From Quartz Hazard to Quartz Risk: the Coal Mines Revisited

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Received 23 June 2000; in final form 21 March 2001

Following the classification of quartz as a human carcinogen by the IARC, many standard-setting committees are currently trying to convert this hazard into their national or EU standards. Since human data to set a safe exposure limit for quartz are limited, we hypothesized that lung burden data on quartz in coal miners' lungs after lifetime exposure could be used to set a non-carcinogenic lung burden of quartz, and that this might be valid for other groups occupationally exposed to quartz. A review of data shows that lungs of coal miners with simple coal workers' pneumoconiosis (sCWP) typically contain up to 30 g of dust, and in one specific study lung burdens between 0.7 and 1.7 g of quartz were associated with macules only, and no sCWP. Assuming independent actions of coal and quartz and no clearance of quartz, and sCWP as a prerequisite for lung cancer due to quartz exposure in coal mine dust, a simple kinetic approach was applied. A no observed adverse effect level (NOAEL) for quartz of between 0.03 and 0.13 mg/m³ (40 yr exposure) is derived, but it is concluded that more refined physiologically based pharmacokinetic modelling is needed for a better estimate, also including interindividual differences in lung clearance. Considering the independent effects of, and the well-known interaction between coal and quartz, these data could be important to other workplaces with usual mixed-dust exposure.

Keywords: quartz; coal; lung burden; risk assessment

INTRODUCTION

In 1996 an IARC Working Group classified crystalline silica (quartz) into IARC's Group 1, i.e. there was sufficient evidence for carcinogenicity in humans (IARC, 1997). This was based mainly on epidemiological evidence and there was no unanimous agreement for this latter classification amongst the working group (not an unusual situation in itself for an IARC Working Group). Disagreement was based largely on several issues, including: (i) the strong association between silicosis and lung cancer; (ii) the use of silicosis as an 'inert' dose estimate for cumulative uptake or intake; and (iii) the negative outcome of coal mine dust as a lung carcinogen, established at the same meeting. In recent reviews (Checkoway and Franzblau, 2000; Soutar et al., 2000) the first issue has been covered extensively and will not be addressed in this paper. Here we attempt to calculate a no observed adverse effect level (NOAEL) for quartz from studies in coal workers, based on two assumptions:

1. Coal and quartz act independently in coal mine dust, so that a NOAEL for quartz can be calculated from the quartz content of coal miners' lungs. Donaldson and Borm (1998) previously argued that the quartz hazard is a variable entity, depending on how and what it is mixed with. Similarly, we know that coal itself can cause pneumoconiosis (Collis and Gilchrist, 1928) and that coal rank (determined by coal quality) does affect the retained lung burden (Douglas et al., 1986) and is involved in the progression of pneumoconiosis (Walton et al., 1977). In addition, the incidence of simple coal workers' pneumoconiosis (sCWP) and progressive massive fibrosis (PMF) at given quartz exposures varies with countries, regions and even within horizons of mine pits (Reisner et al., 1985; Heppleston, 1988; Gautrin et al., 1994).

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2. We assume that protecting against fibrosis in the form of simple coal workers’ pneumoconiosis (sCWP) will also protect against lung cancer. This assumption is discussed in the next section.

PNEUMOCONIOSIS AND LUNG CANCER IN COAL MINERS

Epidemiological studies in coal miners have indicated that the risk of dust-related disease is subject to considerable variation. The incidence of sCWP and PMF varies with countries, regions and even within horizons of mine pits (Reisner et al., 1985; Hepplston, 1988; Gautrin et al., 1994). German epidemiological studies showed that the risk of contracting sCWP between coal fields varied between 2 and 40%, although miners had comparable levels of exposure (for a review see Morfeld and Piekarski, 1998). Neither mineral content nor percentage of quartz could account for these differences and in fact a low prevalence of sCWP sometimes occurred in collieries with higher gravimetric concentrations of quartz. In attempting to explain these differences, many studies have been conducted comparing the quartz content, the biological activity of the coal mine dusts and the incidence of CWP or PMF (Davis et al., 1982; Rosmanith et al., 1982), but no consistent relationship has been observed between any in vitro or in vivo test of biological activity and quartz content or epidemiological outcome.

