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 have shown the variable of birth date to be a 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.

During the Boeing and 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 Keneale 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 the number of survivors 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 the number of variables in recognizing 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. G W KNEALE
A M STEWART
Department of Public Health and Epidemiology, University of Birmingham, Edgbaston, Birmingham B15 2TT

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,3 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 of Acre Mill was requested 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 disease revealed from post-war exposures. The introduction cites Bertram Mann as making some reference to problems resulting from asbestos exposure. He states that Acre Mill was commanded by the ministry to rout 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 its history into Acre Mill, although concerned only 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 closed, it was occupied by another manufacturer for several more years, in a not entirely decontaminated state.

In the discussion section we are informed that between 3000 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. Others 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 this extrapolation of 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 in this area are healthier than to malignant mesothelioma than in the “dust bowls” of Barking and North Western Cape province.

Asbestos fibres 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 different 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 manifested in 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 not just looking at the filters 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 any fibre that has been shown not to be conducted on the various asbestos species to relate their carcinogenic effects, dose for dose, fibre for fibre when equal dimensions are assumed. Most fibre studies have involved 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 wide 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 work and those with no ascertainable exposure.

As for the authors’ more sanguine attitude to chrysotile, the reader would be well advised to refer to 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.

MORRIS GREENBERG
74 New End Road
London NW11 7SY

The 1960s. Access was given to the employees' rolls although employment details were not available. The war was virtually non-existent. We think that the information gathering process when taken together with the records of the coroner and the histopathology review was as detailed as any other similar study in existence.

As the "non-exposed" group was classified as such by history it is obvious to most readers that we are unable to state how they acquired excessive amounts of amphibole fibres within their lung tissues. If these eight cases with high amphibole concentrations are deducted the rate of mesothelioma becomes 1-6 million a year which is similar to the generally estimated background rate.

Greenberg seems to be unaware that high aspect ratio amphibole fibres have been found in the pleura. By contrast with animal studies, which rely on the administration of enormous doses and overload of the respiratory defences, human studies have been remarkably consistent in showing a strong association between amphibole exposure and mesothelioma whereas dust from chrysotile has been weak or non-existent.

Even in chrysotile miners and millers, in whom there have been few mesotheliomas, the evidence indicates that they were related to tremolite rather than chrysotile exposure. To the best of our knowledge the forthcoming review of chrysotile by the International Programme on Chemical Safety will not present any new evidence although it might give a different opinion. Other reviews conclude that amphibole as a much greater potency than chrysotile for producing mesothelioma.

E. T. Edwards
Royal Halifax Infirmary, Halifax, Nova Scotia
D. Whittaker
Queen Elizabeth II Medical Centre, Perth, Western Australia
K. Brown
Formerly Medical Advisor to Cape Industries, Leicester House, North Craigs, Northumberland
F. D. Pooley
School of Engineering, Division of Materials and Minerals, University of Wales, Cardiff

Department of Pathology and Environmental Lung Disease Research Unit, Llandough Hospital, Penarth, South Glamorgan


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 mg 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/mg creatinine. It will be helpful if Ong et al could provide explanation for this apparent discrepancy.

Eric S Johnson
School of Public Health and Tropical Medicine, Tulane University Medical Centre, New Orleans, Louisiana, USA


Author's reply—The overall objective of our article was to evaluate the usefulness of five common biomarkers for low level exposures (<0.25 ppm) to benzene and to stipulate in the conclusion all the biomarkers were unable to provide sufficient specificity for biomonitoring at the low concentration range. All data indicated that these markers should not be used for estimation of exposure to low level environmental exposure to benzene, particularly <0.25 ppm. Our earlier data showed that urinary 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.

CHOO-NAM ONG
Department of Community, Occupational, and Family Medicine
National University of Singapore


Offspring sex ratios and reproductive hazards

Editor—Weijin and Olsen write: "A conception closely associated with ovulation has been suggested to result in more boys". There seems to be an error here because to substantiate this statement, these authors cite France et al who write: "The birth sex ratio favored males when intercourse preceded ovulation/fertilization by two days or longer". Indeed the data of France et al give some corroboration to the conclusion of Gray who, after a meta-analysis of human data, suggested that the regression of offspring sex ratio (proportion male) on time of insemination within the cycle is U shaped. I have cited evidence that:

1. There is a positive relation between offspring sex ratio and parental coital rate in several mammalian species (including humans).
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 P max (the probability that a zygote is male) is not from one zygote to another within litters.

Interpretation of the data is not established, but it seems likely that the variation of P max 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 constructed 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 decline very rapidly during the first year of marriage). If I am right, the sexes of mammalian (including human) offspring are partially controlled by the hormone concentrations of both parents across the female cycle through the process 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 commonly used as indicators of adverse occupational exposures to men and women.

William J James
The Galton Laboratory, University College London, W1N 3JY, London, UK


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