

LETTER TO THE EDITOR

Reply to Dr. Dunnigan

Dr. Dunnigan's commentary (1988) raises some very important points, both about the issue of chrysotile as a mesothelial carcinogen in man, and about the interpretation of studies of lung mineral content. As Dr. Dunnigan is undoubtedly aware from his long association with the Quebec chrysotile industry, the distinction between disease caused by chrysotile and that caused by amphiboles (amosite and crocidolite) has often been ignored, both in the scientific literature and in the regulatory process. I agree with him entirely that this distinction is crucial, because it is clear that chrysotile and the amphiboles do have different potential for inducing disease. I have recently reviewed, in detail, elsewhere [Churg, 1988] the topic of chrysotile, tremolite, and their relation to mesothelioma in man, and, rather than repeat all of the detail and numerous references here, I shall just summarize the main conclusions as they relate to Dr. Dunnigan's presentation.

A basic question of immediate importance in this regard is: "Does chrysotile cause mesothelioma in man at all, and, if so, what dose is required?" Dr. Dunnigan's review seems to imply that because various epidemiologic studies have concluded that amphibole is *mainly* responsible for mesothelioma in man, this implies that amphibole is *entirely* responsible for mesothelioma in man. However, there is a crucial difference between saying that a certain type of asbestos is a *weak* mesothelial carcinogen and saying that it is *not* a mesothelial carcinogen (between "little or no" to use Dr. Dunnigan's last sentence), and Dr. Dunnigan appears to be equating these terms.

One of the major problems in addressing this issue, of course, is the frequent existence of coexposures to both chrysotile and amphibole. However, in my review [Churg, 1988], I was able to find 53 cases in which a reasonable argument (based in part on analysis of mineral content, see below) could be made that a mesothelioma was caused by chrysotile. In saying this, it is worth noting that, of those 53 cases, 41 were found in individuals exposed to chrysotile ore in some form, usually from mining and milling. Ten cases occurred in chrysotile factory workers, and in two cases there was evidence of chrysotile exposure in other settings (albeit these two cases were included more for the sake of argument than as proven examples). Given the interest in the question of chrysotile and mesothelioma in man, the fact that I was only able to find 53 possible cases of chrysotile induced mesothelioma reinforces the idea that chrysotile by itself is not a very powerful carcinogen.

From the limited information available, the greatest incidence of chrysotile

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induced mesotheliomas appears to be in Quebec chrysotile workers, and this group is known to have been exposed to extremely high levels of dust for long periods [McDonald et al., 1980]. The cases in chrysotile factory workers have also all occurred in settings which, by today's standards, represent high exposure. It is worth emphasizing, as does Dr. Dunnigan, that a variety of studies of workers exposed at much lower regulated levels have failed to demonstrate chrysotile-induced mesotheliomas. Furthermore, studies of the nonmining/milling population living in the asbestos mining townships in Quebec, a population with substantial environmental exposure to chrysotile, have failed to show an increased risk of mesothelioma [McDonald, 1985]. Thus, review of the epidemiologic data suggests that chrysotile does produce mesothelioma in man, but that such tumors are only seen with high exposure.

This problem can be approached in another fashion, namely by examining the mineral content of lung tissue. This approach has the advantage of ruling out occult exposure to amosite or crocidolite. In 11 of the 53 cases mentioned above [Magee et al., 1986; McConnochie et al., 1987; Churg and Wright, 1988], mineralogic analysis was performed and only chrysotile ore components (chrysotile plus its natural contaminant tremolite) were found. In this circumstance one can hardly argue with the notion that chrysotile (at least chrysotile ore) can cause mesothelioma in man, and I fail to understand how Dr. Dunnigan can interpret my own published data as indicating anything but this.

Mineralogic analysis also sheds light on the question of dose. When we compared the pulmonary asbestos content of nine Quebec chrysotile miners and millers with mesothelioma with that of a group of exposure-period matched miners and millers with asbestosis, we found that the median chrysotile plus tremolite burden for the group with mesothelioma was about three times the median level for the group with asbestosis [Churg and Wright, 1988]. By contrast, comparing the chrysotile mesothelioma group to a group of shipyard workers with mesothelioma and amphibole (amosite and crocidolite) exposure, the chrysotile/tremolite fiber content of the lungs of the chrysotile-exposed workers was more than two orders of magnitude greater than the amphibole content of the lungs of the shipyard workers. These data again imply that induction of mesothelioma with chrysotile requires an extremely high exposure, an exposure of the magnitude (or at least a residual lung burden of the magnitude) sufficient to induce asbestosis. This is markedly different from the situation for amosite and crocidolite, where the shipyard mesothelioma cases had much lower amphibole burdens than matched shipyard asbestosis cases.

Dr. Dunnigan notes that, in a previous publication [Churg et al., 1984], we had raised the possibility that the tremolite component of the chrysotile ore was the agent responsible for mesothelioma (McConnochie et al. [1987] have also made the same suggestion), but I believe he has mistaken what we intended as thought-provoking speculation for a statement of established fact.* Although the data are suggestive, the fact is far from established.

To understand this situation, it is necessary to remember that chrysotile itself does not accumulate in human lung to any great extent, particularly compared to

*Exactly the same comment applies to the sentence that Dr. Dunnigan has highlighted concerning miners vs other workers with chrysotile exposure.

amphiboles. It is very important to understand this point, because otherwise one can easily conclude that only amphibole is causing disease, and, in fact, Dr. Dunnigan cites several studies in which those with asbestos disease have elevated amphibole but not elevated chrysotile burdens, despite known exposure to both amphiboles and chrysotile. From this he appears to conclude that chrysotile is playing no role in mesothelioma. However, this conclusion reaches the stage of *reductio ad absurdum*, since one could easily take the same data, and, using the values for asbestosis, decide that chrysotile does not cause asbestosis. What these data do indicate is that the chrysotile content of the lung may be a very poor marker of the amount of chrysotile exposure.

