Editorial

On talc, tremolite, and tergiversation

Asbestos is a generic term applied to several silicates that can be separated into long, thin fibres and woven into cloth. The minerals that constitute the various types of asbestos also exist as non-asbestiform variants. Some of these minerals have a different name attached to them according to whether they are asbestiform or non-asbestiform. Thus the non-asbestiform counterpart of chrysotile is antigorite. Chrysotile, crocidolite, and amosite have specific names for their non-asbestiform counterparts but anthophyllite tremolite, and actinolite asbestos do not.

In 1986 the United States Occupational Safety and Health Administration promulgated a new asbestos standard that reduced the acceptable exposure concentration for all types of asbestos to 0·2 f/ml.[1] This standard defined asbestos as mineral fibres composed of crystalline hydrated silicates with a length of 5 μm or longer and an aspect ratio greater than 3:1. The standard recognised the distinction between asbestiform and non-asbestiform types of mineral, but the methods of differentiating the two forms were not specified. It was stated, however, that the non-asbestiform variants of three amphibole minerals would be treated as if they were asbestos. A standard that regulates non-asbestiform anthophyllite, tremolite, and actinolite in the same manner as their asbestiform counterparts assumes that they constitute as great a hazard as exposure to asbestos.

The manner in which fibres induce mesothelioma or lung cancer is unknown. Wagner first showed that mesothelioma could be induced by the intrapleural installation of free fibres.[2] No insight into the biological activity of common non-asbestiform tremolite resulted from these experiments. Subsequently Wagner *et al* showed that one form of asbestiform tremolite injected into the pleural cavity of rats produced mesotheliomas, whereas an equal dose of two non-asbestiform tremolites did not.[3] Several non-asbestiform fibres, including glass, were capable of inducing mesotheliomas provided the diameter of the fibres was less than 0·5 μm, but non-asbestiform actinolite, biotite, and talc did not produce tumours.[4] A relation was found between fibre size and the development of mesothelioma and it was concluded that the fibrous structure was the pre-eminent influence in the induction of malignant tumours of the pleura. Later, Stanton and Wrench carried out experiments using various forms of asbestos—namely, fibrous glass, and the fibrous earths including attapulgite and sepiolite.[5] The various agents were inoculated into the pleural cavity. It seemed that carcinogenicity was related to dimensional distribution of the fibres with those longer than 8 μm and width 0·25 μm or less being the most hazardous.[6] Although this hypothesis has much in its favour, at the present time it remains unproven. The relative infrequency of mesothelioma in man is probably best explained by the fact that few fibres of the required length and width find their way to the pleura, and this is especially true for chrysotile. Stanton *et al*[7] reported on further studies in rats in which both asbestiform and non-asbestiform minerals were used including samples of talc containing non-asbestiform tremolite. Asbestiform tremolite induced tumours in virtually 100% of the treated rats but non-asbestiform tremolite proved non-carcinogenic. Smith *et al*[8] carried out similar experiments, giving two different doses to hamsters. Again, asbestiform tremolite was a powerful carcinogen but the animals that were injected with non-asbestiform tremolite remained free of tumours. More recently Addison and Davis injected different forms of asbestiform and non-asbestiform tremolite into the peritoneal cavities of rats. A high proportion of respiratory tumours was found in the group given tremolite asbestos but not in the group treated with non-asbestiform tremolite.[9] Other studies have produced similar findings.[10 11]

Several investigations have been carried out among workers exposed to cummingtonite grunerite (the non-asbestiform analogue of amosite). For example, McDonald *et al* evaluated the mortality of gold miners with long tenure of employment.[12] Overall, excess deaths in the cohort were from pneumoconiosis, tuberculosis, and heart disease; non-malignant respiratory disease showed a trend with estimates of exposure but no excess or trend was evident for cancers of the respiratory system. Brown *et al* studied gold miners who had worked underground at the same mine for at least one year and found similar results.[13] Cooper *et al* studied taconite

