CORRESPONDENCE

Cancer mortality and exposure to crocidolite

SIR,—De Klerk *et al* (1988;45:5-13, 1989;46:461-7, 529-36) are on rather unsafe ground in relying heavily on a single, relatively short period, occupational hygiene survey of the Wittenoom crocidolite mine and mill¹ in formulating various models relating risk for asbestos diseases and airborne exposure levels.

When he retired in 1984 Major gave me the long running thermal precipitator slides that formed the basis for the estimates of exposure for the few occupational groups he was able to study. I have reassessed some of these using modern light and electron microscopy and the results will be the subject of a future publication but it is clear that the estimates made 20 years ago underestimated the exposure considerably—up to a single order of magnitude.

Major informs me that the large number of non-fibrous compact particles on the LRTP slides degraded the performance of the (early) phase contrast microscope he used which, no doubt, reduced its resolution of the fine crocidolite fibres. At the time he had no established counting rules for guidance and is not surprised that his 27 f/ml could become closer to 200 f/ml when a microscope satisfying modern resolution criteria and currently agreed counting rules is used. On recounting, the highest light microscopy result indicated exposures of some 300 f/ml greater than 5 μ m in length and in addition some 800 f/ml less than 5 μ m in length. Results from the general area outside the plant produced up to 2 f/ml greater than 5 μ m in length.

For comparison with contemporary fibre counts additional factors such as the collection efficiency of the LRTP relative to that of the modern membrane filter method and static/personal sample differences must be considered; these also would increase the estimate of airborne fibres.

De Klerk *et al* apply Major's published estimates of airborne fibre for a few occupants in one crocidolite mill to 87 job classifications in another mill (discontinued in 1957) believed to have been dustier. The authors ac-

knowledge that this could be a considerable source of error but taken with the underestimates of dust conditions measured in 1966 and my experience in measuring other exposures in the occupational environment, it is my view that the quantitative data in their papers cannot be supported.

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- 1 Major G. Asbestos dust exposure. In: Major G, ed. *Proceedings of the first Australian pneumoconiosis conference in Sydney, 1968*. Sydney: Joint Coal Board, 1968:467-74.

Authors' reply:

We would like to make the following comments on Rogers' letter.

(1) The main emphasis in our dose response level estimates relies on the internal comparisons within the cohort and depends more on the ranking of the different jobs in the two mines and mills than on the absolute dust concentration measurements and more on the duration of exposure than the absolute dust concentrations. We have always recognised that comparisons with other studies would be much less supportable than internal comparisons and we have emphasised this.

(2) The data used in our analyses have been the only estimates available of fibre concentrations in the Wittenoom environment and have been published in refereed journals. Our use of them was discussed with Major before their being used and he helped us with our rankings of the various occupations (along with senior staff who worked in the Wittenoom industry during its period of production).

(3) We are keen to use Rogers' analyses of dust concentrations once they have been published and subjected to adequate peer review.

The thrust of our work has not been to rely on absolute dust concentrations but on relative levels of exposure between occupational groups. We believe that our internal comparisons are as valid as it will ever be possible to make them whereas external comparisons will always be difficult by the changing methodology between different industrial hygienists at different times.

Comparing biological effects of mineral fibres

SIR,—I read Dunnigan's editorial with interest (1989;46:681-2). I support his proposition that it is absolutely necessary in the research concerning mineral fibres to depend on fibre counts instead of gravimetric data. I cannot agree, however, with his implicit statement, based on arbitrary and disputable assumptions about fibre counts, that some manmade mineral fibres (glass wool, rock wool) are at least as dangerous as chrysotile.

Most evidence available points to the opposite conclusion. Most manmade mineral fibres have an amorphous chemical structure whereas chrysotile fibres are crystalline. This has serious implications for their durability. Scholze and Conradt have shown that manmade mineral fibres exhibit relatively poor durability and usually have short life times. By contrast, natural fibres were persistent against the attack of biological fluids. It is generally accepted that the durability of fibres after deposition in the respiratory system is one of the important determinants of the intensity of their biological activity and hence their ability to produce disease. In this respect it must be emphasised that a thorough review of animal inhalation studies with high airborne concentrations of glass and rock wool has not led to the conclusion of a statistically significant increase in the risk of lung cancer or fibrosis, by strong contrast with chrysotile fibres.

Assumptions about absolute fibre concentrations based on gravimetric data, such as Dunnigan presents in the cumulative dosage table, are inaccurate and not supported by evidence based on exact fibre diameters and length. Dunnigan's observation that exposure levels in the production of rock/glass wool reached 1 f/ml is not supported by occupational hygiene reports, in which it is stated that an attempt to quantify fibre levels during the earlier periods of the industry would, at best, be crude.¹

I agree with Dunnigan that threshold limit values for toxic fibres should be expressed in fibre number per unit volume rather than in a gravimetric standard. I cannot, however, concur with his conclusion that this must lead to the same threshold limit values for chrysotile and manmade mineral fibres. As I have

tried to point out in this letter, structural differences between manmade mineral fibres and chrysotile asbestos and the resulting biological evidence do not lead to the conclusion of comparable toxicity. In addition Bellman *et al* have added important knowledge regarding the considerable differences between fibre types in respect of their persistence in rat lungs: calculated half times of manmade mineral fibres in animal lungs were relatively short (for glass and rock wool about 280 days). After intratracheal instillation of the same concentrations of chrysotile fibres, the number of fibres longer than 5 µm increased continuously over two years to about 15-fold due to splitting in elementary fibrils.⁵ It is difficult to understand why this conflicting evidence should lead to similar threshold limit values for chrysotile and manmade mineral fibres because this would mean that much higher effective concentrations of chrysotile are accepted in human lungs.

