CORRESPONDENCE

Offspring sex ratio as an indicator of reproductive hazards associated with pesticides

Editor—De Cock *et al*[1] note that waiting times to conception are significantly longer in the wives of men exposed to pesticides. They cite the evidence that the nematocide dibromochloropropane (DBCP) is associated with diminished sperm counts.[2] It is worth noting that there is other evidence of hazard in these men. They reportedly have significantly high gonadotrophin concentrations although their testosterone concentrations remain normal.[3] I have hypothesised that the sexes of human offspring are associated with the hormone concentrations of their parents at the time of conception, high testosterone producing boys, and high gonadotrophin, girls.[4-7] In conformity with this hypothesis, there is a highly significant excess of daughters among the offspring of male DBCP applicators.[8]

So it would be interesting to know whether there was an excess of daughters among the 91 children sired by the pesticide workers studied by de Cock *et al.*[1] More generally, workers in industrial medicine might consider offspring sex ratios as a criterion of reproductive hazard: they are cheaply and painlessly ascertained, and are not subject to the measurement errors and biases that characterise assessments of sperm quality and hormone concentrations. It should be noted that although a bias towards daughters may be indicative of hazard in male workers, there are no grounds for supposing this in female workers. At any rate, in any such analysis, the sex of offspring should be categorised by sex of parent.

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1 de Cock J, Westveer K, Heederik D, Velde E te, Kooij R van. Time to pregnancy and occupational exposure to pesticides in fruit growers in the Netherlands. *Occup Environ Med* 1994;**51**:693–9.
2 Whorton D, Krauss RM, Marshall S, Milby TH. Infertility in male pesticide workers. *Lancet* 1977;**ii**:1259–61.
3 Whorton D, Milby TH, Krauss RM, Stubbs HA. Testicular function in DBCP exposed pesticide workers. *J Occup Med* 1979;**21**: 161–6.
4 James WH. The human sex ratio. Part 2: a hypothesis and a program of research. *Hum Biol* 1987;**59**:873–900.
5 James WH. Parental hormone levels and mammalian sex ratios at birth. *J Theor Biol* 1989;**139**:59–67.
6 James WH. The hypothesized hormonal control of human sex ratio at birth—an update. *J Theor Biol* 1990;**143**:555-64.
7 James WH. The hypothesized hormonal control of sex ratio at birth—a second update. *J Theor Biol* 1992;**155**:121-8.
8 Potashnik G, Yanai-Inbar I. Dibromochloropropane (DBCP): an 8-year re-evaluation of testicular function and reproductive performance. *Fertil Steril* 1987;**47**:317–23.

Author's reply:

Editor—We would like to thank James for his letter on offspring sex ratio among children of fruit growers in our study on time to pregnancy.[1] In his letter James refers to a highly significant and large excess of daughters among the offspring of male 1,2-dibromo-3 chloropropane (DBCP) applicators[2] and wonders if information on sex ratio is also available for the fruit growers in our study. In our initial survey, we did not gather these data. As data on sex ratio are easy to obtain, we gathered this information recently by telephone. We asked wives of fruit growers the outcomes of their pregnancies. Except for one pregnancy, we were able to gather all the information on 140 pregnancies. The total number of pregnancies was 127 (excluding 12 miscarriages for which the sex ratio was unknown and one pregnancy before the period of study). The overall sex ratio was 0·51 with a 95% confidence interval (95% CI) of 0·43–0·59 (based on a binomial distribution with expected population value for sex ratio (proportion of males) was 0·514[3]). For the 91 pregnancies in our time to pregnancy study, the overall sex ratio was also 0·51.

In a more detailed analysis we first related the sex ratio to the exposure variables that were also studied in the time to pregnancy study. A decrease in sex ratio was found when recent years of birth were compared with earlier pregnancies. Also, time to pregnancy increased with more recent years of birth (table 1).

