

PATHOLOGY AND EXPERIMENTAL PATHOLOGY

Pathologic Reactions to Chrysotile and Their Mineralogic Correlates

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This presentation briefly considers the correlations between pathologic reactions to chrysotile and the corresponding mineral content of the lungs. Most of these comments on the effects of chrysotile are derived from the analysis of the lungs of a series of Quebec chrysotile miners and millers, and a comparison group of shipyard workers and insulators with amphibole exposure. It should be appreciated, however, that there exists considerable epidemiologic evidence, and some mineralogic evidence, which suggests that processed (milled) chrysotile ore has different biologic properties.¹ Thus comments that apply to disease seen in chrysotile mining industry workers may not hold true for individuals with other types of chrysotile exposure.

FATE OF CHRYSOTILE IN THE LUNGS

A variety of studies have made it clear that chrysotile and amphiboles differ markedly in their ability to concentrate in lung tissue. Wagner *et al.*² have shown experimentally that, in rats constantly exposed to amphiboles, fiber concentration in the lung steadily increases; but with exposure to chrysotile, there is only a brief increase in chrysotile concentration, and this is followed by a leveling off of concentration. Whether this phenomenon reflects proximal deposition in airways because of the curled shape of the fibers, dissolution of the fibers in lung tissue juice, or extremely rapid macrophage-mediated fiber removal, is unclear. In any event, mineralogic analysis indicates that a similar phenomenon must occur in humans. For example, Wagner *et al.*³ showed that, in a series of workers with exposure to both chrysotile and amosite or crocidolite, the amphibole concentration averaged 100 times the chrysotile concentration at the time of examination. I have observed a similar effect in shipyard and insulation workers from the Pacific Northwest of North America (Table 1).

The same processes.^{4,5} Most of these are crocidolite, but were exposed (referred to, for convenience) as very minor constituent. There is no pathologic evidence of exposure of about 30 $\times 10^6$ fibers/g dry lung fibers/g dry lung, a trend. In a group of chrysotile was about 10:1 (see reference) that pulmonary tremor exposure than chrysotile the possibility that the in disease.

DIFFERENCES AS A FUNCTION OF

Much less is known of workers exposed to various agents. We examined a series

TABLE 1. Asbestos

Population
95th Percentile for 20 males from the general population of Vancouver ⁷
7 Long-term residents of Thetford never employed in the asbestos industry ¹⁰
9 Thetford chrysotile miners and millers with no asbestos-related lung disease ⁸
9 Thetford chrysotile miners and millers with only airway fibrosis ⁸
10 Thetford chrysotile miners and millers with asbestosis
14 Shipyard and insulation workers with asbestosis
5 Thetford chrysotile miners and millers with mesothelioma ⁶
32 Shipyard and insulation workers with mesothelioma not asbestosis

* Fibers $\times 10^6$ /g dry lung.

The same process also occurs in Quebec chrysotile industry workers.^{4,5} Most of these workers have not been exposed to amosite and crocidolite, but were exposed to the amphiboles tremolite and actinolite (referred to, for convenience, as tremolite) which form a natural but very minor constituent of the chrysotile ore. In a group of workers with no pathologic evidence of asbestos-related lung disease and an average exposure of about 30 years,⁵ the mean chrysotile concentration was 23×10^6 fibers/g dry lung and the mean tremolite concentration 58×10^6 fibers/g dry lung, a tremolite-to-chrysotile ratio of about 2:1 (Table 1). In a group of chrysotile workers with mesotheliomas, the mean ratio was about 10:1 (see reference 6, Table 1). These observations suggest that pulmonary tremolite burden may serve as a better marker of total exposure than chrysotile in chrysotile industry workers, and also raise the possibility that the tremolite component of the ore may play a role in disease.

DIFFERENCES IN PULMONARY CHRYSOTILE FIBERS AS A FUNCTION OF DIFFERENT TYPES OF OCCUPATIONAL EXPOSURE

Much less is known about the chrysotile content of the lungs in workers exposed to various forms of processed (milled) chrysotile products. We examined a series of 21 workers exposed in shipyard, insulation,

