

Malignant Mesothelioma Caused by Childhood Exposure to Long-Fiber Low Aspect Ratio Tremolite

F. Magee, MD, J.L. Wright, MD, N. Chan, MD, L. Lawson, MD, and A. Churg, MD

A 41-year-old man was found to have a malignant mesothelioma of the pleura. During childhood in Corsica, he had been exposed at home to chrysotile ore from the Canari mine. Analysis of lung mineral content revealed background levels of chrysotile but an elevated level of tremolite and actinolite asbestos. The latter had a geometric mean length of 3.7 μm , a value considerably longer than we have found for tremolite and actinolite from Quebec chrysotile miners but roughly the same as the mean length of amosite and crocidolite in workers with occupational amphibole exposure. No tremolite or actinolite fibers of length greater than 8 μm microns and width less than 0.25 μm were observed. The mean aspect ratio of the tremolite and actinolite fibers was 7, a value similar to that found in chrysotile miners with mesothelioma but considerably less than the mean aspect ratio of amosite and crocidolite from those with occupational exposure. These data suggest that long-fiber tremolite is a potential mesothelial carcinogen in humans, and that fiber length is more important than fiber aspect ratio in this regard.

Key words: asbestos, chrysotile, tremolite, mesothelioma

INTRODUCTION

There is considerable epidemiologic evidence that the amphibole fibers amosite and crocidolite are more dangerous in regard to human mesotheliomas than are fibers of chrysotile [Becklake, 1983; Churg et al, 1984]. Chrysotile ores commonly contain a small percentage of the amphibole asbestos minerals tremolite and actinolite. The possible effects of these latter fibers on the mesothelium are uncertain. In animals, long-fiber high aspect ratio tremolite is a powerful mesothelial carcinogen [Stanton et al, 1981; Wagner et al, 1982]. Yazicioglu et al [1980] have reported human mesotheliomas apparently caused by tremolite in material used as stucco. We have shown that Quebec chrysotile miners with mesothelioma have considerably elevated lung burdens of tremolite compared to miners without mesothelioma, which suggests that tremolite may play a role in mesotheliomas occurring in chrysotile miners.

Department of Pathology and UBC Health Sciences Centre Hospital, Departments of Medicine and Pathology, St. Paul's Hospital, University of British Columbia, Vancouver, British Columbia, Canada. Address reprint requests to Andrew Churg, MD, Department of Pathology, University of British Columbia, 2211 Westbrook Mall, Vancouver, B.C., Canada V6T 1W5.

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TABLE I. Fiber Concentrations in Present Case and Mean Concentrations in Other Reported Series ($\times 10^6/\text{g}$ dry lung)

Group	Chrysotile	Tremolite amphiboles
Present case	0.3	2.1
General population of Vancouver [Churg and Wiggs, 1986]	0.3	0.4
Chrysotile miners with no asbestos- related disease [Churg, 1983]	23	58
Chrysotile miners with mesothelioma [Churg et al, 1984]	64	540
	Amosite	Crocidolite
Shipyard and insulation workers with mesothelioma [Churg and Wiggs, 1984]	9.9	2.9

TABLE II. Tremolite Fiber Sizes and Aspect Ratios (Sizes in Microns; Values as Geometric Means (geometric standard deviations))

Group	Length	Width	Aspect ratio
Present case	3.7 (2.1)	0.52 (1.9)	7.0 (1.8)
General population of Vancouver [Churg and Wiggs, 1986]	1.6 (2.0)	0.24 (1.8)	6.5 (1.9)
Chrysotile miners without asbestos- related disease [Churg, 1983]	2.0 (2.1)	0.21 (2.0)	10 (2.2)
Chrysotile miners with mesothelioma [Churg et al, 1984]	1.8 (2.0)	0.17 (2.0)	11 (2.0)
Shipyard/insulation workers [Churg and Wiggs, 1984]			
Amosite	3.9 (2.2)	0.19 (1.9)	22 (2.6)
Crocidolite	2.8 (2.2)	0.10 (1.9)	33 (2.8)

TABLE III. Cumulative Percentage of Tremolite Fibers in Various Length Categories

Width $< (\mu\text{m})$	Length (μm)	
	> 8	> 5
0.1	0	0
0.25	0	0.5
0.4	0.5	2
0.5	3	4
0.75	6	18
1.0	6	18
1.5	12	36

Table III shows the cumulative percentage of tremolite and actinolite fibers meeting a variety of size criteria, including those proposed by Stanton et al [1981]. Figure 1 provides data on proportions of fibers in all length and width categories. No fibers longer than $8 \mu\text{m}$ and narrower than $0.25 \mu\text{m}$ were observed.

