Crystalline Silica: Variability in Fibrogenic Potency

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INTRODUCTION

There is a growing body of evidence supporting the contention that the ability of respirable crystalline silica to cause silicosis can vary according to the surrounding circumstances of exposure (Fubini, 1998). This has implications for targeting regulatory activities to those industries and processes of most concern in relation to exposure to crystalline silica. The UK Health & Safety Executive (HSE) has therefore undertaken a systematic review of the literature to determine the state of the evidence for this contention. Clearly, if crystalline silica does vary in its fibrogenic potency according to the surrounding features of occupational exposure, then there cannot be a single exposure–response relationship that defines the risks of developing silicosis. This review therefore addresses two related issues: (i) whether or not the fibrogenic potency of crystalline silica is variable, and if so, what are the factors which influence its variability; (ii) in the light of currently available information, what is the most reliable view that can be formed of the exposure–response relationship(s) for the development of silicosis. The main conclusions on these issues are briefly summarized below. The supporting evidence for these conclusions is detailed in the forthcoming review (HSE, 2002).

OVERVIEW OF EXPERIMENTAL AND HUMAN EVIDENCE ON THE FACTORS WHICH INFLUENCE THE TOXICITY OF CRYSTALLINE SILICA

Variability according to polymorphic type of crystalline silica

Experimental evidence indicates that the toxicity of crystalline silica varies according to polymorphic form; cristobalite and quartz appear more reactive and more cytotoxic than coesite, shishovite and tridymite. Quartz is by far the most commonly encountered polymorph of crystalline silica, although in some circumstances there can also be occupational exposure to cristobalite, e.g. from the conversion of quartz under the high temperature conditions of industrial furnaces and kilns. There has been a widespread belief that cristobalite is more toxic than quartz, largely based on an early study which we consider to be unreliable. The chemical reactivity and toxic properties of crystalline silica appear to relate to the presence of silanol groups (SiOH) protruding from the crystal surface. Cristobalite and quartz possess a similar density of surface silanol groups, hence there are no obvious theoretical grounds to suggest that there would be a difference in their toxic potency. The weight of evidence from experimental studies in vitro and in vivo shows no differences in the cytotoxic, inflammatory or fibrogenic properties of these polymorphs. Epidemiological evidence relating to the risks of silicosis from exposure to cristobalite, as judged by chest radiography, is limited in extent. The main results of relevance derive from a study in diatomaceous earth workers, with some limited supporting evidence from a study in pottery workers in which a sub-group of workers with the highest potential for exposure to cristobalite could be identified. The results of these studies suggest relatively low or similar risks of silicosis compared with a number of studies involving exposures to quartz (for similar estimates of exposure). Overall there is no clear epidemiological evidence indicating that cristobalite is more fibrogenic than quartz.

It is therefore concluded that the risks of developing silicosis from occupational exposure to quartz and cristobalite are likely to be similar, providing the surrounding circumstances of exposure are similar.

Variability due to the presence of other minerals

Occupational exposure to quartz may occur as a result of its close geological association with aluminium-containing clay minerals, such as muds, marls or

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shale-based clays. Such materials are used in the heavy clay industry to make bricks, tiles and pipes. Aluminium-containing minerals are also encountered in the pottery industry. In some coal mines some of the quartz present may be coated with aluminium-containing clay minerals such as kaolinite and illite, found in dirt bands associated with coal deposits. There is experimental, animal and human evidence all consistently pointing in the same direction to indicate that the toxic effects of quartz are reduced in the presence of such aluminium-containing clay minerals. It has been suggested that this is due to the binding of aluminium ions (Al\(^{3+}\)) to the surface silanol groups of quartz. Over the millions of years of geological formation of coal the surface of quartz grains in dirt bands associated with coal strata can become coated or intergrown with clay minerals. This reduces the amount of ‘free’ or unexposed quartz surface present. These quartz grains may be merely liberated and not fractured during coal-getting activities and thus retain their clay mineral coating. It may well be that it is the amount of ‘free’ quartz surface, rather than the total amount of quartz present in respirable coal mine dust which is of relevance to the risk of coalworker’s pneumoconiosis.

However, there is evidence from a number of animal studies indicating that the protective effect of aluminium-containing minerals may not be permanent. This is presumably due to the differential clearance of Al\(^{3+}\) and quartz from the lungs. The retained ‘cleaned’ quartz eventually begins to express its pathogenic properties. There is a lack of clear human evidence on this point.

Overall, the available evidence consistently indicates that aluminium-containing minerals will protect against the toxicity of quartz as long as co-exposure to these minerals continues. However, it seems possible that this protective effect may become less in the months and years following cessation of exposure, giving concern for the possibility of delayed silicosis development.

Variability due to particle number, size and surface area

Current knowledge suggests that regardless of the type of dust, the total surface area of dust retained in the lungs is an important determinant of toxicity. Surface area is related to particle size; smaller particles possess a larger surface area per unit mass compared with larger sized particles. Hence, smaller particle size fractions (very fine dusts) of respirable crystalline silica would be expected to produce more lung damage than equal masses of larger respirable size fractions. The available experimental evidence, although limited in extent, supports this conclusion. The available epidemiology studies do not directly inform on this issue. Overall, in view of the theoretical considerations outlined above and the limited experimental support, it would be prudent to consider that there would be a greater risk of silicosis in workers exposed to very fine particles of crystalline silica, such as might be found in silica flours, compared with exposure to equal masses of larger size respirable particles.

