PostScript

LETTERS

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Sex ratio at birth and exposure to petrochemicals

Saadat and colleagues¹ reported a significantly high sex ratio (proportion male) in births to people exposed to oil and natural gas from an Iranian oilfield. These authors cited a study of Yang and colleagues² of sex ratios near a petroleum refinery plant in Taiwan. In that study Yang *et al* failed to find any disturbance in the sex ratios of two polluted municipalities as contrasted with Taiwanese national data. However Saadat *et al* failed to mention another, more powerful, study by the same group of authors. Yang and colleagues³ contrasted the sex ratios at birth in 16 municipalities in which there was substantial involvement in the petrochemical industry with sex ratios in the other 345 municipalities in Taiwan. Overall, the offspring sex ratios of the polluted municipalities were highly significantly higher ($p = 0.003$). Thus in both Iran and Taiwan, significantly high offspring sex ratios have been associated with exposure to petrochemical pollution. This seems an established phenomenon for which an explanation is needed.

In view of the evidence that mammalian (including human) sex ratios at birth are dependent on parental hormone levels around the time of conception,⁴ caution would dictate that we regard these chemicals as potential endocrine modifiers (or "disruptors"). In general, where an adverse exposure is associated with a raised offspring sex ratio, it is reasonable to suspect modification to maternal (rather than paternal) endocrines. So in accordance with my hypothesis,⁴ one may suspect that exposed women have raised oestrogen levels. Alternatively they may have lowered progesterone levels, which reportedly occurred in ducks fed on petroleum.⁵ Or they may have both. The hormones of the women in both these polluted areas should be assayed to test the present suggestion.

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Authors' reply

Possible effect of maternal hormones and GST genotypes on sex of offspring

We would like to thank Dr James for his letter. Dr James may well be correct in that maternal oestrogen and progesterone levels may play a part in determining the sex of offspring.

We know that parental exposure to toxicants can influence offspring sex ratio. The glutathione S-transferase (GST) family is one of the major detoxification systems in mammalian tissues. The GSTs contribute in the protection against a broad range of compounds, including pesticides and environmental pollutants.¹ On the other hand, there is considerable evidence that genetic polymorphisms of some members of the GST family are risk factors for recurrent early pregnancy loss and spontaneous abortions.^{2,3} Very recently, we showed that in the general population of Shiraz (south of Iran), offspring sex ratio is not associated with parental GSTT1 and GSTM1 genotypes.⁴

We studied the parental GSTM1 and GSTT1 genotypes of families who were resident in the contaminated area of Masjid-I-Sulaiman (MIS) which participated in our previous study.⁵ Since some families were unwilling to

participate, the number of participating families decreased from 51 to 35. In the participant families we identified 214 offspring. Using the PCR based method, the GSTT1 and GSTM1 genotypes were determined.⁴ Table 1 shows the association between maternal genotypes and offspring sex ratio. In the general population, the sex ratio is not associated with parental GSTM1 and GTT1 genotypes⁴; the observed sex ratios in each combination of maternal genotypes were therefore compared with the sex ratio in the general population of MIS (0.504).⁵ Interestingly there was significant association between maternal combination of active GSTM1/null GSTT1 genotype and increased offspring sex ratio ($\chi^2 = 5.601$, $df = 1$, $p = 0.018$). There was no significant association between other genotype combinations and sex ratio (table 1). It should be noted that paternal genotypes did not show any significant association with offspring sex ratio (data not shown).

Therefore, we suggest that an interesting study would be the analysis of variations of offspring sex ratio at birth in relation to maternal hormones and maternal GST genotypes in the polluted areas of Iran and Taiwan. Such a study is presently underway in MIS.

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Table 1 Association between the combination of GST genotypes of mothers and offspring sex ratio in polluted areas of MIS

Genotype		Sons	Daughters	χ^2 *	p value
GSTM1	GSTT1				
Present	Present	12	14	0.186	0.666
Present	Null	24	10	5.601	0.018
Null	Present	46	45	0.000	1.000
Null	Null	30	33	0.206	0.650

χ^2 was performed using sex ratio equal to 0.504 in general population of MIS.

* $df=1$