

# Asbestos-Related Pleural Disease Due to Tremolite Associated With Progressive Loss of Lung Function: Serial Observations in 123 Miners, Family Members, and Residents of Libby, Montana

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**Background** *The community of Libby, Montana has recently been the focus of national attention secondary to widespread amphibole contamination associated with vermiculite mining and processing.*

**Methods** *Patients who had occupational and non-occupational exposure to amphibole asbestos in Libby, Montana were evaluated for progressive loss of pulmonary function.*

**Results** *Of the 123 patients evaluated, 94 demonstrated average age-corrected accelerated loss per year of vital capacity at 3.2%, total lung capacity (TLC) 2.3%, and DLCO 3.3%. All patients all had predominantly pleural changes with minimal to no interstitial disease.*

**Conclusions** *The study demonstrates a progressive loss of pulmonary function in patients exposed to tremolite asbestos. Am. J. Ind. Med. 46:219–225, 2004. © 2004 Wiley-Liss, Inc.*

**KEY WORDS:** *tremolite; asbestos; pulmonary function; Libby; vermiculite; environmental; exposure; mining; dust*

## INTRODUCTION

In November 1999, it was reported that the community of Libby, Montana was experiencing an epidemic of pulmonary disease associated with occupational and environmental contamination of asbestiform amphibole materials within the community. Investigations revealed that the asbestos contamination was associated with a vermiculite mining and processing operation. Tremolite is an amphibole which has very little commercial value but is a contaminant of the vermiculite ore source in Libby [McDonald et al., 1986a]. This report will reference the high incidence of asbestos related pleural changes and their progression associ-

ated with tremolite exposure from the vermiculite mining and processing activity in Libby. The amphibole of the Libby mine has been characterized by mineralogists as a tremolite–actinolite–richterite–winchite transition fiber and will henceforth be referred to as tremolite [US Geological Survey, Bulletin 2193, 2002].

The vermiculite bed seven miles northeast of Libby was discovered in 1916 and mined initially for asbestos by the Zonolite Corporation and then subsequently for vermiculite. It was mined by W.R. Grace & Co. from 1963 to 1990 and was for a long period of time the world's largest producer of vermiculite.

Vermiculite is a hydrated, laminar, aluminum-non-magnesium micaceous silicate, which when heated expands to between 10 and 20 times its original proportions and is excellent as an insulator, soil conditioner, and fertilizer additive [Moatamed et al., 1986].

In the process of mining and processing this material, W.R. Grace Company had multiple sites in proximity to Libby including an expanding and shipping facility. The ore body contained 21–26% tremolite and was initially pro-

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cessed on the mountain. The concentrated unexpanded ore, which contained over 2–6% tremolite [Amandus et al., 1987] was then loaded in railcars and shipped throughout the nation to over 200 regional processing or expanding sites. With the application of heat, the ore expands to an accordion like configuration. The expanded vermiculite had up to 1–3% tremolite [Amandus et al., 1987].

Both expanded and unexpanded forms of vermiculite from the mine were made freely available to the community. Many of the homes in the community were insulated with vermiculite. Vermiculite was placed on the ball fields, school track, and children played in piles of vermiculite, which were near the mining and processing facilities. The vermiculite was also used as insulation for plywood dryers in the local lumber mills and could be found in the rail yards where ore cars were loaded for shipping.

Studies of occupational exposure and disease among former vermiculite mine workers found significantly increased rates of asbestosis and lung cancer [Amandus et al., 1987]. A mortality study of the Libby area by the Agency for Toxic Substances and Disease Registry (ATSDR) found that deaths due to asbestosis were among the highest in the country at 40–60 times the expected national rate [DHHS/ATSDR, 2000].

Medical screening in the year 2000 of approximately 6,200 residents of the Libby area who lived there prior to 1990 found over 14% of all participants had radiographic changes consistent with asbestos related abnormalities. These findings represent a significant public hazard in view of the long term health impact known to be associated with amphibole exposure. Additional medical screening in 2001 added more patients, now estimated at over 1,000 plus the 491 patients in this clinical practice who are not part of the 1,000 and who have been followed for up to 14 years. These 491 patients demonstrate isolated pleural plaques to diffuse pleural or interstitial disease including 40 known deaths from asbestos-related diseases. They were examined and followed by a two physician practice specializing in pulmonary disease. The patients were either referred by internists and family practitioners or were self referred. These patients have not been previously reported. Initially, they were mostly employees of W.R. Grace as well as some family members of employees. More recently, non-occupational exposed residents of the community have been identified with asbestos-related health abnormalities. Because of extensive longitudinal medical data in this clinical practice setting, a study was undertaken to determine if there was accelerated loss of pulmonary function in this group of patients.

