LETTERS TO THE EDITOR

RE: "DOSE-RESPONSE ASSOCIATIONS OF SILICA WITH NONMALIGNANT RESPIRATORY DISEASE AND LUNG CANCER MORTALITY IN THE DIATOMACEOUS EARTH INDUSTRY"

In an update by Checkoway et al. (1) of mortality among diatomaceous earth workers, asbestos exposure misclassification and asbestos-silica interactions may have influenced study results and interpretation. In a reanalysis (2) of the original cohort mortality study to examine confounding by asbestos exposure, workers employed before 1930 were excluded because asbestos was definitely used in the facility, but specific jobs and exposure levels could not be identified. In this updated study, pre-1930 workers were included, and Checkoway et al. reported that they "extrapolated the 1930 job-specific intensity estimates to earlier years of plant operation" (1, p. 682). In fact, no asbestos was used in the facility in 1930, and measures of asbestos exposure were assigned to maintenance workers only (3). Thus, production workers employed before 1930 were considered "nonexposed" when some may have been exposed to high levels of asbestos. High levels of exposure to asbestos are well established as carrying their own risk of lung cancer. In addition, confounding by asbestos exposure for the pre-1930 workers cannot be dismissed, because confounding was investigated only in workers whose main asbestos exposure occurred after 1950 (2), when levels were considerably lower than would have been anticipated during the pre-1930 period.

Because non-asbestos-exposed workers do not require adjustments for the effects of asbestos, they are perhaps the most relevant to an assessment of silica risks. As shown in table 7 of Checkoway et al. (1), the only non-asbestos-exposed workers who exhibited a rate ratio exceeding 1.00 (13 deaths, rate ratio = 2.03) were those in the highest silica exposure category (≥5.0 mg/m²-years). Because five lung cancer deaths occurred among pre-1930 hires, a key question not answered in the paper is this: How much of this increased lung cancer risk is due to the pre-1930 deaths?

In the “reanalysis” to examine confounding, the standardized mortality ratios were 1.34 for non-asbestos-exposed silica workers, 1.15 for silica workers exposed to 0–<2.7 fibers/ml-years of asbestos, 1.99 for workers exposed to silica and 2.7–<6.8 fibers/ml-years of asbestos, and 4.4 (confidence interval (CI) 1.20–11.3) for workers exposed to silica and ≥6.8 fibers/ml-years of asbestos (2). The standardized mortality ratio for workers not exposed to asbestos but with the highest level of exposure to silica was 2.00 (CI 0.73–4.35). The standardized mortality ratio for the highest category of exposure to asbestos and to silica was 8.32 (CI 1.71–24.3). In the more recent mortality update (1), the chosen categories of asbestos exposure were >0–1.2 and >1.2 fibers/ml-years. Clearly, this choice of asbestos exposure categories may have diluted the effects at higher asbestos concentrations and influenced the conclusion of no asbestos effect.

REFERENCES

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RE: "DOSE-RESPONSE ASSOCIATIONS OF SILICA WITH NONMALIGNANT RESPIRATORY DISEASE AND LUNG CANCER MORTALITY IN THE DIATOMACEOUS EARTH INDUSTRY"

In a retrospective study, such as the diatomite worker study of Checkoway et al. (1), data reconstruction is always difficult at best, resulting in a high potential for exposure misclassification. The paper detailing the reconstruction acknowledges that sources of potential error relating to exposure misclassification were "... present to a substantial degree in the history of the cohort addressed here, and inherently limit the accuracy of the final results" (2, p. 601). In a 1952–1954 survey by the US Public Health Service, Cooper and Cralley noted that "the absence of adequate data on levels of dust concentration by specific operation during the past 15 years made an accurate assessment of the past weighted dust exposures impossible" (3, p. 41).

For the earliest years (the 1920s through the 1940s), Checkoway et al. (1) used crude historical dust (total and respirable) data to extrapolate quantitative exposures to crystalline silica for the years 1948–1988 (4) (impinger testing, 1948–early 1970s; gravimetric testing, early 1970s–1988). Job-specific exposures for the years prior to 1948 were estimated by regression modeling extrapolation and the use of a somewhat arbitrary scaling factor of 2.5 (log scale) for dust concentrations to jobs prior to 1944. Crystalline silica concentrations were assumed for all years. Limited industrial hygiene data on the crystalline silica component of the dust were available but were not used.

Use of the above multiplier placed most of the early workers in the higher exposure categories and most of those hired prior to 1930 in the highest exposure category. This placement may not be consistent with the early work experience and may have resulted in overestimation of exposure.
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 percent 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 existed prior to 1948, and exposures for that period could only be estimated. Thus, serious questions arise regarding the assignment of crystalline silica assessments to all workers in the cohort, the extent of crystalline silica exposure among the earliest workers, and the validity of the scale factor used to assign exposures prior to 1944.

Limitations of the industrial hygiene data for the later years and the lack of industrial hygiene data in the earlier years make the assessments of individual exposures less valid, particularly during the earliest years of employment. The study findings (1) are driven by the increased risk observed in the highest exposure cell, in which a significant percentage of the lung cancer deaths occurred among workers hired prior to 1930 (table 1). Any significant degree of exposure misclassification and the resulting shift in the number of lung cancer deaths in any of the exposure cells could lead to substantially different conclusions. The impact of exposure misclassification on the study findings should be examined more fully by the scientific community.

References


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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

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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 to respirable crystaline silica (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).