Variability between freshly fractured and ‘aged’ surfaces

Cleavage of crystalline silica particles into smaller fragments results in the formation of reactive free radical species at the newly generated particle surfaces. This leads to an increase in cytotoxicity in short-term in vitro tests independent of particle size reductions. However, the activity of the free radicals decays with time, a process referred to as ‘ageing’. This occurs slowly in air, but more rapidly in water. This phenomenon has not been well studied in animals, but the available evidence does demonstrate enhanced lung damage with freshly fractured quartz. Inferences drawn from human studies are consistent with the contention that exposure to aged surfaces may be less hazardous than exposure to freshly cut surfaces of quartz. Overall, there are enough grounds to conclude that occupational exposures to freshly cut surfaces of crystalline silica will pose greater health risks than exposures to ‘aged’ surfaces. From what is understood about particle ageing, the use of ‘wet processes’ should help to reduce the reactivity of freshly cut quartz surfaces, by quenching the formation of free radicals at the cut surfaces. However, this will depend on the effectiveness of the wetting process and the time interval between dust generation and inhalation. In the seconds (or less) between generating the dust and deposition of the dust in the lungs it is unlikely that wet processes could markedly alleviate the enhanced reactivity of freshly cut surfaces. Freshly cut surfaces are likely to be generated in abrasive processes such as grinding, drilling and crushing.

EXPOSURE–RESPONSE RELATIONSHIP(ES) FOR THE DEVELOPMENT OF SILICOSIS

The HSE review (in preparation) identified 12 epidemiological studies covering a range of industries in which exposure to crystalline silica occurs and in which the quantitative risks of silicosis were investigated. Useful commentaries on the strengths and weaknesses of most of these studies are available (Pilkington et al., 1996; Finkelstein, 2000). Among these studies, widely different risk estimates for the development of silicosis were reported. Much of this variation is likely to be due to inaccuracies in assessments of past exposure, uncertainties in the identification of cases of silicosis and differences in study design. However, in some studies it seems plausible that the low risk estimates for silicosis...
relative to other studies may be due to the presence of aluminium-containing minerals as well as to the absence of significant exposure to freshly cut surfaces of cristobalite silica.

In order to come to a view on the exposure–response relationship(s) for silicosis, the approach taken has been to identify the most robust study in terms of the reliability of the exposure assessment and the diagnosis of silicosis and to use this study as the starting point for comparison with other studies reflecting other circumstances of exposure. The study selected was one in Scottish coal miners (Miller et al., 1998; Buchanan et al., 2001). The miners in this cohort encountered major seams of sandstone (almost pure quartz) between which lay one of the coal seams. Coal-getting machinery cut into the sandstone and generated high exposures to respirable quartz uncontaminated with other minerals over a period of ∼8 yr. It should be emphasized that this study is not typical of most coal mining situations, in which the quartz present is usually more closely admixed with other minerals. Numerical risk estimates derived from this study are shown below (Table 1). Note that they apply to the risks of developing silicosis (defined at category 2/1+ on the ILO scale) 15 yr after exposure ends, reflecting the long period of radiographic follow-up in this workforce.

It should be noted that the risk predictions shown in Table 1 only apply when average exposures do not exceed 2 mg/m³. If average exposures exceed this value, even for periods of just 2 months, then the risks of developing silicosis are likely to rise to exceptionally high levels. This is presumably due to an overwhelming of lung defence mechanisms at high rates of dose delivery. As discussed in the analysis of Buchanan et al. (2001), the dose metric of cumulative exposure (the sum of exposures to time-weighted concentrations over a period of time) is not appropriate in circumstances where there have been periods of exposure to high absolute concentrations (>2 mg/m³).

It needs to be considered to what extent the risk estimates presented in Table 1 might be representative of silicosis risks in other industries with different circumstances of exposure. The risk estimates shown apply to conditions in which workers are exposed to freshly cut uncontaminated surfaces of quartz. Such conditions occur in many industries where abrasive processes take place (e.g. grinding, cutting, crushing and drilling). Hence, these risks are likely to apply to many exposure circumstances. However, in some industries lesser risks might pertain, depending on the presence or absence of factors (potency factors) that could influence the toxicity of crystalline silica.

The ‘potency matrix’ (Table 2) proposes how various factors might influence the toxicity of respirable crystalline silica in different circumstances of occupational exposure. In this matrix exposures to...
freshly cut surfaces of uncontaminated quartz are taken as the starting point or baseline for comparison with other circumstances of exposure, given that the most reliable quantitative risk estimates for silicosis development derive from a study reflecting these conditions. The matrix might be developed for use as a simple qualitative guide to assist in decisions on what regulatory stance should be taken in relation to particular industries or processes involving exposure to respirable crystalline silica.

REFERENCES