TABLE 1. Asbestos Fiber Concentrations in Various Populations*

Population	Chrysotile	Tremolite	Amosite + Crocidolite
95th Percentile for 20 males from the general population of Vancouver ⁷	1.0 (Mean = 0.3)	1.0 (Mean = 0.4)	0.01
7 Long-term residents of Thetford never employed in the asbestos industry ¹⁰	1.7	5.3	0
9 Thetford chrysotile miners and millers with no asbestos-related lung disease ⁵	23	58	0.06
9 Thetford chrysotile miners and millers with only airway fibrosis ⁵	47	106	0.23
10 Thetford chrysotile miners and millers with asbestosis	74	143	0.10
14 Shipyard and insulation workers with asbestosis	0.5	0.9	31
5 Thetford chrysotile miners and millers with mesothelioma ⁴	64	540	0
32 Shipyard and insulation workers with mesothelioma but not asbestosis	0.7	0.8	5

* Fibers $\times 10^6$ /g dry lung. Values are means except as noted.

textile, friction products, and manufacturing industries, and found, by comparing fiber concentrations in the workers to concentrations in a nonexposed population, that tremolite as well as chrysotile must have been present in the various end products.⁷ The pulmonary ratio of tremolite-to-chrysotile in Quebec chrysotile industry workers is fairly constant;^{5,6} however, in workers exposed to processed products, the ratio varies widely and the marked residual predominance of tremolite is not seen in their lungs,⁷ suggesting that processing of the original fibers for different commercial applications results in removal of tremolite from the final product. If tremolite really is important in the genesis of mesothelioma, the relative lack of tremolite may account for the virtual absence of mesotheliomas in those exposed to chrysotile in the textile and friction products industries.

One additional interesting point which emerged from this study was the observation that there were marked differences in the sizes of chrysotile and tremolite fibers found in workers with exposure in different types of industries. The shortest fibers were found in shipyard workers; the longest in textile, brake, and manufacturing workers; and fibers of intermediate length in insulators. It is possible that these length differences will be found to correlate with epidemiologic evidence of different disease rates in different chrysotile-using industries.⁸ Incidentally, analysis of fiber length proved to be the most reliable method of determining mineralogically whether an individual had been exposed to chrysotile by breathing urban air or in an asbestos-using occupation: fibers in the occupationally exposed group were distinctly longer (Table 2).

RELATIONSHIP OF ASBESTOS FIBERS IN VARIOUS POPULATIONS TO DISEASE PATTERNS

Table 1 shows concentrations of chrysotile and tremolite in various chrysotile-exposed populations, and a comparison group of amosite and crocidolite-exposed shipyard and insulation workers. Because, as noted, everyone in the population is exposed to all these forms of asbestos by breathing urban air, reference ("background") values for the general population of Vancouver are also recorded.

A number of interesting conclusions emerge from these data. One conclusion is that, on average, increasing amounts of fibrosis in the lung are associated with increased burdens of chrysotile/tremolite, a finding

which has previously been noted for crocidolite,² but not shown in data with regard to chrysotile.

Another important finding is that, in humans, exposure to chrysotile alone does not result in pleural mesothelioma. There is no evidence of pleural mesothelioma during the period 1940-1960 in workers exposed to chrysotile and no amosite exposure, and the ratio of chrysotile to amosite and the ratio of chrysotile to tremolite in mesothelioma is strikingly different from that in workers with only fibrosis, and the ratio of chrysotile to amosite and the ratio of chrysotile to tremolite in the genesis of mesothelioma.

An additional observation is that disease is seen at much lower levels of exposure to crocidolite compared to chrysotile, that much less amosite is required to produce the same level of disease as even applies to those exposed to chrysotile seen in the series in Table 1 would, if the ratio of chrysotile to amosite and the ratio of chrysotile to tremolite in mine dust appears to be the same as whether this is also true for chrysotile. The epidemiologic evidence implies that such fibers

A last conclusion, which is in contrast to current controversy, is that very low levels of asbestos exposure can result in disease from the data shown in the town of Thetford Mines, Quebec, Canada.¹⁰ These individuals were exposed to asbestos for years to a lifetime. They were elevated some 10 times above the level of Vancouver, a population with no background atmospheric asbestos. Furthermore, the mean size of the fibers were considerably longer but were quite similar to those of workers (Table 2). None of these workers had disease, and a variety of other factors suggest that there is no increase in the incidence of the asbestos-related diseases, therefore, that asbestos is not considerably longer (asbestos fibers) than those carried by the

TABLE 2. Geometric Mean Fiber Lengths (μ m) in Various Populations

Population	Chrysotile	Tremolite
General population of Vancouver ⁷	1.3	1.6
Long-term Thetford residents ¹⁰	2.4	2.1
Thetford chrysotile miners and millers ⁷	2.5	2.1
Workers exposed to processed chrysotile ⁷	2.5	2.5

which has previously documented in those exposed to amosite¹ and crocidolite,² but not shown for chrysotile. We are currently analyzing this data with regard to severity of asbestosis.

