CORRESPONDENCE

Fibrogenic effect of wollastonite compared with asbestos dust and dusts containing quartz

Editor—I would like to comment on a recent paper by Cambelova and Juck on the fibrogenic effect of wollastonite compared with asbestos dust and dusts containing quartz.¹

Having studied the biological effects (actually lack thereof—neither fibrosis nor neoplasia) after long-term (10 mg/m³ for 6 a day, 5 days a week for 12 months plus 12 months observation, or for a full 24 months) inhalation exposure of wollastonite in rats (McConnell et al, 1991), I was surprised to read of the results obtained in a study by Juck and co-workers.²

It is difficult to determine from the report what their rats were actually exposed to or the total exposure. The authors reported that they obtained their wollastonite sample by crushing and grinding (crushing, denaturation, etc.) and reported a geometric mean length of 11.57 ± 1.34 μm (wollastonite-China) and 9.22 ± 1.21 (wollastonite-NYCO). Although this size of fibres could be deposited into the alveolar region of the lung through inhalation, the authors do not report what else was present in the sample injected into the lung—such as, the number, size, and other characteristics of the particulates that would also be produced by “crushing” and would also be injected into the lung. Was any effort made to clean up the sample of wollastonite so that only particulates of relevant size were injected? Moreover, if a crushed sample would not be in an aerosol and all of those particulates >1.5 μm diameter in the aerosol would be filtered by the nose and upper airways and never reach the alveolar region. Also, although the authors report that each instillation contained “about 3 × 10⁶ particles sample” and that the “Exposure lasted three months”, it is impossible to determine the number of exposures—that is, 1, 2, or 3 instillations a week for 1, 2, 3, weeks, or for the full 3 months?

Notwithstanding the lack of adequate description of the protocol, I offer the following in an effort to explain the findings of Cambelova and Juck. Before conducting our inhalation studies of wollastonite we also attempted IT instillation (20 mg/rat/week for 13 weeks), but had to abandon it in favour of inhalation because of early deaths, which we ascribed to severe acute bronchiolitis obliterans. It seemed that the sample of wollastonite we used (NYCO) was contaminated into masses of non-fibrous as well as fibrous particles that plugged the small airways. There was an immediate attempt by the host to deal with these clumps of wollastonite with a foreign body fibrogenomalous type reaction. The fibres and non-fibrous particulates were clearly visible in these lesions. Interestingly, there was minimal alveolar reaction, except in areas where the airway had been completely occluded with resultant atelectasis. I have also noted this phenomenon after IT injection of other types of particulates and fibres. I am confident that if rats are given a high enough dose of most particulates by IT injection, a similar inflammatory response will be found.

Although we did not conduct hydroxyproline measurements in our study, I am sure these would have been increased due to the collagen in these foreign body granulomas in the airways. Unfortunately (and importantly), the authors did not report any histopathological findings in their study that would settle the question of the location of the increased amounts of collagen. One normally uses the lung for histopathology and the other half or even a single lobe for quantifying collagen. This is of utmost importance because the pathology induced by inhaled fibres (all types) is not in the alveoli and virtually always found in the terminal bronchioles and proximal alveolar ducts or alveoli. In contrast, IT instillation of particulates often causes these bolus type lesions higher up in the airways, which is a situation to be of potential hazard assessment because they cannot occur after inhalation; the route of human exposure of most concern. After inhalation, only respirable wollastonite fibres are found in the alveolar region and they are diffusely distributed. Also, when distributed evenly wollastonite is highly soluble in lung fluids and tissues (Bellemann and Muhle).³

The authors refer to the consensus paper produced by the health authorities in the field of fibre toxicology (McClellan et al) as giving credibility to IT instillation as a potential “... gauge of fibrogenic potential ...”.⁴ One of the most important conclusions of the workshop that impacts directly on the interpretation of the Cambelova and Juck study states that “Numerous studies have demonstrated that inhalation models best simulate the pathological responses borne only respirable-sized fibres reach the parenchymal regions of the lung. Physiological mechanisms of fibre clearance and/or inflammation depend on deposition, translocation, and clearance mechanisms. Alternate routes, including intracutaneous and intratracheal methods of fibre exposure, can provide useful information on the potential toxicity of fibres. However, the results obtained using these artificial routes can differ from those observed following inhalation exposures.” They also pointed out that “Studies using injections routes of exposure may indicate the pathogenic potential of fibres; however, these experimentalisms are either overloaded through a bolus effect or simply bypassed, bringing into question the role of such studies for assessing human risk.”⁵

Finally, while the results of this study are in conflict with the results of intratracheal (IP) injection studies (Pott et al),² these authors injected the same types and similar amounts (>20 mg) of wollastonite into the abdomen of rats and failed to produce either a significant amount of fibrosis or tumours. The IP model is very sensitive and readily reaches the peritoneum with the induction of mesothelomas. In fact, it has been suggested that the IP model is over-sensitive and therefore, like the IT model, is not appropriate for hazard or risk assessment. Nevertheless, a negative IP result would be incongruous in the light of a positive (fibrosis) result after IT injection.

In summary, I am convinced that what the authors actually produced in their studies was a fibrogenomalous bronchiolitis (probably occlusive) that had not occurred if the fibres were given by inhalation, and therefore these results have no relevance for determining the potential health effects of wollastonite in humans.

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