## MATERIALS AND METHODS

Pulmonary function studies including spirometry with bronchodilator, plethysmographic lung volumes, and single breath carbon monoxide diffusion (DLCO) were conducted.

The studies prior to 1998 were performed on a Sensormedics model 6200 and subsequently on a Medgraphics model 1085. All studies were done before and after bronchodilator utilizing Albuterol. The same technician was used throughout the entire period. Lung volumes and DLCO were measured after bronchodilator.

Normal values of pulmonary function results used spirometry as described by Knudson et al. [1983], lung volumes established by the Intermountain Thoracic Society [Kanner et al., 1984], and DLCO (non-adjusted values) by Miller et al. [1983]. All studies were reviewed to be certain that height, which was measured to the nearest half inch, and age at test date were correct, and if differences in height were present they were adjusted to match across study dates. American Thoracic Society (ATS) pulmonary function testing guidelines were used throughout [American Thoracic Society, 1995]. In total, 30 patients were removed from the study for the following reasons: chronic obstructive pulmonary disease with elevated residual volumes (14), previous thoracic surgery (1), unacceptable pulmonary function tests because of patient unreliability and inability to meet ATS acceptability criteria (9), and/or the presence of a significant non-asbestos related condition such as sarcoidosis or congestive heart failure (9). Several patients had multiple disqualifying diagnoses. The first and last set of pulmonary function tests were compared for all patients tested (153).

Since the patient values were all age corrected against the normative predicted values, changes in the percentage of predicted over time reflected changes of pulmonary function beyond that accounted for by aging. Differences between the first and last pulmonary function were tabulated and changes per year were calculated. Changes were recorded in percentage change per year because of the wide variation in ages and the usual way of presenting this data in a clinical practice setting.

Repeated measures of analysis of covariance was used to statistically test changes in pulmonary function over time with time modeled linearly. To account for individual differences in the period between assessments, the time between the first and last assessments was entered into the statistical analysis as a covariant.

The initial postero-anterior chest X-ray was graded for extent of pleural changes by the principle investigator and also by a board certified radiologist (Dr. Teel). The extent of pleural changes were graded as follows. The percentage of the lateral chest wall involved with pleural changes was measured and the average of both sides of the chest calculated. All patients were weighed at each visit and body mass index calculated.

## RESULTS

Of the 491 subjects, 220 were employees of the vermiculite facilities, 121 were family members, and 150 were

environmental exposures. Two or more sets of pulmonary functions were available on 153 patients. These subjects are representative of the Libby area population and the practice group of 491 patients. All had lived in Libby the majority of their life prior to 1990.

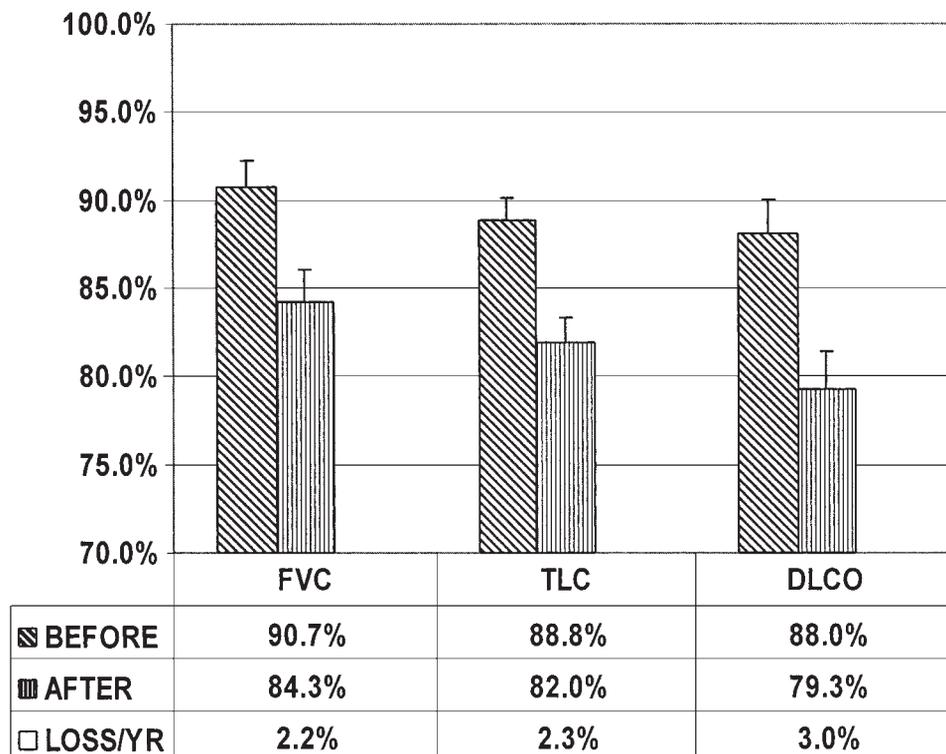
The majority of the 123 patients were ex-smokers with 8 of 123 (7%) being current smokers. Also, 27 (21%) never smoked. In total, 86 (70%) were former employees of W.R. Grace, 27 (22%) were family members of employees, and 10 of 123 (8%) were characterized as Libby environmental exposures only. In total, 99 were males (80%), 24 females (20%), and the average age was 66 years at first pulmonary function study.