DISCUSSION

As noted in the Introduction, the effects of tremolite in humans are uncertain. The present case provides an unfortunate but instructive "biological experiment" in

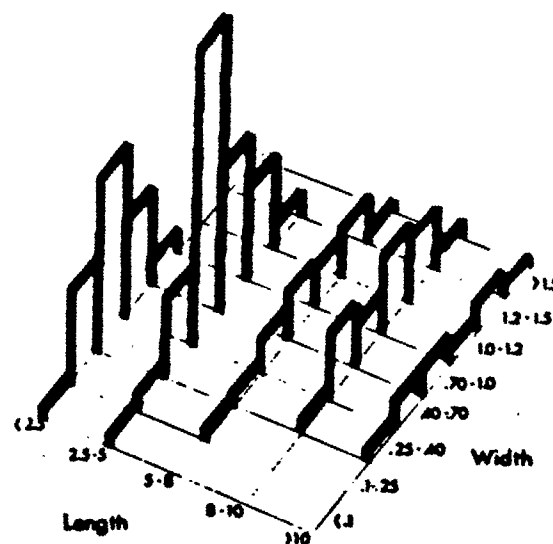


Fig. 1. Relative proportion of tremolite and actinolite fibers as a function of length and width. Fiber sizes are in microns.

this regard. We presume that the important exposure in this case was to the chrysotile product of the Canari mine, although, given the widespread presence of asbestos outcrops in Corsica and the use of crushed serpentine for paving roads in that area [Viallat and Boutin, 1980], other exposures are also possible. Whatever the exact source of exposure, by the time of our examination some 30 years later, the patient's pulmonary chrysotile fiber burden was well within the range of the general population, and the size distribution of his chrysotile fibers also resembled that found in the general population (data not shown). By contrast, his lung contained more tremolite than chrysotile. This phenomenon, which appears to reflect either low deposition of chrysotile in lung or rapid clearance of chrysotile from lung, has been reported in long-term chrysotile miners [Rowlands et al, 1982; Churg, 1983].

What is particularly interesting in this case is the relatively small amount of tremolite present and the long size but low aspect ratio of the fibers. The concentration data can be appreciated by examining Table I which shows that the present case has a slightly elevated tremolite level compared to the general population, but a level 2 orders of magnitude less than was found in five chrysotile miners with mesothelioma [Churg et al, 1984]. The concentration of tremolite was, however, quite similar to the mean values for amosite and crocidolite found in a series of shipyard and insulation workers with mesothelioma [Churg and Wiggs, 1984].

The size data (Table II) show that the geometric mean fiber length is much longer than that of the tremolite found in chrysotile miners with or without mesothelioma [Churg, 1983; Churg et al, 1984] and is much closer to the amosite and crocidolite fibers found in the shipyard and insulation workers [Churg and Wiggs, 1984]. However, the aspect ratios of the tremolite fibers are very similar to those of chrysotile fibers in the chrysotile miners and much lower than the values for amosite (Table II).

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The issue of fiber size and mesothelial carcinogenesis has attracted considerable attention. The early work of Stanton et al [1977] suggested that fibers longer than 8 μm and narrower than 1.5 μm were carcinogenic if the fiber involved was durable. However, the later work of Stanton et al [1981] showed that fibers longer than 8 μm and narrower than 0.25 μm were the most dangerous, and fairly similar size ranges have been derived from the work of Pott [see Harington, 1981]. How well these size criteria apply to human exposures is uncertain. That mesothelioma has never been reported in humans after exposure to anthophyllite, a relatively broad fiber, suggests that the 0.25- μm (or even narrower; see Harington [1981]) cutoff is more important than the 1.5 μm value. However, the present case implies that the 8/0.25- μm cutoff may not apply to humans, since no fibers meeting these criteria were found (Table III; Fig. 1).

Obviously it is difficult to draw conclusions from a single case, but our data imply that long-fiber low aspect ratio tremolite is a mesothelial carcinogen at about the same lung burden as equally long but much higher aspect ratio amosite or crocidolite. The observations suggest that fiber length may be more important than high aspect ratio in human mesothelial carcinogenesis.

ACKNOWLEDGMENTS

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