American Journal of Industrial Medicine 14:247–249 (1988)

LETTER TO THE EDITOR

Tremolite, Other Amphiboles, and Mesothelioma

The importance of asbestos fiber type in the etiology of malignant mesothelioma has been a major scientific and practical issue since it was first noted by Wagner et al [1960]. Over the years, epidemiological evidence has accumulated sufficient to persuade many of us that the amphiboles, not chrysotile, are mainly to blame. We recently reviewed this evidence [McDonald and McDonald, 1987] and some has been cited by Dr. Jacques Dunnigan [1988]. The introduction of analytical transmission electron microscopic analyses of lung tissue has added a new dimension of greater specificity than was possible in the past when exposure was, of necessity, assessed from work histories and scanty environmental measurements. Even so, this approach too has its limitations and uncertainties:

1. Fibers present in lung tissue at death, at varying periods after first or last exposure, do not necessarily reflect the past, qualitatively or quantitatively. We know, indeed, that amphibole fibers are not only retained more readily than chrysotile but for much longer. It follows that only studies well controlled for time-related variables can be interpreted.
2. Lung tissue studies depend on the availability of post mortem and surgical material, both of which are liable to many types of selection bias. This problem is compounded by the need for similar tissue from comparable referents.
3. Inhaled and retained fibers are not evenly distributed throughout the lung and investigators, who must be thankful for what they can get, seldom, if ever, take this source of variation (error) into account.
4. The significance of fibers in lung tissue at death will depend on the carcinogenic mechanism. If the fibers act as the primary carcinogens, retention may be of critical importance. If they act in some other way, for example as a transport medium for chemical carcinogens (e.g., polycyclic hydrocarbons from tobacco smoke) to the target organ, or by activating some latent virus already present, long-term retention may have little relevance.

For these reasons, lung burden studies provide just one more element in the jigsaw of causation but do not necessarily outweigh other types of evidence. Nevertheless, their potential significance has been sufficient for our group to give priority to this approach in recent epidemiological work. This is because we are primarily interested in objective, quantitative, and discriminatory indicators of past exposure rather than carcinogenic mechanisms.

Address reprint requests to J. Corbett McDonald,MD, Professor, Department of Clinical Epidermiology, The Cardiothoracic Institute, University of London, Fulham Road, London SW36HP, United Kingdom.
Accepted for publication February 16, 1988.

The results of two large surveys, completed but unpublished, bear directly on the questions raised by Dr. Dunnigan. The first concerns the remarkable difference in lung cancer risk observed in Quebec chrysotile miners and millers [McDonald et al., 1980] and in South Carolina chrysotile textile workers [Dement et al., 1982; McDonald et al., 1983a]. Analysis of postmortem tissue from nearly 200 deceased members of these cohorts showed that the miners and millers had many times more chrysotile and tremolite fibers in their lungs than the textile workers. While this was compatible with there having been twelve mesotheliomas in the Quebec cohort and only one on South Carolina, it clearly did not explain the fact that the SMR for lung cancer was five times higher in South Carolina than in Quebec. This forces us to speculate on the possible presence of some other factor in the textile industry, such as sprayed mineral oil, not reflected in either environmental or biological estimates of fiber exposure. We may note in passing that the lung cancer experienced by workers in another textile plant in Pennsylvania, where, in addition to chrysotile, small amounts of amosite and crocidolite were used, was almost the same as in South Carolina but, instead of one mesothelioma, there were at least fourteen [McDonald et al., 1983b].

The second unpublished survey of relevance has entailed electron microscopic examination of some eighty mesothelioma cases and individually matched referents from across Canada (excluding British Columbia) from deaths in 1980–84. Statistical analyses indicate that long amphibole fibers ($\leqq 8$ μm) strongly discriminated between cases and referents, with no additional information from shorter fibers. No significant discrimination was given by chrysotile fibers per se; however, an important component of the amphibole contribution was from long tremolite fibers, a proportion but not all of which may well represent chrysotile contamination.

The potential importance of the tremolite factor, noted by Pooley [1976] and Rowlands et al. [1982], was directly demonstrated in vermiculite miners and millers whose only mineral fiber exposure was from contaminating tremolite [McDonald et al., 1986]. The lung cancer and mesothelioma experience of this cohort was, dose for dose, many times worse than that of Quebec chrysotile miners and millers. The contribution of fibrous tremolite to mortality from these causes was also suspected in New York State talc miners many years earlier [Kleinfeld et al., 1967].

Tremolite is commonly found in association with many mineral deposits, some of which are exploited for industrial use and others, not. Much further research will be needed to estimate the proportion of occupational, para-occupational, and background cases of mesothelioma caused by fibrous tremolite and the relative importance of the various possible sources, including chrysotile contamination.

On present evidence, Dr. Jacque Dunnigan's last sentence, taken literally, would appear to be true: most epidemiological studies, including those with lung burden analysis, suggest that "amphiboles are mainly responsible, whereas chrysotile alone has little or no mesothelioma-producing potential". Although tremolite is an amphibole and some of it may come as part of the industrial chrysotile package, this does not detract from the essential thrust of Dr. Dunnigan's conclusion.

J. Corbett McDonald, MD, FRCP,
Department of Clinical Epidemiology,
Cardiothoracic Institute, Brompton Hospital,
London SW36HP United Kingdom

REFERENCES

Dement JM, Harris RL, Symons MJ, Shy C (1982): Estimate of dose-response for respiratory cancer among chrysotile asbestos workers. Ann Occup Hyg 26:869–887.

Dunnigan J (1988): Linking chrysotile asbestos with mesothelioma. Am J Ind Med 14:205–209.

Kleinfeld M, Messite J, Kooyman O (1967): Mortality experience in a group of asbestos workers. Arch Environ Health 15:177–180.

McDonald AD, Fry JS, Woolley AJ, McDonald JC (1983a): Dust exposure and mortality in a American chrysotile textile plant. Br J Ind Med 40: 361–367.

McDonald AD, Fry JS, Woolley AJ, McDonald JC (1983b): Dust exposure and mortality in an American factory using chrysotile, amosite and crocidolite in mainly textile manufacture. Br J Med 40:368–374.

McDonald AD, McDonald JC (1987): Epidemiology of malignant mesothelioma. In Antman K, Aisner J (eds): "Asbestos-Related Malignancy". London: Grune & Stratton Inc., pp 31–55.

McDonald JC, Liddell FDK, Gibbs GW, Eyssen GE, McDonald AD (1980): Dust exposure and mortality in chrysotile mining. 1910–75. Br J Ind Med 37:11–24.

McDonald JC, McDonald AD, Armstrong B, Sébastien P (1986): Cohort study of mortality of vermiculite miners exposed to tremolite. Br J Ind Med 43:436–444.

Pooley FD (1976): An examination of the fibrous mineral content of asbestos lung tissue from the Canadian chrysotile mining industry. Environ Res 12:281–298.

Rowlands N, Gibbs GW, McDonald AD (1982): Asbestos fibres in the lungs of chrysotile miners and millers—A preliminary report. Ann Occup Hyg 26:411–415.

Wagner JC, Sleggs CA, Marchand P (1960): Diffuse pleural mesothelioma and asbestos exposure in the North Western Cape Province. Br J Ind Med 17:260–271.