The most recent period (1987–90) showed a lower sex ratio of borderline significance (0·33) compared with the previous periods (0·56) (Fisher's exact test, two sided, P = 0·08). A similar trend in sex ratio was found for the total group of 127 pregnancies. We also found a change in sex ratio dependent on gravidity. For the first, second, third, and subsequent children, sex ratios of 0·60, 0·57, 0·42, and 0·31 were found respectively. The first two pregnancies of a couple in comparison with next pregnancies showed a sex ratio of 0·58 and 0·38 respectively (Fisher's exact test, two sided, P = 0·08).

*Table 1 Offspring sex ratio and time to pregnancy according to year of birth (n = 85)**

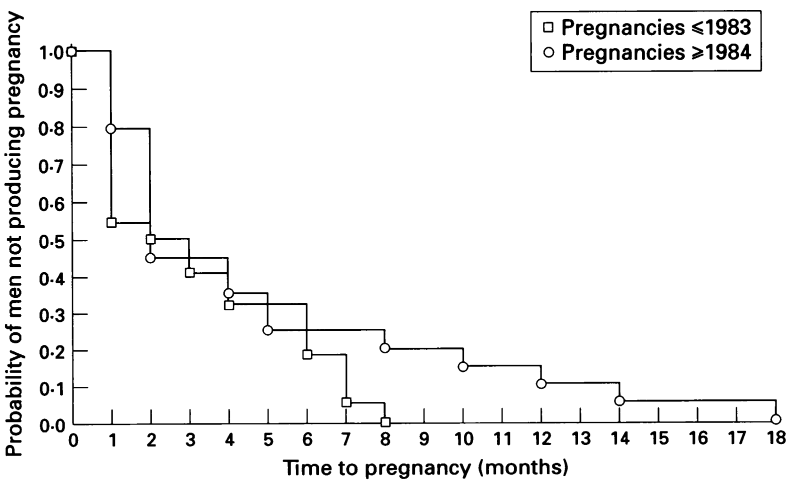
Year of birth	Pregnancies n	Sex ratio	Time to pregnancy (months)
1978–80	18	0·56	2·9
1981–83	22	0·55	3·5
1984–86	24	0·58	4·2
1987–90	21	0·33	4·1

*n = 91 pregnancies from the time to pregnancy study, excluding six miscarriages of unknown sex.

This raises the question whether gravidity acts as a confounder in this analysis, as does time to pregnancy. Because of small numbers, stratification of sex ratio according to gravidity and year of birth was not possible. Surprisingly, a difference in time to pregnancy according to year of birth was found for boys but not for girls. The figure is a Kaplan-Meier curve (PROC LIFETEST) by year of birth for boys. The curves, did not differ significantly. A univariate survival analysis with the PHREG SAS procedure as described in our study on time to pregnancy,[1] for the period of birth comparing pregnancies occurring in 1983 or before (1) with more recent pregnancies (0) as the independent variable, showed a fecundability ratio of 1·61 (95% CI 0·83–3·13) for boys and 1·13 (95% CI 0·59–2·15) for girls. No differences in age at the time of conception of men or women, or the age difference between both parents were found in our study. Therefore, a role of age dependent hormone concentrations of the parents on offspring sex ratio at the time of conception is not a very likely explanation for these findings.

In our study on time to pregnancy, we focused on seasonal effects of exposure of men. No significant differences according to season were detected in the sex ratios. Observed sex ratios for the quarter of a year in which conception took place were: 0·64 (January-March), 0·44 (April-June), 0·48 (July-September), and 0·52 (October-December).

As no relation between sex ratio and any of the exposure variables used in our study on time to pregnancy was found, other available information on exposure was considered as well. Because offspring sex ratio is a dichotomous variable, we studied outcome in a case-control like design with maximum likelihood logistic regression models by computing odds ratios (ORs) with SAS PROC LOGISTIC. As the odds



Time to pregnancy by year of birth for boys (n = 44).