to crystalline silica among workers hired prior to 1944. Products containing higher percentages of crystalline silica, that is, calcined powders, did not appear until the mid- to late 1920s (5). Natural (uncalcined) products remained dominant in production into the 1930s (3). Natural diatomaceous earth products contain only small amounts of crystalline silica in the form of quartz. The first rotary kiln for calcining (heat treating) diatomaceous earth powder was not installed until late 1923, and production of calcined and flux-calcined products did not begin in earnest until 1925, and then only in limited quantities (5). Through 1929, natural products still accounted for more than 60% of the production at the California plant studied by Checkoway et al. (1). Although beehive and scove kilns that could produce calcined bricks were in place beginning in the early 1920s, the business did not take hold until 1927. While heat treatment for aggregate and brick products occurred prior to 1930, calcined bricks were always maintained as much as possible in the amorphous state, so that the undesirable expansion/contraction properties of cristobalite were minimized (6). Thus, it is unlikely that the earliest exposures to dust in this plant included any significant quantities of crystalline silica, and the assignment of high levels of crystalline silica exposure to this segment of the cohort remains highly suspect. Furthermore, it is during this time period that Checkoway et al. (1) reported little asbestos exposure, when there is evidence that pre-1930 workers were exposed to asbestos (7).

A comparison of the subjective exposure assessments used in a 1993 study (8) on the same cohort with the semiquantitative estimates used in the current study (1) showed a large degree of undesirable overlap across all categories, suggesting a potential for misclassification (2). This is of special concern, since no industrial hygiene data available dust measurement data and judgments of the effectiveness of interventions to reduce exposure (e.g., improved ventilation) that were documented in the plant's historical dust exposures in the diatomaceous earth industry. Warman, NJ: Johns-Manville Corporation, 1973. (Internal document).


Mel J. Mirliss
International Diatomite Producers Association
Long Beach, CA 90803

**THE AUTHORS REPLY**

Mirliss (1) and Gibbs (2) question the validity of two aspects of our mortality study of diatomaceous earth workers (3). Mirliss suggests that for the earliest years of the study, estimates of worker exposure to crystalline silica may have been erroneous because of insupportable assumptions about exposure modeling, and Gibbs raises the possibility that uncontrolled confounding by asbestos exposure may have biased our findings of a dose–response association between crystalline silica and lung cancer mortality.

Mirliss (1) correctly notes that silica dust exposures for the years before 1944 were estimated by extrapolating from measurement data obtained during later years (1948–1988). The exposure modeling that formed the basis of the extrapolation incorporated exposure intensity time trends from available dust measurement data and judgments of the effectiveness of interventions to reduce exposure (e.g., improved ventilation) that were documented in the plant’s history (4). The scaling factor ultimately used for the earlier years (2.5 on the log scale) was derived simply as an

---

**TABLE 1. Lung cancer mortality trends, lagged 15 years, by cumulative exposure to respirable dust and cumulative exposure to respirable crystalline silica, 1942–1994**

<table>
<thead>
<tr>
<th>Cumulative exposure mg/m²-years</th>
<th>No. of deaths</th>
<th>RR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.5</td>
<td>22</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>0.5–&lt;1.1</td>
<td>12</td>
<td>0.96</td>
<td>0.47–1.98</td>
</tr>
<tr>
<td>1.1–&lt;2.1</td>
<td>9</td>
<td>0.77</td>
<td>0.35–1.72</td>
</tr>
<tr>
<td>2.1–&lt;5.0</td>
<td>14</td>
<td>1.26</td>
<td>0.62–2.57</td>
</tr>
<tr>
<td>&gt;5.0</td>
<td>20†</td>
<td>2.15</td>
<td>1.08–4.28</td>
</tr>
</tbody>
</table>