miners employed for at least three months and found no association between respiratory cancer and tenure of work or latency.[14] Central to the issue of carcinogenicity of asbestos analogues are the studies on talc miners and millers in New York. A proportionate mortality study of talc workers was first published by Kleinfeld *et al* in 1967[15] and, later, for the same workers in 1974.[16] The study group consisted of all talc workers employed in 1940 with 15 or more years exposure. There were 108 deaths including 12 attributed to lung cancer, one to fibrosarcoma of the pleura and one to peritoneal mesothelioma. The proportionate mortality for respiratory cancer was 12% compared to 3·7% expected. The excess was seen only in the 60–79 age group and mainly in the period 1945–69. Although they give rise to suspicions, such small numbers are difficult to interpret without necropsy data, history of smoking, and environmental information. Brown *et al* conducted a retrospective cohort mortality study of 398 workers in one New York talc mine and mill from which bulk samples contained 30–60% tremolite and 5–15% anthophyllite. The main findings were nine deaths from bronchogenic cancer (standard mortality ratio (SMR) = 270) and one likely unrelated mesothelioma. No histories of smoking were available, five of the lung cancer cases had been employed at the facility for one year or less, and four men had less than two months employment. The authors concluded that the working environment posed a significant risk for the development of lung cancer, likely due to exposure to tremolite in the talc.[17] Stille and Tabershaw[18] reported on a cohort of 655 workers employed at the same location as those studied by Brown *et al* during 1948–77. An analysis was performed separating the cohort into two strata: for those with prior employment, the SMR for cancer of the respiratory system was raised at 214 (based on only two deaths). As with that of Brown *et al*,[17] this study had several limitations including the absence of data on cigarette smoking and no analysis of exposure by latency. The dichotomous analysis of cases with and without prior employment used to implicate other unknown work exposure is questionable. A further analysis of essentially the same data was performed by Lamm and coworkers and this gave similar results.[19] These authors concluded that the evidence was not consistent with a significant risk of lung cancer as a result of exposure at the facility in question.[18 19] Gamble and Piacitelli[20] updated the original cohort of talc workers from upstate New York. Their analysis added eight more years of follow-up to the study by Brown *et al*,[17] an exposure by latency analysis, and a nested case-control study to account for possible confounding by smoking and other occupational exposures. The case-control study focused on 22 cases of lung cancer each matched with three controls on date of birth and date of hire and who must have survived the case. No relation was seen between mortality from lung cancer and non-talc employment. When the data were stratified by smoking, the odds ratio decreased with tenure and the trend analysis was significant. The analysis showed a strong association between lung cancer and cigarette smoking and there appeared to be an inverse relation between exposure and the development of lung cancer. The authors have acknowledged shortcomings in their analysis, but it is none the less far more complete than similar mortality studies and provides an argument against a causal relation between lung cancer and exposure to non-asbestiform tremolite.

In the United States, the Consumer Products Safety Commission (CPSC) is charged with the control of unreasonable hazards or injuries resulting from consumer products. In late 1986, the CPSC was petitioned to ban limestone products with a tremolite content of more than 0·01%. The petition was refused with a statement from the CPSC that "there is a clear mineralogical distinction between asbestiform minerals and non-asbestiform cleavage fragments no matter whether the persistence and dimension of the so called fibres may be similar." If the sole information on the hazards of non-asbestiform tremolite was mineralogical, clearly caution would be advisable. The fact that non-asbestiform tremolite has failed to induce mesothelioma when injected into animals suggests, however, that it would be inappropriate to treat all forms of tremolite as being equally hazardous.

It is also interesting to note that the recent standards for air quality proposed by the United States Mine Safety and Health Administration[21] exclude the non-asbestiform variants of anthophyllite, tremolite, and actinolite from the asbestos portion of their standard; it is suggested that they should be regulated under the proposed respirable mine dust standard, presumably at 5 mg/m^3.

In summary, there is no evidence to suggest that the non-asbestiform mineral counterparts of asbestos are carcinogens in animals. Although the results from animal studies may not necessarily establish a lack of carcinogenicity for non-asbestiform amphiboles for humans under all exposure conditions, they do suggest that if a risk is present, it is markedly less than that for asbestos. The studies on mortality of workers exposed to non-asbestiform cummingtonite grunerite are uniformly negative. Whereas early studies of talc workers from upstate New York showed excess death rates from respiratory malignancies, exposure to dust and cigarette smoking were not taken into account; hence, the cause of the excess respiratory malignancy in these workers is highly speculative. Later studies suggest that other exposures may have been important factors in the rates of lung cancer seen. Lastly, the lack of a trend in a latency by

exposure analysis, a significant odds ratio for cigarette smoking, and an inverse relation between lung cancer and exposure when controlling for smoking have been noted. Thus the overall results argue convincingly against a causal connection between lung cancer and non-asbestiform tremolite.

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