Despite the significant percentage of quartz in coal mine dusts and its accumulation in the lungs, no excess mortality from lung cancer in coal miners has been shown in numerous reports reviewed at the IARC (IARC, 1997). A recent meta-analysis of lung cancer from 14 studies on mortality in coal miners (Morfeld et al., 1996, 1999) showed a pooled relative risk of 0.96 (0.92–1.00), but it was noted that all follow-up studies were negative, whereas the odds-ratio case–control studies demonstrated an elevated lung cancer risk. Studies in Germany (Morfeld et al., 1997, 1999) and France (Auburtin, 1998) showed a significant increase of lung cancer among those with CWP in comparison to those without CWP, and suggested that a healthy worker survivor effect could mask excesses in total cancer and lung cancer in follow-up studies. However, two large epidemiological studies among British (Miller et al., 1997) and Dutch (Swaen et al., 1995) coal miners were unable to identify any relationship between CWP and lung cancer.

Returning to our second basic assumption, this would mean that a possible lung cancer risk due to quartz would be prevented by protecting against fibrosis in the form of CWP. In standard setting for chrysotile it has been argued that mechanisms for fibrosis and lung carcinogenesis are linked in a similar way (Meldrum, 1996). This also implies that if we know the amount of dust, including quartz, causing CWP in coal miners, we could calculate a safe exposure level for quartz in CWP and lung cancer. Further, if this quartz threshold load were a general one, this might also be used to set a safe exposure limit for workers exposed to mixed dusts containing quartz.

LUNG FIBROSIS AND CANCER IN COAL DUST-TREATED ANIMALS

Few animal studies have been conducted with coal dust that can be used for risk assessment in humans. Inhalation studies (Lewis et al., 1989; Nikula et al., 1997) in rats and monkeys exposed to a low concentration of coal dust (2 mg/m³, 7 h/day, 5 days/week, 24 months) did show alveolar hyperplasia in the rat, but no excess of lung tumours. Also, no lung tumours were reported in rats exposed to coal mine dust at 6.6 and 14.9 mg/m³ (6 h/day, 5 days/week) for up to 20 months (Busch et al., 1981), despite large deposits of coal dust in macrophages and the interstitium. In contrast, lung tumours have been found after inhalation for 24 months (5 h/day, 5 days/wk) of 200 mg coal dust/m³ (Martin et al., 1977) by rats, although the incidence of tumours (11%) was not significant due to a limited number (n = 6) of control animals investigated. Lung tumours have also been found after repeated intratracheal instillations of five different coals up to cumulative doses of 60 and 120 mg (Borm et al., 2000; Pott et al., 2000). In the latter study lung tumours were found in 34–72% of the animals at 129 weeks and the coal mine dust with the highest quartz content (16.7%) caused the lowest tumour rate. At similar intratracheal doses (50 mg, single instillation) of 30 different coal mine dust samples with different quartz content (0.3–15.1% quartz) no lung tumours were reported after a histological investigation of two rats per group (Rosmanith et al., 1982).

At the applied dose rates, saturation and retardation of macrophage clearance seems a fact since alveolar clearance was found to be impaired after two weekly injections of 10 mg coal dust (<3 µm) for 2 weeks (Martin et al., 1977). Such an impairment of macrophage clearance is known to lead chronically to lung overload, since at a particle volume of ~6% of the normal macrophage the function starts to become impaired (Morrow, 1988). Particle overload in long-term inhalation assays in rats is known to result in lung tumours for poorly soluble non-toxic dusts (PSPs), whereas a lung tumour response in mice and hamsters under similar conditions has not been found (ILSI Risk Science Institute Workshop Participants, 2000). Thus, there is clearly a species difference with respect to the response of a particle-overloaded lung and the development of lung tumours. A major ques-
Table 1. Overview of autopsy studies in coal miners that have documented lung dust and quartz burden

