CORRESPONDENCE

Sex ratio of offspring of men exposed to sodium borates

Editor—Whorton et al report 529 births (250 sons and 279 daughters) sired by men exposed to sodium borates.[1] With official data on the comparable non-exposed United States population (adjusted for maternal age, race, parity, and calendar time) these authors estimate an expected 466·6 births. They took the unusual step of contrasting the observed sex ratio (proportion male) with the numbers of the two sexes expected assuming simultaneously both: a United States live birth sex ratio of 0·512; and the comparable United States fertility rates.

They thus calculate expected values of sons and daughters that are less than both the observed values. So they are able to conclude that the unusual observed sex ratio is not due to a deficit of boys. This, they considered, would allay suspicions that borates represent a reproductive hazard to male fertility.

I should like to present an alternative argument based on their data. It would be more conventional to contrast the observed sex ratio (250 boys, 279 girls) directly with the expected sex ratio of 0·512. This gives an associated χ^2 value of 3·3. Bearing in mind the suspicion of reproductive hazard cited by Whorton et al,[1] and the evidence that occupational reproductive hazards to men may manifest themselves in low sex ratios of offspring,[2] it would seem appropriate to use a one-tailed test. (In this case P < 0·05.) So I would conclude that indeed there are grounds for suspicion that borates affect the male reproductive system. More data should be gathered on the sex ratios of offspring of men exposed to these materials. If these prove to be low too, then more invasive investigation (sperm counts, hormone assays) would be justified.

Lastly, the excess fertility in the exposed men was estimated by adjusting United States national fertility rates for maternal age, parity, race, and time. These men were employed in the Mojave Desert. Would not fertility be greater in such areas than in urban areas? If so, the excess fertility may be illusory.

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1 Whorton MD, Haas JL, Trent L, Wong O. Reproductive effects of sodium borates on male employees: birth rate assessment. Occup Environ Med 1994;51:761–7.
2 James WH. Occupations associated with low offspring sex ratios. Am J Ind Med 1994; 25:607–8.

Author's reply—James' comments on our sex ratio analyses need closer scrutiny on several counts. Firstly, contrary to James' comments, in our sex ratio analysis, we did not assume comparable fertility rates between our study and the United States general population. On the other hand, in his comparison between the observed overall sex ratio in our study and the ratio for the United States, James implicity made the assumption of comparable fertility rates between our study and that for the United States.

The primary purpose of our study was to determine if there was a deficit or excess of births by sex rather than the sex ratio itself. As such, a direct comparison of the two sex ratios would have been appropriate only if the underlying fertility rates in our study and in the general population were comparable. As shown through the use of the standardised birth ratio, the fertility rates in our study were significantly higher than those in the general population. From the methodological point of view, the problem of directly comparing sex ratios is similar to that of applying the proportional mortality ratio (PMR) in mortality analysis. It is well known that PMR compares proportions of deaths from specific causes between two groups, and it is a valid measure for mortality risk only if the underlying death rates are comparable in the two groups.[1 2] Similarly, a direct comparison of sex ratios determines whether there is a deficit or excess by sex only if the underlying fertility rates are comparable in the two populations being compared.

James' rationale for a one tailed test assumes an original hypothesis of a lower sex ratio (proportion male) associated with exposure to sodium borates. Based on previous data on sodium borates, we had no preconceived idea whether the sex ratio (proportion male) should be higher or lower. Thus, James' argument for a one tailed test was based on a retrospective examination of the data, which would render the conventional P value of 0·05 inappropriate, and the χ^2 of 3·3 calculated by James would not have been significant.

James implied that male reproductive hazards would most likely result in an altered sex ratio. Among the papers cited in another letter to the editor by James,[3] one report by Potashnik and Yanai-Inbar[4] was due to a chemical exposure (dibromochloropropane). Potashnik and Yanai-Inbar reported an increase in girls born to men exposed to dibromochloropropane who had recovered from either azoospermia or severe oligospermia. The mechanism for this is unknown although James believed this effect to be due to an increase in gonadotrophin concentrations.[3] Men who are azoospermic from exposures to dibromochloropropane have raised gonadotrophin (FSH and LH) concentrations due to direct testicular damage.[5] There is no evidence at the present to think that there is a causal relation between the increase in gonadotrophins as a result of direct testicular toxicity and the increase in female offspring.

James' entire proposition relied on only one statistic: the sex ratio for the entire group. He ignored detailed exposure-response analyses. As reported in our paper, the highest female sex ratios (proportion female) were observed in the lowest exposure categories (table 7), and there was no

statistical trend of sex ratio by exposure. Furthermore, the female sex ratio for participants during the period of high exposure (0·525) was practically identical to that for the rest of the participants (0·528).

James also questioned the appropriateness of comparing fertility rates of workers in our study who lived in the Mojave Desert to those in the general population. There is no evidence that people who live in the Mojave Desert communities are more fertile than the rest of the nation. Although the location of the factory is rural, most of the employees live in small, urban communities and commute to work. Furthermore, James again does not seem to consider the fact that we also compared fertility ratios internally by exposure category (tables 4 and 5).

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1 Wong O, Decouflé P. Methodological issues involving the standardized mortality and proportional mortality ratio in occupational studies. J Occup Med 1982;24:299–304.
2 Wong O, Morgan RW, Kheifets L, Larson SR. Comparison of SMR, PMR, and PCMR in a cohort of union members potentially exposed to diesel exhaust emissions. Br J Ind Med 1985;42:435–48.
3 James WH. Occupations associated with low offspring sex ratios. Am J Ind Med 1994;25: 607–8.
4 Potashnik G, Yanai-Inbar I. Dibromochloropropane (DBCP): an 8-year re-evaluation of testicular function and reproductive performance. Fertil Steril 1987;47:317–23.
5 Whorton D, Milby TH, Krauss RM, Stubbs HA. Testicular function in DBCP exposed pesticide workers. J Occup Med 1979;21: 161–6.

Assessment of risk of lung cancer among mild steel and stainless steel welders

Editor—I have read with great interest the paper by Sjogren et al.[1] The authors carried out a meta-analysis of five epidemiological studies—three case-control[2–4] and two historical cohort[5 6] studies—on the occurrence of lung cancer among stainless steel (SS) welders. The results clearly indicated a relation between SS welding and lung cancer, the pooled relative risk being 1·94 (95% confidence interval (95% CI) 1·28–2·92). The authors concluded that "it is time to reconsider the IARC (International Agency for Research on Cancer) statement from 1990[7] and to separate SS welding fumes from other welding fumes".

Here I compare the risks of lung cancer of mild steel (MS) welders v SS welders with additional results from the studies included in the meta-analysis of Sjogren et al[1] and from other studies not included in this meta-analysis.[8–12]

The observed odds ratio (OR) among MS welders in the Danish case-control study was 1·65 (95% CI 1·03–2·65),[3] which is similar to that of SS welders, 1·54 (95% CI 0·83–2·84). In the French cohort mortality study the standardised mortality ratio (SMR) for lung cancer was slightly higher for MS welders than for welders predominantly exposed to chromium VI—that is, 1·59 (95% CI 0·73–3·02) v 1·03 (95% CI 0·12–3·71).[5]

Some other studies did not detect high risks of lung cancer among SS welders. Becker et al followed up a cohort of SS welders compared with an internal reference group of turners. The welders had a