Another important conclusion is that, at sufficiently high levels of exposure, chrysotile ore must be judged capable of causing mesothelioma in humans. There is no other explanation for the fact that, of six cases of pleural mesothelioma in Thetford chrysotile workers analyzed by us during the period 1980-1984,⁶ five contained only chrysotile ore components and no amosite or crocidolite. The very high tremolite-to-chrysotile ratio and the very large lung burden of tremolite in those with mesothelioma is striking when compared to those with no disease or with only fibrosis, and certainly raises the possibility of a role for tremolite in the genesis of mesothelioma.

An additional observation is that, for any of the diseases listed, disease is seen at much lower pulmonary concentrations of amosite/crocidolite compared to chrysotile/tremolite (Table 1). Thus it appears that much less amosite/crocidolite compared to chrysotile/tremolite is required to produce either asbestosis or mesothelioma. This conclusion even applies to those with no disease: the levels of chrysotile and tremolite seen in the series of nine chrysotile miners without disease⁵ cited in Table 1 would, if the fibers were amosite and crocidolite, be in the range for both mesothelioma and asbestosis. Thus Quebec chrysotile mine dust appears to be relatively innocuous. It is unclear, however, whether this is also true of certain types of processed chrysotile products. The epidemiologic evidence in regard to the textile industry in particular implies that such fibers may be considerably more dangerous.⁸

A last conclusion, and one which is particularly interesting in regard to current controversies in North America about the dangers of inhaling very low levels of asbestos in public buildings such as schools, emerges from the data shown in Table 1 on seven long-term residents of the town of Thetford Mines who were never employed in the chrysotile industry.¹⁰ These individuals lived in Thetford for anywhere from 25 years to a lifetime. Their mean chrysotile and tremolite concentrations were elevated some 10 to 15 times over those of the general population of Vancouver, a population which is probably reasonably representative of background atmospheric exposure to asbestos in North America. Furthermore, the mean sizes of fibers in the lungs of the Thetford residents were considerably longer than those of the population of Vancouver, but were quite similar to the fibers found in the chrysotile industry workers (Table 2). Nonetheless, these individuals had no asbestos-related disease, and a variety of epidemiologic studies have shown quite clearly that there is no increased incidence of mesothelioma in long-term residents of the asbestos mining townships.⁹ The data just cited imply, therefore, that asbestos burdens composed of considerably more and considerably longer (and, hence, theoretically more dangerous) fibers than those carried by the general population of North America do not

produce disease. These observations should produce reassurance about the lack of danger from exposure to very low levels of asbestos in public buildings or urban air.

SUMMARY

In chrysotile industry workers, tremolite concentration exceeds chrysotile concentration by large ratios. In those exposed to processed chrysotile products, tremolite is also present, but the chrysotile-to-tremolite ratios in the lung suggest that tremolite is removed in milling the chrysotile ore. Chrysotile and tremolite concentrations are higher in those with asbestosis than those without. Analysis of lung tissue indicates that chrysotile mine dust can induce mesothelioma in humans, but extremely high lung burdens appear to be required for this process. In such workers, the ratio of tremolite-to-chrysotile is much higher than in those with parenchymal fibrosis, raising the possibility that tremolite is important in the genesis of mesothelioma. For both mesothelioma and asbestosis, the disease appears at much lower lung burdens of amosite/crocidolite than chrysotile/tremolite. Long-term residents of Thetford Mines, a chrysotile mining town, carry lung burdens that are composed of more fibers and longer fibers than residents of most North American cities, but residents of the town of Thetford who have not worked in the chrysotile industry do not have elevated lung cancer or mesothelioma rates. These observations imply that the burden of asbestos which the general population carries as a result of exposure in public buildings will not produce disease.

ACKNOWLEDGMENT

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Pulmonary Fibrosis in Chrysotile

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Asbestos exposure increased mortality from pleural and peritoneal the gastrointestinal tract asbestos-associated diseases of all asbestos type and the

In recent years, the estimate risks for asbestos dose-response scale.¹ from mortality data requires inaccurate compared to fatal conditions. Asbestos thus, it may not be recommended that mortality data have previously low levels of attempted to increase the observing pathologic approach enables detect significance but would pathogenesis of asbestos derived from a cohort previously studied epidemiologically determining exposure (old level) and in demonstrating present correlation cumulative exposure, and

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