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- 1 Scholze H, Conradt R. An in vitro study of the chemical durability of siliceous fibres. *Ann Occup Hyg* 1987;31:683-92.
- 2 Leineweber JP. Solubility of fibres in vitro and vivo. In: *Biological effects of man-made mineral fibres. Proceedings of a WHO/IARC conference, Copenhagen, 1982*. Copenhagen: World Health Organisation, 1984;2:87-101.
- 3 International Agency of Research on Cancer. *IARC monographs on the evaluation of carcinogenic risks to humans*. Vol 43. *Man-made mineral fibres and radon*. Lyon: IARC, 1988.
- 4 Cherrie JW, Crawford NP, Dodgson J. Problems in assessing man-made mineral fibre concentrations in relation to epidemiology. *Ann Occup Hyg* 1988;32:715-23.
- 5 Bellmann B, Muhle H, Pott F, König H, Klöppel H, Spurny K. Persistence of man-made mineral fibres (MMMF) and asbestos in rat lungs. *Ann Occup Hyg* 1987;31:693-709.

Author's reply:

I am pleased that Meijers agrees that "...it is absolutely necessary in the research concerning mineral fibres to depend on fibre counts instead of gravimetric data." This was, after all, the main message of the editorial and I should like to add that it applies not only to mineral fibres but to all res-

pirable fibrous materials, natural and synthetic, inorganic and organic.

Meijers' disagreement centres mainly on my "implicit statement that some manmade mineral fibres are at least as dangerous as chrysotile..." and that "...it follows that this must lead to the same threshold limit values for chrysotile and manmade mineral fibres" (sic).

Firstly, I hasten to emphasise that any statement to the effect that some respirable fibrous materials are as potent (or less, or more, or equally potent) as chrysotile must be qualified by adding "...on a fibre for fibre basis." To illustrate this qualification, I suggest an examination of the data from Kevlar (pulp) inhalation studies in the rat, recently published by the International Labour Office which indicates that fibrosis was seen in animals dusted for two weeks with 18 mg/m³, and that in rats exposed chronically (24 months) to 100 and 400 f/ml doses squamous cell tumours were found, and that dose dependent fibrosis was found in rats exposed to 25, 100, and 400 f/ml but no adverse effects were found at the 2.5 f/ml exposure level (ILO meeting of experts on safety in the use of mineral and synthetic fibres, Geneva, 1989. (Working document.))

In the first study the authors indicate that a dust cloud of 18 mg/m³ corresponds to 2000 f/ml. Compare this with the number of fibres (L ≥ 5 µm, D ≤ 0.1 µm) that have been counted in 1 mg of UICC chrysotile: 13 300 × 10⁶. If one were to disperse 18 mg of UICC chrysotile fibres in one cubic metre some 239 400 f/ml of chrysotile would be found. On the other hand, if 239 400 f/ml (chrysotile) is equivalent to 18 mg/m³ then 100 f/ml would correspond to 0.007 mg/m³.

On the basis of these numbers, I submit that if Kevlar (pulp) fibres, at exposure levels of 100 and 400 f/ml—that is, 0.9 mg/m³ and 3.6 mg/m³—produce fibrosis and tumours it would be surprising if exposure to 100 and 400 f/ml of chrysotile (0.007 and 0.028 mg/m³) produced similar effects. This example illustrates the importance of comparing biological effects of all respirable fibrous materials not only on a gravimetric basis but more appropriately on the basis of fibre number.

With respect to manmade mineral fibres, specifically glass fibres (including special purpose fibres) or rock wool in inhalation studies conducted

to data, the ILO working document referred to above states: "In several of the relevant studies, an increase in lung tumours that was not statistically significant was found in exposed animals. In all of the carcinogenicity bioassays conducted to date similar mass concentrations of chrysotile asbestos have clearly induced lung tumours, whereas crocidolite asbestos has induced few or no tumours. However, available data are insufficient to draw conclusions concerning the relative potency of various fibre types, because the true exposure (number of respirable fibres) was not characterised in most of these studies" (page 11, emphasis added).

I agree with Meijers that durability is of paramount importance in determining long term potency. This appears to be the key factor separating chrysotile asbestos from the amphiboles, the latter persisting (and thus accumulating with repeated exposures) for a whole lifespan. But it seems that the final word on the relative in vivo solubilities of different fibres has not yet been said. Indeed, the ILO working document indicates: "The solubility of man-made mineral fibres in vitro and their durability in vivo vary with chemical composition. While, in general, glasswool fibres appear to be relatively non-durable, one sample (editor's note: fibres of alkali free borosilicate glass) was shown to be very insoluble in vitro. Conversely, while in one study ceramic fibres were very durable, one sample proved to be as soluble as glasswool used for comparison in the same experiment in vitro. Insufficient samples of slagwool and rockwool have been tested to allow a prediction of their overall range of solubility in tissues. On the available evidence, no generalisation can be made regarding the durability of any single class of man-made mineral fibres" (page 12, emphasis added).

I would submit that this whole issue should not be regarded as a matter of controversy but rather as a subject of future well designed experimental research investigations.

- 1 Palekar LD, Most BM, Coffin DL. Significance of mass and number of fibers in the correlation of V79 cytotoxicity with tumorigenic potential of mineral fibers. *Environ Res* 1988;46:142-52.