* Adapted from table 6 of Checkoway et al. (1).
† mg/m²-years, milligrams per cubic meter x years; RR: rate ratio adjusted for age, calendar year, duration of follow-up, and ethnicity (Hispanic vs. non-Hispanic); CI, confidence interval.
‡ Eight of these workers were hired prior to 1930 (9).
extension of the data-derived values for subsequent time periods and yielded a plausible range of respirable dust concentrations (1–7 mg/m³) (4). Moreover, contrary to Mirliss’s suggestion that early silica exposures were overestimated, it is not possible to predict with any accuracy whether these exposures were underestimated or overestimated. There is undoubtedly some error in the estimated percentages of crystalline silica in respirable dust, as we acknowledged (3). In estimating the crystalline silica component of dust, we relied on information supplied by the company, which included crystalline silica concentrations in various product mixes and annual diatomite production values by type (natural, calcined, flux-calcined) (5). Furthermore, cohort members’ job history records, reaching back to the earliest years of plant operation, were sufficiently detailed to distinguish jobs according to their relative exposures to amorphous and crystalline silica. In brief, we consider the extrapolated exposures best estimates based on empirical data and reasonable occupational hygiene judgment. Given that exposure was assessed in a blinded manner with regard to health outcome, it is more likely that our findings for lung cancer and nonmalignant respiratory disease mortality underestimate, rather than exaggerate, the true associations (6).

Gibbs’s (2) comments focus on asbestos exposure among a group of 66 workers (including eight lung cancer deaths) hired before 1930. These workers experienced a large excess of lung cancer, but their asbestos exposures are uncertain. To address how including these workers influenced the findings, we performed additional analyses that excluded the pre-1930 hires. After we excluded these workers, the estimated lung cancer rate ratio in the highest exposure stratum of crystalline silica (≥5.0 mg/m³-years) relative to the reference category (<0.5 mg/m³-years) was 1.74 (12 and 22 observed, respectively). A nearly identical result (rate ratio = 1.73) was found after adjustment for asbestos exposure. Compared with national rates for white US males, the standardized mortality ratio for workers with the highest crystalline silica exposure was 2.05. These results are only slightly lower than findings reported for the entire cohort (3). We also performed standardized mortality ratio analyses on the reduced cohort, considering jointly crystalline silica and asbestos exposures and stratifying by the asbestos levels recommended by Gibbs (2). The standardized mortality ratio was 2.21 (seven observed) among workers with ≥5.0 mg/m³ of crystalline silica exposure and no asbestos exposure, whereas no lung cancer deaths occurred in the joint stratum of lowest crystalline silica (<0.5 mg/m³-years) and highest asbestos exposure (≥6.8 fibers/ml-years). In fact, all four lung cancer deaths among those with the highest asbestos exposures occurred among workers in the two highest crystalline silica strata (2.1–<5.0, ≥5.0 mg/m³- yrs). These findings confirm the previously reported (7) absence of confounding by asbestos exposure after 1930. The lack of measurement data on asbestos exposure before 1930 limits our ability to assess confounding in the most direct manner. However, data on radiographically determined pleural abnormalities (plaques or diffuse thickening) are markers of asbestos exposure and can provide some indication of potential confounding. A panel of three readers has read historical radiographs for interstitial fibrosis and pleural disease to analyze silicosis, which will be reported on subsequently. The prevalence of pleural abnormalities among workers hired before 1930 (4.2 percent) was very similar to that in workers hired during 1930–1939 (4.9 percent), a period when asbestos presumably was not used in diatomaceous earth production (8). Furthermore, employment before 1930 accounted for relatively small fractions of the total duration of employment among the eight lung cancer deaths (18 percent) and 58 other workers (13 percent) hired before 1930. For these two groups, mean crystalline silica exposures after 1930 were 10.4 and 9.11 mg/m³-years, respectively, which would place them in the highest exposure stratum, irrespective of pre-1930 exposures. Therefore, exclusion of these workers from the analysis is not justified on the basis of potential confounding by asbestos and would result in an unnecessary sacrifice of data. We maintain that confounding by asbestos exposure is a very unlikely explanation for the observed dose-response relation of lung cancer mortality with crystalline silica among diatomaceous earth industry workers.

REFERENCES

Harvey Checkoway
Nicholas J. Heyer
Noah S. Seixas
Department of Environmental Health
University of Washington
Seattle, WA 98195–7234

Paul A. Demers
Occupational Hygiene Programme
University of British Columbia
Vancouver, BC V6T 1Z3, CANADA