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LETTER TO THE EDITOR

Paternal Occupational Exposure and Spontaneous Abortions: A Closer Look at Paternal Recall and Vinyl Chloride

Key words: paternal exposure, recall bias, spontaneous abortion, vinyl chloride

We commend Savitz et al. [1994] for their effort at summarizing the epidemiology literature regarding paternal occupational exposure and spontaneous abortion, especially as it pertains to methodological issues. They identified three major methodological issues: (1) accurate ascertainment of the occurrence of a spontaneous abortion, (2) validity of the father's exposure assignment, and (3) potential confounding by parental lifestyle factors that may be correlated with paternal occupation. Concerning the first issue, it should be noted that an article was recently published by Fikree et al. [1993] that assessed the recall agreement of pregnancy outcomes among 857 couples. Using the wives' reports as the standard, Fikree et al. [1993] found 71.2% sensitivity and 98.8% specificity for husbands' recall of spontaneous abortions. We have also observed differences in recall of spontaneous abortions by male employees. These observations showed that 20 spontaneous abortions were recalled among 96 (20.8%) lifetime pregnancy outcomes (live births, still births, and spontaneous abortions) by male employees who had their spouses/partners assist with a reproductive health survey. There were only six spontaneous abortions among 114 (5.3%) lifetime pregnancy outcomes recalled by male employees who chose not to involve a spouse/partner. These data support the opinion of Savitz et al. [1994] that paternal occupational exposure studies "should routinely seek reproductive outcome information from the woman, whenever possible."

Based on the Infante et al. [1976a] data collected from male employees only, Savitz et al. [1994] suggested that further epidemiologic research be initiated on paternal occupational exposure to vinyl chloride and spontaneous abortion. Infante et al. [1976a] reported an age-adjusted fetal death loss of 15.8%, as recalled by male workers (N = 95) who had potential exposure to vinyl chloride, compared to 8.8% recalled by rubber and polyvinyl chloride fabrication male workers (N = 158). When the analysis was restricted to men under age 30, they reported 20.0% fetal death loss for the vinyl chloride group compared to 5.3% for the nonexposed group.

Although they alluded to the fact that the risks reported by Infante et al. [1976a]

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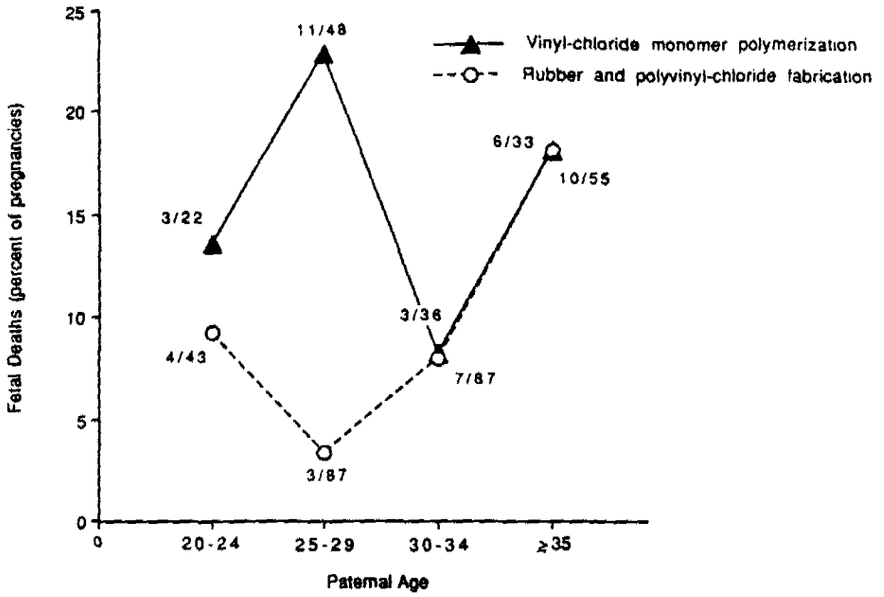

Fig. 1. Fetal deaths by paternal age and potential exposure to vinyl chloride monomer as defined by Infante et al. Note: the rubber and polyvinylchloride fabrication group was considered not exposed to vinyl chloride monomer. The ratios in the graph are the number of fetal deaths divided by pregnancies per each age group (adapted from Infante et al., 1976a,b: Stallones, 1987].

were observed primarily among the younger male employees, Savitz et al. [1994] were apparently unaware of additional paternal age-specific fetal death loss data requested by Paddle [1976] and subsequently published by Infante et al. [1976b]. These additional data demonstrated that the difference in the overall age-adjusted risks (15.8% vs. 8.8% in the original published work) was the result of divergent age-specific fetal death loss percentage in only one of the four 5-year age strata (Fig. 1).

The late Reuel Stallones, in a commentary on the use and abuse of subgroup analyses in epidemiology [1987], asked the following questions concerning the Infante et al. [1976a] data: "Why was the harm limited to the 25- to 29-year age group? Why was the rate higher in the exposed 25–29-year age group than in either of the two older exposed age groups? Why was the rate lower in the nonexposed 25–29-year age group than in the younger, nonexposed age group?" Stallones' conclusion was "No answers to these questions are evident; a sensible conclusion is that something went wrong in the study, resulting in aberrant findings, and that the study therefore should be discarded. If published at all, the data should appear in a textbook of epidemiology as a most pertinent example of the value of a subgroup analysis in discovering a problem, internal to the research, which renders invalid the results obtained for the total group and which might have been accepted had the subgroup analysis not been done." Hatch et al. [1981] have also raised other concerns about the analyses in Infante et al. [1976a].

Savitz et al. [1994] suggested that the dominant lethal test may be the animal study most relevant to human spontaneous abortion. In this regard we note that Short et al. [1977] reported a negative result for vinyl chloride in the dominant lethal assay

in male rats exposed to vinyl chloride levels as high as 1,000 ppm for 6 hours daily over an 11-week period. Anderson et al. [1976] found no response to vinyl chloride in the dominant lethal assay in male mice exposed briefly to levels as high as 30,000 ppm.

In summary, we again commend Savitz et al. [1994] for their ambitious and comprehensive review of the literature concerning paternal occupational exposures and spontaneous abortion. However, we concur with Stallones' [1987] conclusions. We believe there is no justification for continuing to use the data of Infante et al. [1976a] to support the suggestion in the epidemiology literature of a positive association between paternal occupational exposure to vinyl chloride and spontaneous abortion. If other epidemiology reviewers do find the conclusions of Infante et al. to be credible, then we believe they should at least offer the reader their answers to Stallones' three questions.

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