Ingestion of herring leads to absorption of pristane in humans

Editor—Pristane (2,6,10,14-tetrahydromenetadecane) is a branched chain hydrocarbon which is thought to be derived from the phyllo moiety of chlorophyll. The compound has been associated with several biological effects. Pristane can induce plasmacytomas,1 and together with some poly cyclic aromatic hydrocarbons, act as promoters in the development of B-lymphoid malignancies and skin tumours in animals.2 3 Intraperitoneal injections have induced arthritis in mice.4 Pristane occurs in marine fish in rather high concentrations, 1% to 3% of the body fat, in certain zooplankton and these plankton are assumed to be the primary source of the pristane found in liver oils of sharks and whales.5 Pristane is also found in herring and the concentration in flesh is about 370 mg/g of wet weight.6 Other fish species such as cod have much lower concentrations of pristane in their flesh, most often <1 mg/g of wet weight.7

One of us (BS) volunteered to ingest Atlantic herring as lunch at 11.00 am. Four different meals contained 125, 140, 250, and 310 g of cooked herring. A reference meal was composed of chicken with potatoes, bread, and water. The quantitative analysis of pristane was performed with gas chromatography equipped with a flame ionisation detector. Pristane was also identified with gas chromatography-mass spectrometry, operated in electron impact mode. The recovery of the complete clean up method was 100% for pristane and the internal standard (dodecylechlohexane). The detection limit of the method was 300 pg.

The serum concentration of pristane increased to 20-3000 mg/g serum 2-4 hours after ingestion of herring. Pristane was not detected before and 24 hours after ingestion of herring and it was not detected after the reference meal.

This experiment showed that pristane is clearly absorbed after the ingestion of Atlantic herring.

Pristane injected intraperitoneally into mice induces seropositive arthritis in susceptible strains. This agent has been proposed as an experimental model for rheumatoid arthritis.4 Swedish fishermen eat more herring than the general population1 and it is an interesting finding that fishermen had a high prevalence of rheumatoid arthritis when this disease was investigated in 66 large occupational groups in Sweden.8

It is also interesting that pristane is absorbed after ingestion of herring and this absorption should be studied in larger groups of humans after ingestion of herring and other species of fat fish. Further work is also needed to scrutinise the possible link between pristane exposure and the occurrence of multiple myeloma and diseases affecting the joints.

HÅKAN CARLSSON
EVA GRIMMVAL
Department of Toxicology and Chemistry,
Swedish National Institute of Working Life,
S-171 84 Solna, Sweden

3 Horton AW, Bolweicz LG, Baskar AW, Butts CK. Comparison of the promoting activity of pristane and s-alleles in skin carcinogenesis with their physical effects on micellar models of biological membranes. Biochim Biophys Acta 1979;559:196-105.

Digestive tract neoplasms among employees with past exposure to brominated dioxins

Previously, we reported biomonitoring, immunological and other clinical findings for a group of 42 employees potentially exposed to polybrominated dibenzo-p-dioxins (PBDDs) and furans (PBDFs) during extrusion blending of resins containing polybrominated diphenyl ether (PBDE) flame retardants.1 2 In the five years since the clinical study was completed, two cases of digestive tract neoplasms have come to our attention within this group of employees and an additional digestive neoplasm was reported in a techni-
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 been criticized for 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.

What is missing is 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 at different stages of life, and whether A-bomb survivors apart from their radiation dose are or are not representative human beings. So it is clearly important not to stink on the possibility of 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.

W G 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,1 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 Bertram Mann 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 of disease resulting from post-war exposures. The introduction cites Bertram Mann as making some reference to problems resulting from asbestos exposure. Am. Kneale was commanded that they had 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 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 closure, 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. Otherwise they would surely 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 dilution by 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 think.

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 might have been healthier with respect to malignant mesothelioma than in the "dust bowls" of Barking and North Western Cape province.

Apropos of asbestos 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 asbestos 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 been deposited in the critical tissues. (Yet it is chrysotile rather than the amphiboles that is more often reported by pathologists to be found juxta-plurally.) Again, although physicians are less sensitive to content of the asbestos fibre because of its rate of clearance from the body, toxicology requires a better understanding of the toxicokinetics and mode of action of asbestos that has not been conducted on the various asbestos species to relate their carcinogenic effects, dose for dose, fibre for fibre when equal dimensions are involved. Much crude studies have insisted 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 exposure and those with no ascertainable exposure.

As for the authors' more sanguine attitude to chrysotile, the reader would be well advised to read O'Donnell's work on 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 North End Road
London NW11 7SY


Authors' reply—Greenberg's repeated concern that parts of our article might be misread is touching but likely to understate the extent of your concern. It is more 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 without some misgivings about the apparent willingness of experts to misread a single dataset.

Two of the authors (ATE and DW) worked alongside Bertram Mann for many years and his paper is well known to us. Despite his claim (in his letter or in writing) about asbestos related disease arising from asbestos pollution from the factory a detailed analysis of tissue proven mesothelioma 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 has 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. This is despite a high rate of deaths from 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 1970. It is difficult. DW carried out personal interviews with many to gather information about the type of asbestos used and the working conditions. Several of DW's interviewees had worked at Acre Mill from the 1940s to