Over the course of the study group observation, average BMI increased less than 1 kg/m<sup>2</sup> and there was no statistical correlation between increasing BMI and loss of lung function. Bronchial asthma was also evaluated as a confounding variable. Many subjects used a variety of bronchodilators prescribed by their personal physician although none carried a diagnosis of bronchial asthma and there was no evidence of significant changes in FEV<sub>1</sub> following bronchodilators.

The majority had pleural changes only, consisting of either pleural plaques or diffuse pleural thickening. Because only about half the patients had high resolution computed tomography (HRCT) scans, it was not possible to differentiate this further with any certainty, due to the variations between the plain PA chest film and the HRCT. A total of 67 of

123 (55%) had no evidence on chest X-ray or HRCT of interstitial changes. The remaining patients (56) had minimal radiographic evidence of irregular interstitial changes involving the bases at profusion category 0/1 or 1/0. Of 123 films reviewed, 4 subject films were felt to be normal or equivocal. Of these, all subsequently developed overt pleural changes within a few years and three of four had pleural changes consistent with asbestos exposure on HRCT.

The parameters that were felt to be most valuable for analysis were forced vital capacity (FVC), (taking the best available and valid number from each set), total lung capacity (TLC), and the single breath diffusion capacity (DLCO). In the group of 123 patients (including those with improved FVC), the average yearly loss was 2.2 % for FVC, 2.3% for TLC, and 3.0% for DLCO as calculated over an average of 35 months (Fig. 1). Using FVC as the primary measure of worsening lung function, 94 of the 123 (76%) had an accelerated loss in this parameter. Analyzing the 94 of 123 who had progressive loss of FVC, the loss per year for FVC was 3.2%, TLC 2.3%, DLCO 3.3% (Fig. 2). In total, 79 of 123 patients with greater than 1% loss of FVC per year the average yearly loss was 3.6% for FVC per year, 2.5% for TLC, and 3.5% for DLCO (Fig. 3). The loss rate in this group could not be explained by increases in weight, extent of disease initially or subsequently or other concomitant illness. For the 67 patients with pleural changes alone and with no interstitial changes, the average yearly loss was 2.2% for



