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only to the FEV_1/Ht^2 slope. It is highly probable that the acceleration of annual decline in FEV_1 by smoking reflects obstructive changes in the respiratory system. In the case of pre-existing pulmonary fibrosis, however, the progression of restrictive disorders might be, at least in part, responsible for the acceleration, although its contribution to the FEV_1/Ht^2 slope was about twofold larger than that of smoking.

In conclusion, no definite evidence was obtained that supports the possibility of an interaction of pre-existing mild pulmonary fibrosis and low exposure to chrysotile asbestos on the accelerated annual decline of FEV_1 and FVC. Even if it is mild and stable, however, pre-existing pulmonary fibrosis is an independent risk factor for accelerated annual decline of FEV_1 irrespective of exposure. As this study was based on only a few subjects, and past exposure before the start of the study was not considered, further investigation is needed to confirm the results.

This study was presented, in part, at the 24th International Conference on Occupational Health, Nice, 1993. Partly supported by Takeda Science Foundation, Japan.

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1 Baker EL, White RF, Pothier L, Berkey CS, Dinse GE, Travers PH, *et al.* Occupational lead neurotoxicity: improvement in behavioural effects after reduction in exposure. *Br J Ind Med* 1985;**42**:507–16.
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Table 2 Odds ratios of 16 cases (more daughters than sons within a family) compared with 27 controls (43 sons) for exposure variables

Variable	*Odds ratio (95% CI)*
Spraying days 1990 (30 days)	18·4 (1·72–196)
Cross current sprayer (10 days/y)	1·7 (1·05–2·59)
Herbicide sprayer (5 days/y)	3·6 (1·10–11·6)
(Manual) knapsack sprayer (5 days/y)	2·2 (1·06–4·66)
Metiram (1 spraying/y)	1·3 (1·05–1·61)
Azinphos-methyl (0/1)	4·4 (1·11–17·3)
Paraquat (0/1)	>5·6* (>5·6-< 13·4)

*Paraquat was used by all families with more daughters compared with 74% in the control group.

ratio for gravidity (OR 1·35, 95% CI 0·92–1·99) was not significant and adjustment did not influence the regression coefficient or standard errors of variables of interest, only crude ORs are given.

No relation was found for most of the variables studied in our time to pregnancy study, but the results suggest a relation between use of a cross current airblast sprayer (days/y) (OR = 1·3, 95% CI 0·96–1·72) and use of a herbicide sprayer (days/y) (OR = 2·0, 95% CI 1·08–3·76) and production of daughters. Also we compared families with more daughters than sons with the other families. Instead of gravidity we corrected for the number of children within a family (OR = 1·23, 95% CI 0·66–2·31). As some families also conceived children before the time of the study (1978–90) number of children is a surrogate measure for gravidity. Because differences with or without adjustment were small, table 2 gives only crude ORs. For the 43 families a relation was found between the number of days with use of a herbicide sprayer (days/y), a cross current airblast sprayer (days/y), and a knapsack sprayer (days/y) and the number of daughters within a family. When comparing families with more daughters than sons (16 families), the number of spraying days a year was 37 compared with 25 for the other families, 7·6 *v* 3·3 days/y for the herbicide sprayer, 16 *v* 5·4 days/y for the cross current airblast sprayer, and 7·1 *v* 3·0 days/y for the knapsack sprayer. In families with more daughters use of the specific pesticides Azinphos-metyl (insecticide), Metiram (fungicide), and Paraquat (herbicide) was higher. Table 2 shows the results of the ORs.

For families with more sons than daughters (17) a significant OR was found for use of a cross current sprayer (yes or no, OR = 0·16, 95% CI 0·03–0·82), and number of spraying days with this type of sprayer (OR = 0·54 per 10 spraying days/y, 95% CI 0·30–0·98).

Discussion

Overall sex ratio was not different from the expected ratio of 0·51. James hypothesised that high concentrations of testosterone at the time of conception produce boys, and high concentrations of gonadotrophin produce girls. Among the offspring of DBCP applicators[3] a highly significant excess of daughters was found. As exposure to pesticides in fruit growing typically includes mixed exposure to many different compounds, similar to that found for DBCP, it is not possible to predict the direction of a shift in sex ratio induced by exposure to pesticides among this group. As the number of subgroups is small it is impossible to draw firm conclusions, but some of the results are of interest. From our results there are some indications that exposure to pesticides in agriculture may affect offspring sex ratio. The shift towards daughters in the most recent period (sex ratio of 0·33) was remarkable. Also the finding that spraying frequency, frequency of use of specific equipment, and use of some specific pesticides are related to a shift towards more daughters within a family may point to an exposure effect. One should be careful in interpreting these results. The fact that use of several pesticides is related to sex ratio does not necessarily imply that individual pesticides are causally related to sex ratio. Fruit growers use a complex mixture of agents and the use of one agent is often correlated with the use of another one. It is unlikely that the shift in sex ratio is caused by the introduction of particular pesticides as all pesticides have been applied to some extent during the study period. Because application techniques changed considerably over time, the introduction of certain techniques seems a more plausible explanation for this finding. It is possible that with certain underlying mechanisms, effects may not be caused by exposure of the male worker only, as most women live near the orchard and they often participate during particular activities like pruning, thinning, and harvesting. No seasonal trends were found in this analysis as was found for time to pregnancy. Our finding that there might be a difference in time to pregnancy for boys and girls as well, may indicate that both sex ratio and time to pregnancy are interlinked. We cannot explain why exposure variables associated with time to pregnancy are not related to sex ratio.

In conclusion, we think that the suggestion by James to analyse sex ratio is a useful one and should be explored further. To consider both sex ratio and time to pregnancy simultaneously may have advantages in elucidating occupational hazards of (pesticide) exposure. Our results do show that other variables such as families with predominantly daughters or sons, which are indicative of a shift in sex ratio, might be more powerful because they use another sampling unit (family instead of a crude stratification by exposure). Especially in this study among agricultural workers an analysis on a family level might be relevant because the exposure might be aggregated at the family level as well. In general, it seems useful to explore, after time to pregnancy and sex ratio, the presence of families with a predominance of one of the sexes as little is known about the underlying biological mechanisms as well as the statistical properties of these indices.

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NOTICE

The Toxicity of Mixtures of Solvents. 13 June 1995. London.

A one day meeting organised jointly by the SCI Health and Safety Group, RSC Toxicology Subject Group, and the Institute of Occupational Hygiene. The meeting will examine the theoretical and practical difficulties in assessing the toxicity of solvent mixtures and effecting control of exposure. Data from experimental studies, occupational exposures and poisoning incidents will be reviewed with an aim of understanding the nature of mixed solvent toxicity. The second half of the meeting will concentrate on industrial experiences, and will consider techniques for assessing and controlling exposures to mixtures of solvents in the workplace.

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