<table>
<thead>
<tr>
<th>Subjects</th>
<th>Exposure period</th>
<th>Lung dust burden (g)</th>
<th>Lung quartz burden (g)</th>
<th>Retained dose (% of respirable dust)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>UK coal miners (PMF: 32; sCWP: 58), mean age: 60</td>
<td>No data, &lt; 1956</td>
<td>PMF: 17.6 sCWP: 12.7</td>
<td>PMF: 0.4 sCWP: 0.3</td>
<td>(Rivers et al., 1960; Nagelschmidt et al., 1963)</td>
<td></td>
</tr>
<tr>
<td>German coal miners (CWP degree 0 or 1), two regions, Ruhr (49), Saar (16), age at death: 17–68</td>
<td>Exposure years: 1–12 yr; 0–10 000 shifts</td>
<td>Ruhr: 15 (2–45) Saar: 7.5 (1–25)</td>
<td>No data No data</td>
<td>(Stöber et al., 1966)</td>
<td></td>
</tr>
<tr>
<td>US coal miners (n = 63)</td>
<td></td>
<td>6.9–8.8/100 g dry tissue</td>
<td>0.16–0.25</td>
<td>(Carlberg et al., 1971)</td>
<td></td>
</tr>
<tr>
<td>UK coal miners (n = 314), mean age: 60 yr</td>
<td></td>
<td>10.6</td>
<td>0.53–2.5</td>
<td>(Bergman and Carswell, 1972)</td>
<td></td>
</tr>
<tr>
<td>UK coal miners (n = 74), soft macules, fibrotics, PMF</td>
<td>1972–1977</td>
<td>M: 7.0 F: 16.5 PMF: 15.0</td>
<td>M: 1.5 F: 4.5 PMF: 5.0</td>
<td>(Davis et al., 1977)</td>
<td></td>
</tr>
<tr>
<td>UK coal miners (n = 49)</td>
<td>1972–1977 (autopsy) exposure &lt; 1972</td>
<td>2.3–24.5% (8.8)/dry lung weight</td>
<td>(Chapman and Ruckley, 1985)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean values cohort (n = 423)</td>
<td>256 g/h/m³</td>
<td>14.4 ± 11.7 g</td>
<td>0.8 g</td>
<td>24.4 mg per g/h/m³</td>
<td>(Tran and Buchanan, 2000)</td>
</tr>
<tr>
<td>US coal miners (n = 131), age at death: 67 ± 9.8</td>
<td>1959–1973, 108± 43 mg/m³</td>
<td>13.8 ± 8.0 0.38 ± 0.25</td>
<td>4%</td>
<td>(Kuempel et al., 1997; Kuempel, 2000)</td>
<td></td>
</tr>
<tr>
<td>Australian coal miners (n = 264), age: 63.4</td>
<td>1966–1983</td>
<td>3.93 (coal)</td>
<td>No data</td>
<td>No data</td>
<td>(Leigh et al., 1994)</td>
</tr>
</tbody>
</table>

The studies of Davies et al., Chapman and Ruckley, Douglas et al. and Tran and Buchanan (Davis et al., 1977; Chapman and Ruckley, 1985; Douglas et al., 1986; Tran and Buchanan, 2000) were all done with the same cohort of coal miners, who died between 1972 and 1977 and who had been exposed underground for at least 20 yr. The cohort comprised 514 men in total, of whom 430 have disease data; classification of disease is: M, soft macules but no fibrosis; F, fibrosis; and PMF, progressive massive fibrosis.

The question is, what is the most appropriate animal model to estimate effects of PSPs in humans?

**LUNG BURDEN OF COAL AND QUARTZ IN COAL MINERS**

A number of studies in coal miners have generated data on lung quartz burden that can be used to calculate a threshold level for quartz in coal. Several post-mortem studies have been done in which the whole lung was digested or ashed, and the total or specific dust in the lung is measured (for an overview see Table 1). These studies show that in coal workers, up to 30 g of total dust may be found in the lungs, with an accumulation rate of 0.4–1.7 g of dust retained each year (IARC, 1997). The retained free silica load is usually a reflection of its content in respirable dust but is ‘concentrated’ in lymph nodes compared with the lung tissue.