**FIGURE 1.** Loss of pulmonary function; all 123 patients, average 35 months ( $P < 0.001$ ).

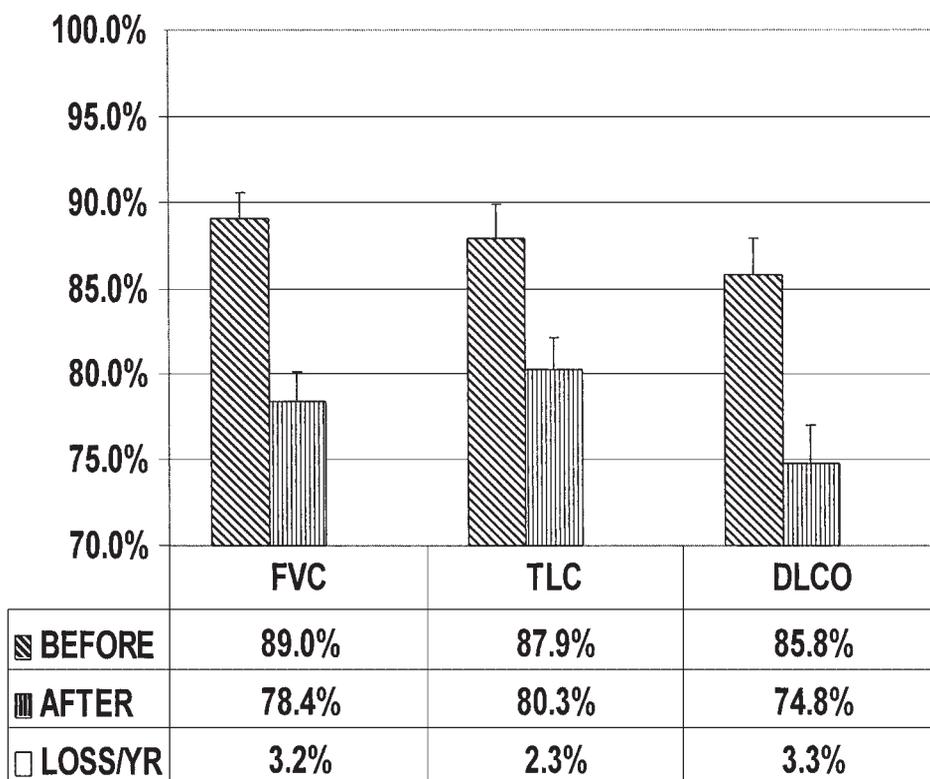


FIGURE 2. Loss of pulmonary function 94/123 patients with worse FVC.

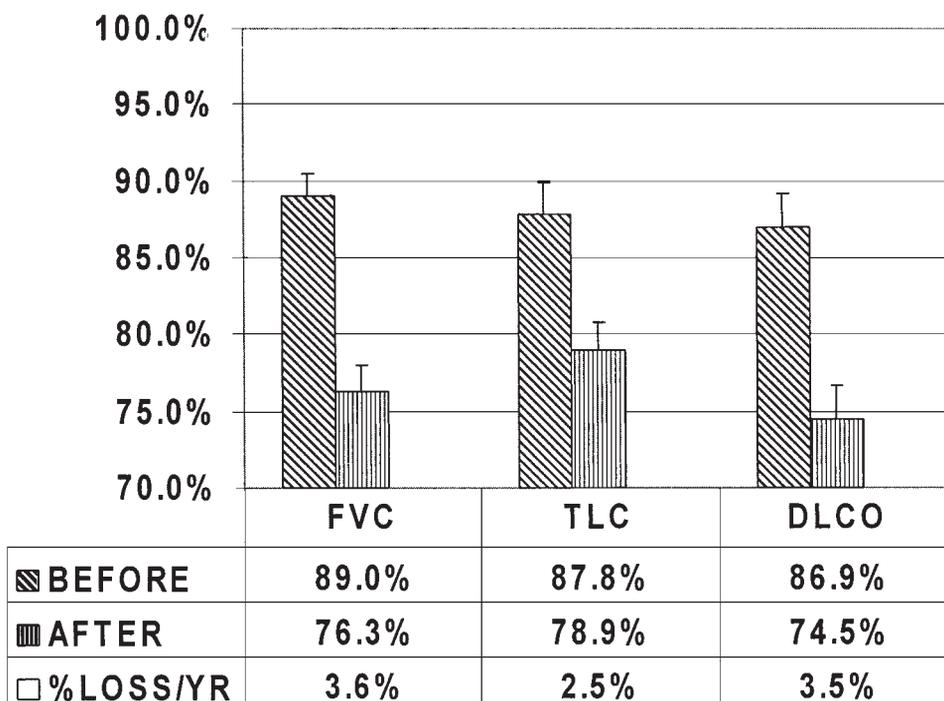
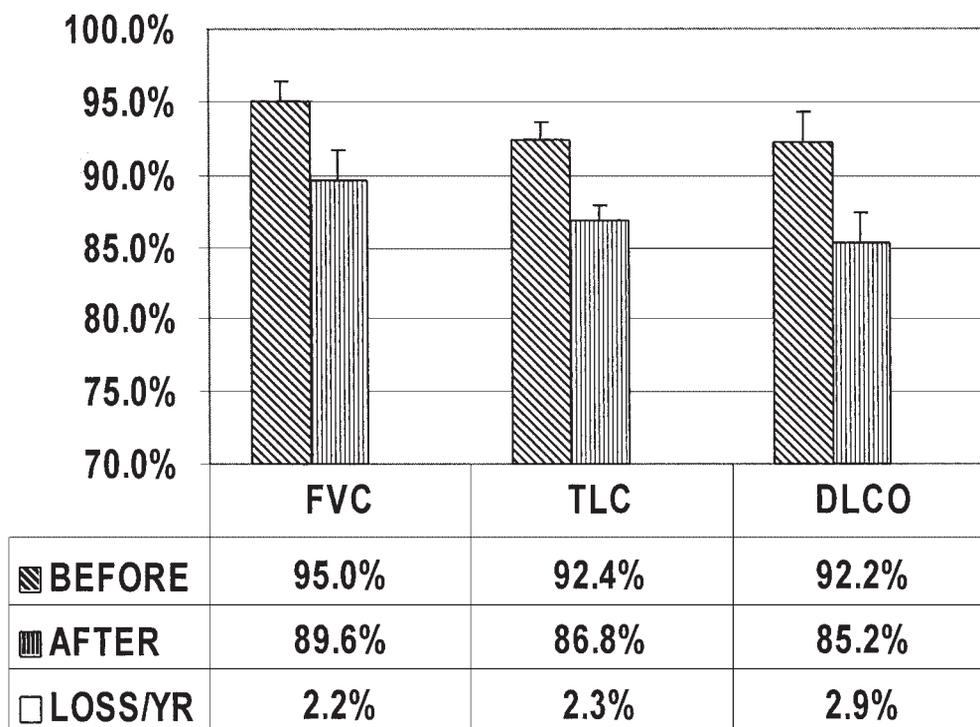