To return to the tremolite issue, analysis of the lungs of chrysotile miners has shown that tremolite, which is a very minor constituent of the ore to start with, equals or exceeds the chrysotile content when one examines the lung tissue [see for example, Churg et al., 1984]. Again, this process reflects the fact that chrysotile does not accumulate as readily as amphibole in human lung. However, by examining the tremolite:chrysotile ratio of fibers in the lung, one can gain some idea of the relative tremolite content of the asbestos to which a worker is exposed, since presumably the less tremolite in the asbestos, the smaller the tremolite:chrysotile ratio in the lung. When this is done [see Churg, 1988; Table 3] then the highest tremolite:chrysotile ratio is seen in chrysotile miners and millers from Quebec, and lower ratios are found in the lungs of workers exposed to various types of processed chrysotile products [Green et al., 1986; Pooley and Mitha, 1986; Churg and Wiggs, 1986]. This observation certainly implies that *some* tremolite is removed during processing the ore. However, it does not imply, as Dr. Dunnigan seems to indicate, that *all* tremolite is removed.

The conclusion I draw from these data is that workers using processed chrysotile products are exposed to relatively smaller amounts of tremolite compared to workers mining and milling the ore, but such secondary workers still have some tremolite exposure. If tremolite is, in fact, the agent of chrysotile-induced mesothelioma, then perhaps this lesser amount of tremolite in secondary products accounts for the lesser incidence of mesothelioma in chrysotile factory workers compared to chrysotile miners and millers.

A further consideration is that tremolite by itself can produce mesothelioma in man, but it appears to do so with any frequency only when the tremolite fibers are relatively long and have a high aspect ratio [See Churg, 1988; Tables 2,4]. By contrast, the tremolite found in Quebec chrysotile ore (and probably that in Cyprus as well, see McConnochie et al. [1987]) is a much shorter, stubbier fiber, a fortunate accident that may be responsible for the low incidence of mesothelioma that such chrysotile does induce [Churg, 1988; Table 4].

The published data are therefore consistent with the idea that tremolite is the agent of chrysotile-induced mesothelioma in man, but they are no more than consistent. The number of cases (especially cases in which pulmonary mineral content has been analyzed) upon which this information is based is very small, and the possibility still remains that chrysotile fiber itself, in sufficiently large doses, is a mesothelial carcinogen. What would be extremely helpful is a study of a mine in which the ore is not contaminated with tremolite, and, thus far, none have been reported.

Dr. Dunnigan's concern about the application of the foregoing data to

individual legal cases is understandable, but I do not believe that this Journal is the place to comment upon legal problems related to specific cases, particularly since such issues are subject to standards of proof which are often quite different from scientific questions. However, it is worth reiterating two points in this regard: 1) at present, the published data are consistent with the notion that, although amosite and crocidolite are much more potent mesothelial carcinogens, *extremely large* doses of chrysotile (with whatever tremolite accompanies it) can produce mesothelioma in man; and 2) there is a distinction between “no” effect and “little” effect.

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REFERENCES

- Churg A, Wiggs B, DePaoli L, Kampe B, Stevens B (1984): Lung asbestos content in chrysotile workers with mesothelioma. *Amer Rev Respir Dis* 130: 1042–1045.
- Churg A, Wiggs B (1986): Fiber size and number in workers exposed to processed chrysotile asbestos, chrysotile miners, and the general population. *Am J Indust Med* 9: 143–152.
- Churg A (1988): Chrysotile, tremolite, and malignant mesothelioma in man. *Chest*, 93:621–628.
- Churg A, Wright JL (1988): Fiber content of lung in amphibole vs chrysotile-induced mesothelioma: Implications for environmental exposure. In “*Mineral Fibres in the Nonoccupational Environment*.” Lyon: IARC, in press.
- Dunnigan J (1988): Linking chrysotile asbestos with mesothelioma. *Am J Ind Med* 14:205–209.
- Green FHY, Harley R, Vallyathan V, Dement J, Pooley F, Althouse R (1986): Pulmonary fibrosis and asbestos exposure in chrysotile asbestos textile workers: Preliminary results. *Accomplishments Oncol* 1: 59–68.
- McDonald JC, Liddell FKD, Gibbs GW, Eyssen GE, McDonald AD (1980): Dust exposure and mortality in chrysotile mining, 1910–1975. *Br J Indust Med* 37: 11–24.
- McDonald JC (1985): Health implications of environmental exposure to asbestos. *Environ Hlth Perspect* 62: 319–328.
- McConnochie K, Simonato L, Mavrides P, Chrisofides P, Pooley FD, Wagner JC (1987): Mesothelioma in Cyprus: The role of tremolite. *Thorax* 42: 342–347.
- Magee F, Wright JL, Chan N, Lawson L, Churg A (1986): Malignant mesothelioma caused by childhood exposure to long-fiber low aspect ratio tremolite. *Amer J Indust Med* 9:529–533.
- Pooley FD, Mitha R (1986): Fiber types, concentrations, and characteristics found in lung tissues of chrysotile-exposed cases and controls. *Accomplishments Oncol* 1: 1–11.