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 that the sex ratio is 0.521:1 in the offspring of men exposed to sodium borates and 0.512:1 in the comparable 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 implicitly 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 ratio (0.500:1). 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 only assesses mortality risk if only the death rates are comparable in the two groups.2 Similarly, a direct comparison of sex ratios determines whether there is a deficit or excess by sex only if the 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 χ² of 3.3 calculated by James would not be 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 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 azoospermia or severe oligospermia. The mechanism for this is unknown although James believed this effect to be due to an increase in gonadotrophin concentrations.4 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 time 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 category (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 (0-25) 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 with 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).


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-control2 and two historical cohort3 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 1.28-2.92). The authors concluded that "it is time to reconsider the IARC (International Agency for Research on Cancer) statement from 1990 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 al1 and from other studies not included in this meta-analysis.25

The observed odds ratio (OR) among MS welders in the Danish case-control study was 1.65 (95% CI 1.03-2.65), 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 predominately exposed to chromium VI—that is, 1.92 (95% CI 0.73-3.02) v 1.03 (95% CI 0.12-3.71).1

Some other studies did not detect high risks of lung cancer among SS welders. Becker et al2 followed a cohort of SS welders compared with a reference group of turners. The welders had a
Correspondence


Urinary N-acetyl-β-D-glucosaminidase (NAG) and exposure to inorganic lead

Editor—Urinary activity of N-acetyl-β-D-glucosaminidase (NAG) had been reported to be one of the earliest markers to be increased in workers exposed to lead. The underlying mechanism for an increase in NAG activity is uncertain. It was suggested that the increase in NAG activity may be due to stimulation of exocytosis. In a recent publication by workers from a lead smelting plant, it was further suggested that increased NAG activity among workers exposed to lead was due to contaminant "albeit slight cadmium exposure". Their conclusion was based on the finding that urinary cadmium concentration (CdU) was the only significant variable in explaining the variation in NAG activity through stepwise regression analysis. Furthermore, the correlation coefficient (r) between NAG and CdU, was 0.41 in the non-exposed and 0.35 among workers.

We obtained data from exposed workers in a polyvinyl chloride lead stabiliser plant did not support this hypothesis. The increases in NAG, the heat labile isoenzyme (NAG A), and the heat stable isoenzyme (NAG-B) were all highly associated with the recent change in blood lead (PbB) concentration over the past six months (PbB). Among several exposure indices derived from serial PbB concentrations, PbB was the only significant variable to account for the variation in NAG, NAG-B, and NAG-A. Furthermore, CdU and blood cadmium (CdB) did not correlate well with NAG and its isoenzymes. When they were forced into the regression model, CdU was in fact negatively correlated (table). Activity of NAG is also increased when other xenobiotics affect the proximal tubules. It is indeed very unlikely that NAG is a specific marker for cadmium. As inorganic lead is known to cause proximal tubular dysfunction, it is therefore not surprising to see an association between lead exposure and NAG.

Among lead smelters, it is possible that there may be significant concomitant exposure to cadmium. This is evident by the fairly wide range of CdB results (0.3 to 5 μg/L) and the significantly higher CdB and CdU concentrations among the workers exposed to lead. Our cohort of PVC lead stabiliser workers had never been exposed to cadmium. Their geometric mean (range) CdB and CdU were much lower than those of the lead smelters (CdB: 0.56 (0.10 to 1.92) μg/L, CdU 0.41 (0.67 to 2.07) μg/L). We have also previously reported that NAG activity was better correlated with CdB and about 40% of the workers exposed to cadmium with a CdB of less than 3.0 μg/L had increased NAG concentrations.

It is possible that where there is significant cadmium exposure, cadmium plays a greater part in increasing NAG activity than does lead, and perhaps even masks the contribution of lead. Our data show that lead does increase NAG activity in the absence of cadmium exposure.

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