Nagelschmidt et al. (1963) studied the lung dust and quartz content in lungs of 32 cases with PMF and 58 cases with sCWP from British coal miners in order to test the silica theory of the origin of PMF in coal dust exposure. The total dust as well as its quartz content were determined, and related to collagen content and age of death. No tumours were reported in any of these cases, while total dust content varied from 4.5 to 39.6 g for PMF (n = 18, mean: 17.6 g), and between 2.4 and 44.1 g (n = 27, mean: 12.7 g) for sCWP. Age, total lung weight and the total quartz content of subjects with sCWP (0.3 g) were not significantly different from those with PMF (mean = 0.43 g). No significant difference in age of death was observed between groups of coal miners when classified at different dust accumulation rates (>1, 0.5–1.0, 0.25–0.5 and 0.1–0.25 g/yr).

Stöber et al. (1966) described lung retention versus exposure years in 49 coal miners from the Ruhr region and 16 cases from the Saar region in Germany who died for various reasons >1 yr after their last exposure, but showed no or only slight pathological changes. Interestingly, lung retention was not related to exposure years but reached a plateau of 16 or 7.5 g after ~15 yr of exposure in Ruhr and Saar miners, respectively (data estimated from figs 3 and 4 in that paper). The clearance rate in both groups was found to be 0.14 per yr, equivalent to a half-life of 5 yr.

Carlberg et al. (1971) reported on the coal and free silica content in lungs and lymph nodes of 63 bituminous coal miners’ lungs. Their study also reviews
data from previous studies in other geographical areas. They list mean values of free silica concentrations of 0.18–0.57 g/100 g dry tissue, while total dust content varied between 3.9 and 12.3 g/100 g dry lung tissue. All studies referred to were published in the 1960s. Their own data showed values between 6.9 and 8.8 g (total lung dust) and 0.16 and 0.25 g (free silica). No exposure history for the investigated cases was described.

Bergman and Casswell (1972) later investigated lung dust in 314 cases who had worked in seven different British coal fields, and found an average of 10.56 g dust per lung at an average age of death of 60.1 yr. The quartz content of the retained dust varied between 2.54 and 11.92%, and was inversely related to the coal rank factor of the coal. This would mean a average quartz content per subject (two lungs) of between 0.53 and 2.5 g.

A number of studies were published on a cohort of 514 British coal miners who died between 1972 and 1977, of which 430 have disease data and 120 also have lymph burden data. Davis et al. (1977) presented graphical data on measured total dust, coal content and quartz in whole lungs of 74 deceased coal miners. Interestingly, they also had the cumulative dust exposures of 58 cases in this group, which allowed calculation of the percentage of retained dust at lifetime exposure. Their graphs show an average retention of total dust or coal in all groups of ~5%, while quartz retention was ~5% in subjects with soft macules, but 9–13% in subjects with fibrosis. The retained quartz amount is ~10-fold higher than those described by Nagelschmidt et al. (1963).

Chapman and Ruckley (1985) examined 180 specimens dissected from 49 lungs of coal miners and reported a mean lung dust content of 8.8% per dry lung weight (range = 2.3–24.5%). They also described striking differences between dusts recovered from lung and lymph nodes. Whereas total lung dust contained 6.1% quartz, the mean quartz in lymph nodes was 20.3%. The lymph nodes themselves contained 11.4% (4.6–21.1) dust expressed per g dry tissue. No exposure data or personal characteristics were listed in this study. The final report, including data from 503 coalminers and exposure data, was given in Ruckley et al. (1989). Tran and Buchanan (2000) recently used these data to derive some kinetic parameters on lung dust burden versus exposure.

Leigh et al. (1994) determined the coal dust and silica content in the lungs of 264 deceased Australian coal workers exposed to mixed coal and silica dust. They described lung coal content of 3.93 g coal and 0.18 g of silica at a mean age of death of 63.4 yr, and a significant relationship in lifelong non-smokers between coal content and age. Lung cancer was not an exclusion criterion in this study. Years at the coal face was investigated as a variable to explain for dust content (significant in all cases), but no absolute values were reported; it was only mentioned that these samples were taken from post-mortem examinations during the study period 1966–1983.

