the 1960s. Access was given to the employees' roll although employment details during the war were 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.¹ 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 for chrysotile it has been weak or non-existent.² 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.^{3,4} 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 amphiboles have a much greater potency than chrysotile for producing mesothelioma.^{5,6}

A T EDWARDS

Royal Halifax Infirmary,
Halifax, Yorkshire

D WHITAKER

Queen Elizabeth II Medical Centre,
Perth, Western Australia

K BROWNE

Formerly Medical Adviser to Cape Industries,
Leicester House, North Creae, Norfolk

F D POOLEY

School of Engineering,
Division of Materials and Minerals,
University of Wales, Cardiff

A R GIBBS

Department of Histopathology and Environmental
Lung Disease Research Group,
Llandough Hospital,
Penarth, South Glamorgan

- 1 Boutin C, Dumortier P, Rey F, Viallat JR, De Vuyst P. Black spots concentrate oncogenic asbestos fibres in the parietal pleura. *Am J Respir Crit Care Med* 1996;153:444-9.
- 2 Gibbs AR. Role of asbestos and other fibres in the development of diffuse malignant mesothelioma. *Thorax* 1990;45:649-54.
- 3 Dufresne A, Harrigan M, Masse S, Begin R. Fibres in lung tissues of mesothelioma cases among miners and millers of the township of Asbestos, Quebec. *Am J Ind Med* 1995;27:581-92.
- 4 McDonald JC, McDonald AD. Chrysotile, tremolite and mesothelioma. *Science* 1995;267:775-6.
- 5 Health risks associated with chrysotile asbestos. Papers from a workshop held in Jersey, Channel Islands, 14-17 November 1993. *Ann Occup Hyg* 1994;38:397-646.
- 6 Meldrum M. *Review of fibre toxicology*. Sudbury: HSE Books, 1996.

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

Editor—Ong *et al*¹ 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 equivalent to exposure to 1 part per million (ppm) is 144.4 or 128.6

ng/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.^{2,3} It will be helpful if Ong *et al* could provide some explanation for this apparent discrepancy.

ERIC S JOHNSON

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

- 1 Ong CN, Kok PW, Ong HY, Shi CY, Lee BL, Phoon WH, Tan KT. Biomarkers of exposure to low concentrations of benzene: a field assessment. *Occup Environ Med* 1996;53:328-33.
- 2 Lauwerys RR, Buchet J-P, Andrien F. Muconic acid in urine: a reliable indicator of occupational exposure to benzene. *Am J Ind Med* 1994;25:297-300.
- 3 Inoue O, Seiji K, Nakatsuka H, Watanabe T, Yin S-N, Li G-L, *et al*. Urinary t,t-muconic acid as an indicator of exposure to benzene. *Br J Ind Med* 1989;46:122-7.

Author's reply—The overall objective of our article¹ was to evaluate the usefulness of five commonly used biomarkers in low level (< 0.25 ppm) exposure 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 (figs 1-3) suggested that they are not to be used for estimation of exposure to low level environmental exposure to benzene, particularly < 0.25 ppm. Our earlier data²⁻⁴ 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.

CHOON-NAM ONG

Department of Community, Occupational, and
Family Medicine,
National University of Singapore

- 1 Ong CN, Kok PW, Ong HY, Shi CY, Lee BL, Phoon WH, Tan KT. Biomarkers of exposure to low concentrations of benzene: a field assessment. *Occup Environ Med* 1996;53:328-33.
- 2 Lee BL, New AL, Kok PW, Ong HY, Shi CY, Ong CN. Urinary trans,trans-muconic acid determined by liquid chromatography: application in biomonitoring of benzene exposure. *Clin Chem* 1993;39:1788-92.
- 3 Ong CN, Lee BL. Determination of benzene and its metabolites: application in biological monitoring of environmental and occupational exposure to benzene. *J Chromatogr* 1994;660:1-22.
- 4 Ong CN, Kok PW, Lee BL, Shi CY, Ong HY, Chia KS, *et al*. Evaluation of biomarkers for occupational exposure to benzene. *Occup Environ Med* 1995;52:528-33.

Offspring sex ratios and reproductive hazards

Editor—Weijin and Olsen¹ 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*² 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*² give some corroboration to the conclusion of Gray³ 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 cited⁴ 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_{male} (the probability that a zygote is male) varies from one zygote to another within litters.

Interpretation of the data is not established, but it seems likely that the variation of P_{male} 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's¹ report of a significant decline of offspring sex ratio with waiting time to pregnancy. This confirms the data of Renkonen⁵ 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^{6,7}).

If I am right, the sexes of mammalian (including human) offspring are partially controlled by the hormone concentrations of both parents around the time of fertilisation.⁸ 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 will be increasingly used as indicators of adverse occupational exposures to men and women.

WILLIAM H JAMES

The Galton Laboratory,
University College London,
Wolfson House,
4 Stephenson Way,
London NW1 2HE

- 1 Weijin Z, Olsen J. Offspring sex ratio as an indicator of reproductive hazards. *Occup Environ Med* 1996;53:503-4.
- 2 France JT, Graham FM, Gosling L, Hair P, Knox BS. Characteristics of natural conceptual cycles occurring in a prospective study of sex preselection: fertility awareness symptoms, hormone levels, sperm survival and pregnancy outcome. *Int J Fertil* 1992;37:244-55.
- 3 Gray RH. Natural family planning and sex selection: fact or fiction? *Am J Obstet Gynecol* 1991;165:1982-4.
- 4 James WH. Factors affecting sex ratios in mammalian offspring: follicular phase length, cycle day of conception and sex ratio of offspring. *Hum Reprod* 1995;10:2529-31.
- 5 Renkonen KO. Heterogeneity among first post-nuptial deliveries. *Ann Hum Genet* 1970;33:319-21.
- 6 James WH. The honeymoon effect on marital coitus. *Journal of Sex Research* 1981;17:114-23.
- 7 James WH. Decline in coital rates with spouses' ages and duration of marriage. *J Biosoc Sci* 1983;15:83-7.
- 8 James WH. Evidence that mammalian sex ratios at birth are partially controlled by parental hormone levels at the time of conception. *J Theor Biol* 1996;180:271-86.

BOOK REVIEWS

Book review editor: R L Maynard

If you wish to order, or require further information regarding the titles reviewed here, please write or telephone the BMJ Bookshop, PO Box 295, London WX1H 9TE. Tel: 0171 383 6244. Fax: 0171 383 6662. Books are supplied post free in the UK and for British Forces Posted Overseas addresses. Overseas customers should add 15% for postage and packing. Payment can