—Ong et al present data on the relation between concentration of benzene in ambient air and urinary muconic acid concentration. With the formula they provided in figure 3, the urinary concentration of muconic acid is equivalent to exposure to 1 part per million (ppm) is 144-4 or 128-6.

(2) Under some models, coital rate would determine the time of fertilisation within the cycle.

(3) Distributions of the sexes within litters of several mammalian species suggest that Pmax (the probability that a zygote male) varies from one zygote to another within litters.

Interpretation of the data is not established, but it seems likely that the variation of Pmax with time across the female cycle is partially controlled by the varying female hormone concentrations across that time. In particular such an interpretation can be construed to explain Weijin and Olsen’s report of a significant decline of offspring sex ratio with waiting time to pregnancy. This confirms the data of Renkonen and may be caused by the different mean times of fertilisation within the cycle associated with different coital rates (which declines very rapidly during the first year of marriage). If I am right, the sexes of mammal (including human) offspring are partially controlled by the hormone concentrations of both parents associated with the sexual cycle and not with the duration of fertilisation. So deleterious environmental agents which are endocrine disruptors may show themselves in biased offspring sex ratios. Thus it may be expected that offspring sex ratios may be a general effect used as indicators of adverse occupational exposures to men and women.