THE OVERLOAD ISSUE

Some investigators have argued that autopsy data cannot be used since the historically high exposures are suggested to cause overload. It is difficult to counteract this argument, which is not based on data, but recent studies (Kuempel, 2000; Tran and Buchanan, 2000) have modelled lung and lymph node dust burden data of US \( (n = 131) \) and UK \( (n = 514) \) coal miners and found that the retained dust values in coal miners lungs were lower than expected from a rodent-based overload model. Using physiologically based pharmacokinetic (PB-PK) modelling, they showed that the model best suited for the US autopsy data included an unimpaired first-order alveolar clearance, together with a lower first-order interstitial rate and a very slow translocation rate to the lymph nodes (Kuempel, 2000). However, a combination of a relatively slow interstitial rate (in comparison with the clearance rate) and a slower dust translocation rate to the lymph nodes led to the interstitium/sequestration compartment being the most prominent compartment of the model. Both studies report that total lung burden increased with cumulative dust exposure, and the UK study suggests that the relationship between lung and lymph node burden is nonlinear, with a decreasing rate of dust translocation to the lymph nodes for increasing lung burden (Fig. 1). No significant change was found in the lung burden with increasing post-exposure time for increasing cumulative dust exposure. These data suggest that the rat-based overload model may not

![Fig. 1. Lymph node dust burden as a function of total lung dust burden measured in biops from 514 UK coal miners (Table 1), of whom 120 had lymph burden data. Clearly visible is the slowing down in the build up rate of the dust burden in the lymph nodes when the dust burden exceeded 20 g.](image-url)
be suitable for interpreting human data since the findings showed that dusts were still retained in a ‘sequestration’ compartment, attributed mathematically to the interstitium. Sequestration of coal dust and diesel has also been observed in the interstitium of higher primates (Nikula et al., 1997).

**CALCULATION OF A SAFE EXPOSURE LIMIT FROM LUNG BURDENS**

Data of Tran and Buchanan (2000) suggest that using the kinetics of total dust in coal miners in a PB-PK model underestimates the quartz burden in total lung and lymph nodes. This implies that the true kinetics of quartz are low clearance together with a translocation rate to the lymph nodes that is initially high (at low lung burden) but becomes increasingly slow under a greater burden (Fig. 1). The slow clearance associated with quartz is likely to be due to its toxicity to macrophages (Donaldson and Borm, 1998). However, since the quartz content of coal mine dusts in these studies is relatively small (5% on average), there is not enough quartz to induce a total impairment of macrophage clearance. Furthermore, impairment of clearance is associated with inflammation and only substantial inflammation is associated with fibrosis. Thus, it is reasonable to assume a low clearance rate of quartz in the absence of fibrosis.

Therefore, it is assumed that, in contrast to coal, the clearance of quartz is already impaired at very low levels, and quartz accumulates in the lung equivalent to the deposited dose. This means that:

\[
\text{lifetime burden (mg)} = \text{conc. (mg/m}^3\text{)} \times \text{deposited fraction} \times \text{ventilation (m}^3/\text{day}) \times \text{workdays (days/yr)} \times \text{duration (yr)} \quad (1)
\]

The deposited fraction for respirable particles (<5 μm) in humans is 0.12 and the lung ventilation is 13.5 m³/day for a Caucasian male undergoing the heavy exercise associated with underground coal mining (IRCP, 1994). If we assume there are 200 working days/yr (allowing sick-leave) and a time underground of 30 yr, we are able to derive the concentration level (C) of quartz from the formula:

\[
C = \frac{\text{lifetime burden}}{(\text{deposited fraction} \times \text{ventilation} \times \text{workdays} \times \text{duration})} \quad (2)
\]

\[
= 1.0 \text{ g} \times 1000/(0.12 \times 13.5 \times 200 \times 30) = 0.10 \text{ mg/m}^3
\]

The mean lung burden of 1.0 g in equation (2) is derived from fig. 4 and table 2 of Davis et al. (1977), which is the only study to include lungs without fibrosis. The graphic data suggest that 4, 10 and 13% of the retained burden in patient with macules, fibrosis or PMF, respectively, is quartz. This, multiplied by their retained dust levels (see Table 2), leads to 0.32, 1.0 and 1.47 g of quartz per lung, respectively. However, the authors also report that the proportion of working dust exposure varied between 15 and 40% of lifetime, and therefore this range was used to calculate the total quartz load of macules, fibrosis and PMF. For macules, this range is estimated to be between 0.7 and 1.7 g, with a mean of 1.0 g (see Table 2). Additional pathological information from 23 coal miners in fig. 6 of the same paper suggest that a quartz load of 0.2–1.0 g in the lungs is associated with high dust packing but a minimal cellular response.

