PATERNAL EXPOSURES AND PREGNANCY OUTCOME: MISCARRIAGE, STILLBIRTH, LOW BIRTH WEIGHT, PRETERM DELIVERY

David A. Savitz

Department of Epidemiology
Campus Box #7400
School of Public Health
University of North Carolina
Chapel Hill, NC 27599-7400

INTRODUCTION

In this overview, the epidemiologic evidence regarding the influence of paternal exposures in the etiology of pregnancy outcomes will be presented. These outcomes, covering the spectrum of fetal survival and development exclusive of birth defects, have been the subject of a number of studies that include paternal factors. Most of the research has focused on miscarriage as the endpoint, and among those, most have been concerned with occupational exposures. Public concern with such issues as Agent Orange exposure among male veterans who served in Vietnam has lead to a concentration on occupational exposures rather than lifestyle factors such as tobacco or alcohol use.

Until very recently, the relationship between father's exposures and pregnancy outcome has been evaluated through the exploitation of existing data or by analyzing data from studies with a focus on some other exposure (typically maternal), with the predictable limitations in the level of detail available regarding paternal factors. However, in the last few years, studies designed explicitly to examine the paternal contribution to miscarriage have appeared (Alcser et al., 1989; Taskinen et al., 1989; Cordier et al., 1991) and yielded some rather interesting results.

In addition to characterizing the state of evidence, an attempt will be made to highlight some of the methodologic issues specific to paternal factors and the pregnancy outcomes of interest. Finally, the needs to advance research in this area will be discussed.

PATERNAL EXPOSURES AND MISCARRIAGE

Research on paternal exposures and miscarriage was initiated in the mid-1970s with surveys of male dentists exposed to anesthetic gases (Cohen et al., 1974) and vinyl...
chloride workers (Infante et al., 1976). In each instance, suggestive evidence was provided that the male's occupational exposures around the time of conception, independent of maternal risk factors, were related to an increased risk of miscarriage. Though the evidence remains inconclusive, in retrospect, these initial efforts opened up an important avenue of research. A total of at least 38 papers have now been published examining the association between father's occupational exposure and miscarriage (Savitz et al., in press), with a modest number of additional papers concerned with paternal tobacco and alcohol use.

As noted above, most of these studies considered paternal exposure and miscarriage as part of surveys with a broader array of interests. As a result, the level of detail on either the father's exposure, the pregnancy outcome, or both is limited. Father's occupational exposures have largely been based on a job title rather than more thorough methods such as detailed workplace descriptions, biological markers, or environmental measurements. Miscarriages have usually been based on maternal report, with paternal reports sometimes used, and in Scandinavia, medical records. Interest has been concentrated on exposure to heavy metals, pesticides, solvents, and anesthetic gases, with limited data on other potentially harmful agents. Selected findings are summarized below, including the most promising or extensively researched topics.

Table 1 summarizes results of three studies addressing paternal mercury and miscarriage, with null results in one (Brodsky et al., 1985) but notably positive associations in two studies that considered exposure in greater detail (Alcser et al., 1989; Cordier et al., 1991). In the latter two studies, a dose-response gradient was observed based on estimated mercury exposure. In addition to the direct information conveyed about paternal mercury and miscarriage, these latter two studies illustrate the potential value of studies that incorporate measures of dose.

Table 1. Summary of Results of Studies of Paternal Exposure to Mercury and Miscarriage

<table>
<thead>
<tr>
<th>Reference</th>
<th>Exposure</th>
<th>RR</th>
<th>95% CI</th>
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</thead>
<tbody>
<tr>
<td>Brodsky et al., 1985</td>
<td>Exposure in dentistry</td>
<td>0.9</td>
<td>0.7-1.1</td>
</tr>
<tr>
<td>Alcser et al., 1989a</td>
<td>Urine Hg 2,000-3,999 ug/l</td>
<td>1.1</td>
<td>0.8-1.6</td>
</tr>
<tr>
<td></td>
<td>Urine Hg 4,000-9,000 ug/l</td>
<td>1.7</td>
<td>1.1-2.5</td>
</tr>
<tr>
<td>Cordier et al., 1991b</td>
<td>Urine Hg 1-19 ug/l</td>
<td>1.3</td>
<td>1.0-1.7</td>
</tr>
<tr>
<td></td>
<td>Urine Hg 20-49 ug/l</td>
<td>1.7</td>
<td>1.0-3.0</td>
</tr>
<tr>
<td></td>
<td>Urine Hg 50+ ug/l</td>
<td>2.3</td>
<td>1.0-5.2</td>
</tr>
</tbody>
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* Cumulative average quarterly urine levels over lifetime.

b Average mercury level in period before conception.

Studies of paternal exposure to anesthetic gases and miscarriage occurred in a rather brief period in the mid- to late-1970s. Summarizing results for only the most highly or clearly exposed group in each study (Table 2) provides a consistent indication of increased risk, with relative risk measures of 1.5 to 1.8. Mitigating the value of this replication somewhat is the similarity in methods of all the Cohen et al. studies (1974, 1975, 1980), with paternal self-report elicited in mail questionnaires. Limited response proportions, in particular, call the results into question. Although the results are sufficiently impressive to warrant more sophisticated study, the increasingly widespread