Correspondence

Long term follow up of workers exposed to beryllium

Sir,—Cotes et al have reported cases of chronic beryllium disease (CBD) in a beryllium refinery and computed from air levels determined between 1952 and 1960 a mean annual beryllium oxide exposure below 2 μg/m³.¹ Their conclusion, however, that this indicates inadequate protection by the adopted TLV of 2 μg/m³ DWA and a 30 minute peak of 25 μg/m³ is not sufficiently supported by the environmental data available to them and is not confirmed by the exposure history of 46 cases of CBD diagnosed among our employees between 1940 and 1983.

In view of today’s much more advanced sampling and analytical technology, low level beryllium concentrations obtained more than 20 years ago must be interpreted with great caution. This caveat appears also justified for the plant environment described by the authors. The recollection of episodes with accidentally or otherwise raised exposures by 17 workers, the fact that 9% of all samples were above 2 μg, the omission of personal or breathing zone sampling, and the occurrence of two cases with acute beryllium pneumonitis during the same period all suggest that raised beryllium levels must have occurred much more frequently than has been assumed by the authors. Breathing zone measurements of airborne, respirable particles may indeed be 10 to 100 times higher than in the general area, and the reported acute cases could not have occurred without exposures high enough to cause CBD as well. The epidemiological analysis of our own chronic cases left no doubt that all were exposed to concentrations significantly above 2 μg/m³ as a daily weighted average.²

The paper, nevertheless, makes a strong, well justified point for the avoidance of short term peaks beyond the adopted limit of 25 μg/m³ for 30 minutes. Concentrations exceeding this level can easily go unnoticed, and frequent personal monitoring and breathing zone sampling in high risk areas play an important part in our present exposure control efforts. Without them, our preventive programme could not have succeeded in reducing the incidence rate from 27 cases per 3000 (1940–60) to 2 per 3000 (1960–83) newly hired employees. The fact that the last two cases resulted from accidentally high exposures lends additional support for the efficacy of the 2 μg/m³ TLV.

The 25 μg short term limit was adopted mainly to prevent disease from acute chemical irritation. The “upper limit of 100 μg” quoted by the authors was never part of the adopted standard. It was used only during the development of environmental control technology as a maximum level beyond which no exposure was to be tolerated and production had to be stopped until the source of contamination had been corrected.

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References


On the relative toxicity of asbestos fibres

Sir,—One of the major controversies in asbestos epidemiology concerns the differential toxicity of the various fibre types, and in particular their potency for the induction of mesothelioma. The United Kingdom Advisory Committee on Asbestos was of the opinion that the amphiboles, and in particular crocidolite, were more likely to produce mesothelioma,¹ whereas in the United States OSHA has proposed an identical control limit for all asbestos fibres.²

Two problems bedevil the analysis of relative hazard. The first relates to the confounding effect of intensity of exposure; few studies have quantitative estimates of worker exposure to asbestos dust and one cannot be certain that the higher risk of mesothelioma observed in one cohort compared with another is not simply due to greater dust exposure. The second pertains to the difficulty of diagnosing this disease and the consequent unreliability of the death certificate diagnoses.

The recent papers of AD McDonald and her colleagues have gone a long way towards overcoming the problem of comparisons of exposure because both factories were concerned with textile production, exposure evaluations were made by the same hygienist, and exposure histories were calculated for each member of the various cohorts.³⁴ Although the authors made an effort to go beyond the death certificate to identify cases, they have pointed out that the problem of undiagnosed cases of mesothelioma remains.⁴ Although the correct diagnosis may not be made in each case of
Cancer mortality in two asbestos textile factories

<table>
<thead>
<tr>
<th>Factory</th>
<th>Dust exposure (mpcf)</th>
<th>&lt;10</th>
<th>10&lt;20</th>
<th>20&lt;40</th>
<th>40&lt;80</th>
<th>&gt;80</th>
</tr>
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<tbody>
<tr>
<td>South Carolina</td>
<td>E</td>
<td>325</td>
<td>44</td>
<td>40</td>
<td>25</td>
<td>12.5</td>
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<tr>
<td></td>
<td>N</td>
<td>73 (31)</td>
<td>12 (5)</td>
<td>13 (8)</td>
<td>11 (7)</td>
<td>11 (8)</td>
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<tr>
<td></td>
<td>P</td>
<td>0.22</td>
<td>0.27</td>
<td>0.32</td>
<td>0.44</td>
<td>0.88</td>
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<tr>
<td></td>
<td>RR</td>
<td>1.0</td>
<td>1.22</td>
<td>1.45</td>
<td>2.0</td>
<td>4.0</td>
</tr>
<tr>
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<td>E</td>
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<td>105</td>
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</tr>
<tr>
<td></td>
<td>N</td>
<td>94 (21)</td>
<td>18 (5)</td>
<td>26 (10)</td>
<td>21 (6)</td>
<td>30 (11)</td>
</tr>
<tr>
<td></td>
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<tr>
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<td>RR</td>
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<td>0.89</td>
<td>1.34</td>
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<td>3.38</td>
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</tbody>
</table>

E = Expected number of deaths of all causes, based on general population rates.
N = Number of deaths from malignant disease (respiratory neoplasms in parentheses).
P = Ratio N / E.
RR = Ratio of cancer deaths relative to the lowest exposure category.

mesothelioma, it is probable that the disease would be recognised as a malignancy and that the death certificate would be coded to one of the categories of malignant disease (with the exception of ICD code 228, in which case the word mesothelioma will appear on the certificate). It is possible to use the data the authors have presented in tables 5 of their papers to assess the comparative potencies of chrysotile and a mixture of chrysotile and the amphiboles for the induction of asbestos associated malignancies.

From these tables one can calculate for each exposure category the number of deaths expected from all causes of death, standardised for age and calendar period. One may then calculate the ratio of observed cancer deaths (all types) to expected all cause mortality for each category of exposure. The proportion of cancers unrelated to exposure to asbestos should remain constant at roughly 20% of expected all cause mortality, whereas the incidence of asbestos associated malignancies will increase with exposure. The table presents the results of these calculations. It can be seen that the risk of death from cancer, adjusted for expected all cause mortality, was the same in both factories. These data suggest that the risk of death from asbestos associated cancer in factories manufacturing similar products is unrelated to the type of asbestos fibre used. This evidence from human populations is similar to the results of animal experiments which have found little difference in relative toxicities.

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References


A problem in looking for relationships between concentrations of urinary components

Sir,—Falck et al report on an investigation between metallothionen (MT), chronic exposure to cadmium (Cd), and renal function. Among other findings, they note statistically significant linear relationships between urinary concentration of MT and those of Cd, total protein, and beta-2-microglobulin, when each is expressed per unit creatinine excretion.

We write to raise a problem that arises in the interpretation of results from this and other studies that investigate relationships between concentrations of solutes in spot samples of urine. While we do not think that the major conclusions of Falck et al should be challenged, the problem raised is a general one which has not to our knowledge been discussed before.

If uncorrected for degree of dilution, concentrations of any two otherwise unrelated solutes of urine must inevitably be positively correlated. Urine that is concentrated overall will tend to have higher concentrations of both solutes, and conversely urine that is dilute will tend to have lower concentrations of both solutes. To aid comparability of urine concentrations, they are often expressed per unit creatinine excretion, on the grounds that creatinine excretion rate is much more constant between and within individuals than urinary dilution. While urinary concentrations thus corrected for dilution should be less subject to spurious correlations of the