Taking the above quartz loads, acquired over 30 yr, as a no-effect burden for fibrosis, substitution in equation (2) leads to a NOAEL of 0.10 mg/m³ of respirable quartz when exposed for 30 yr underground. At 40 yr this would be 0.08 mg/m³. This calculation assumes that total lung dust has no effect on quartz clearance in the lung and that quartz clearance is effectively zero. Interestingly, the subjects in the same study with fibrosis or PMF have lung dust burdens of >15 g that are associated with saturation of the lymph node clearance (Fig. 1), whereas lymph node clearance is expected to be normal in those with soft macules. This means that we are probably underestimating the safe exposure limit, since there will be some clearance associated with low levels of quartz burden.

<table>
<thead>
<tr>
<th>Classification</th>
<th>Exposure CMD&lt;sup&gt;a&lt;/sup&gt; (g)</th>
<th>Exposure—quartz&lt;sup&gt;b&lt;/sup&gt; (g)</th>
<th>Retained dust&lt;sup&gt;b&lt;/sup&gt; (g, both lungs)</th>
<th>Retained quartz&lt;sup&gt;b&lt;/sup&gt; (g, both lungs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soft macules</td>
<td>197 ± 25</td>
<td>7.9 ± 1.4</td>
<td>7.0 ± 2.5</td>
<td>1.0 (0.7–1.9)</td>
</tr>
<tr>
<td>Fibrotic lesions</td>
<td>243 ± 18</td>
<td>10.4 ± 1.6</td>
<td>16.5 ± 2.0</td>
<td>6.0 (4.1–11)</td>
</tr>
<tr>
<td>PMF</td>
<td>284 ± 26</td>
<td>11.3 ± 1.5</td>
<td>15.0 ± 2.0</td>
<td>7.1 (4.8–13)</td>
</tr>
</tbody>
</table>

<sup>a</sup>The proportion of working lifetime exposure varied between 15 and 40%. Exposures must have been massive considering that 20 yr of exposure (10 mg/m³, 200 days/yr) would lead to 80 g exposure.

<sup>b</sup>Calculated from data in fig. 4 of Davis et al. (1977) showing 4, 10 and 13% of original lung dust burden in patients with macules, fibrosis or PMF is quartz and allowing for the above (a) partial coverage (mean = 27.5%) of lifetime exposure to quartz. The indicated range is based on the estimated coverage of exposure 15–40%.
DISCUSSION

This rather simple approach shows how lung burden data of coal miners can be used to estimate a safe exposure level for quartz. Using the quartz load in coal miners with maucules only a low effect level for pneumoconiosis was calculated assuming: (i) saturation of clearance of quartz at very low levels of exposure; (ii) no effect of coal on the biological activity of quartz; and (iii) no effect of the coal dust lung burden itself. A number of autopsy studies have been described with similar total lung dust burdens in miners with sCWP (Table 1), but the burden used to calculate the NOAEL for quartz-induced fibrosis (0.7–1.7) was derived from the well-documented exposure and pathology in Davis et al. (1977). Using this approach, a NOAEL for quartz-induced CWP and lung cancer would be somewhere between 0.05 and 0.13 mg/m³ (over 40 yr).

Surprisingly, the above estimates from coal miners are close to risk estimates suggested by available studies on (high) quartz exposure (Rice and Stayner, 1995; Miller et al., 1998).

Miller et al. (1998) extrapolated a silicosis risk of 5% at an average exposure of 0.1 mg/m³ for 15 yr of exposure (1740 h/yr) to respirable quartz, but the uncertainty of the model was judged to be too great to calculate a threshold. However, in making such calculations one should keep in mind the assumptions of the study and the uncertainty in the data. First, it is still questionable whether CWP and lung cancer are related at all (Swain et al., 1995; Morfeld et al., 1999). Secondly, quartz is not the only factor influencing the risk of fibrosis, since coal also has this capability. This may cause that real quartz exposure limits should be higher than calculated range. However, we also know that coal is able to mask the fibrogenic activity of quartz (for a review see Donaldson and Borm, 1998), which phenomenon would act in a different direction and drive the exposure range downwards. The current data and approach do not allow us to discern between these two effects since a lung burden of quartz, at equal dust burden, was taken as a starting point. However, another set of data comparing the lungs of patients with PMF with those with simple CWP (Nagelschmidt et al., 1963), suggests lower quartz lung burdens to cause sCWP. The individual data in their paper allow calculation of individual lung quartz load in 18 cases with PMF and 27 cases with sCWP from the weight of the dust in the lungs and the percentage of quartz in the dust (mean = 3.1%). The mean lung dust burdens of 12.7 (sCWP) and 17.6 g (PMF) are similar to those found by Davis et al. (1977). However, the mean quartz burden in sCWP is 0.31 ± 0.34 g (both lungs) and 0.43 ± 0.36 g in PMF. These lung burdens are 3- to 10-fold lower than those reported by Davis et al. (1977). Using these data in equation (2) would lead to a low observed adverse effect level (LOAEL) for sCWP of <0.03 mg/m³ and certainly a much lower NOAEL when using normal risk assessment procedures.

As a third issue, the accuracy of our estimates is dependent on the quality of the data used. Whereas one study (Davis et al., 1977) reports quartz levels at a specific pre-defined disease status, the quartz load from the other autopsy study (Nagelschmidt et al., 1963) was derived from lung dust burden and quartz percentages of whole lung. In addition, it is unknown how valid the use of autopsy data is in the calculation of lung burdens in association with specific pathology. For instance, it has been reported that quartz appears to be concentrated in the lymph nodes (Chapman and Ruckley, 1985). This means that the actual quartz load may be greater than estimated and that the lower level of the range, such as in the Nagelschmidt et al. study, is higher in reality. On the other hand, when radiological findings were compared with pathological data obtained by autopsy, silicosis could not be diagnosed radiographically in 40% of the miners exposed for 30 yr to 0.4 mg of respirable quartz/m³ with slight-to-moderate silicosis at autopsy. Their data also show that at higher exposures the proportion of false-negatives increases (Hnizdo et al., 1993). This supports the use of data from the Davis et al. study, since diagnosis was supported by pathological examination.

A basic comment on our approach would also be that, although mechanisms of quartz- and coal dust-induced fibrosis are similar, distinct pathological differences are present between simple pneumoconiosis and silicosis (Heppleston, 1988). However, it is unknown whether this difference is relevant to the total lung burden of quartz and its relevance to this risk assessment procedure. Both coal and quartz can induce fibroblast collagen production, leading to replacement of normal parenchyma with collagen, with a crucial role for alveolar macrophages, which release various soluble factors that are able to cause cytotoxicity, secondary mediator release and cell proliferation (for reviews see Schins and Borm, 1999; Castranova, 2000). We therefore suggest that the difference in pathology is due mainly to differences in the biopersistence and the intrinsic activity of both substances. Finally, the values used in deriving a NOAEL or LOAEL for quartz are based on the average human. Such values are known to vary considerably between individuals (e.g. breathing rate, deposited fraction, clearance rate), leading to a range of deposited doses. Also, the critical quartz burden will likely vary between individuals. The current approach does not take the issue of inter-human variations into account; however, this approach may form the basis for an expanded analysis.

In conclusion, the approach of using quartz burdens of coal workers without CWP proved useful as an initial evaluation of a range of safe exposure...
levels for quartz and might be relevant to other workplaces, since mixed dust rather than pure quartz exposure is typical, and also mixed dust-type pneumoconiosis is often observed. However, the clearance model for quartz needs to be refined to perform more accurate simulations of exposures that fit this lung burden in humans, and allow adjusting for inter-individual variability in lung clearance.

Acknowledgements—The authors thank Drs Peter Morfeld (RAG, Dortmund, Germany) and Trevor Ogden (editor) for helpful suggestions and references. The initial research to undertake this effort was sponsored by the Industrial Mineral Association, Brussels, Belgium.

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