FIGURE 3. Loss of pulmonary function 79/123 patients with greater than 1% loss rate per year of FVC.



**FIGURE 4.** Loss of pulmonary function 67/123 patients, pleural disease only.

FVC, 2.3% for TLC, and 2.9% for DLCO (Fig. 4). These results are very similar to those of the entire 123 patients (compare Figs. 1–4).

All values as noted above for decline of pulmonary function were statistically significant at  $P \leq .01$ . There did not appear to be any difference between the patients with pleural changes who had minor interstitial changes versus no interstitial changes. It is also noted that in the entire group the decline in the diffusion capacity was more rapid than the decline in either the FVC or TLC.

Extent of pleural changes as measured as described on the chest X-ray was evaluated in relation to the loss of lung function. There was no statistical correlation between the extent of pleural changes measured on the chest X-ray and the loss of pulmonary function. The only clearly discernible event leading to accelerated loss of pulmonary function in this entire group was benign asbestos related effusions (three patients). These were treated vigorously with tube drainage and pleurodesis and the rate of loss equated to the 76% who lost function (2.2–3%).

## DISCUSSION

The progressive loss of pulmonary function in 76% of the 123 patients with pleural changes followed in this group of patients with Libby tremolite exposure is excessive compared to other published reports. Progression of asbestos disease in patients with exposure to chrysotile asbestos is

well documented. Jones et al. [1989] demonstrated declines in FVC and FEV<sub>1</sub> in men who had progressive pleural thickening. Of this group, 31% demonstrated progression of parenchymal small opacities in patients with pleural thickening and smoking was not a significant determinant of pleural progression. The amphibole crocidolite was present in one of the two plants studied and there was a higher rate of progression with crocidolite present. Miller and Miller [1983] demonstrated that patients with longstanding clinically inconsequential plaques remain at risk for diffuse pleural thickening and associated impairment of pulmonary function, which was the case in three patients with pleural effusions. Furthermore, in this group, there was no evidence of progression of small opacities. Decreases in vital capacity have been described by Lillis et al. [1991] and Schwartz et al. [1994]. Ohlson et al. [1985] described 4 year declines in FVC and FEV<sub>1</sub> in a group of asbestos cement workers. The average 4-year decrement of FVC in exposed subjects was 1.9% greater than the reference (control) subjects. Rom [1992] studied 77 asbestos insulators and found that losses of FVC averaged 92 cc per year, FEV<sub>1</sub> 66 cc per year, and TLC 14 cc per year. Kouris et al. [1991] found decreased pulmonary function associated with pleural plaques and more significantly with diffuse pleural thickening. Schwartz et al. [1990] demonstrated loss of FEV<sub>1</sub> and FVC associated with both plaques and diffuse pleural thickening and they concluded that “pleural fibrosis” among asbestos exposed patients is an independent predictor of spirometric patterns

consistent with restrictive lung function. Brodtkin et al. [1996] further correlates loss of pulmonary function associated with increasing respiratory symptoms. Lockey et al. [1984] described changes in weight as a confounding variable measuring pulmonary function in the workplace. There was no evidence of significant weight changes in this group [McKay et al., 1999].

There are fewer articles on exposure to amphiboles. Shepherd et al. [1997] showed progression of pleural and parenchymal abnormalities associated with amosite. Sluiz-Cremer and Hnizdo, 1989] studied crocidolite workers in South Africa, and was able to demonstrate that once a dose of amphibole asbestos sufficient to initiate disease had been retained it was a naturally progressive process. Cookson et al. [1986] studying crocidolite workers demonstrated that asbestosis was actively progressing even after more than three decades. Erlich et al. [1992] demonstrated in amosite exposed workers that there was progression of pleural abnormalities 20 years after exposure. They found exposure of as little as 1 month was sufficient to produce radiologic signs of parenchymal and pleural fibrosis and progression was detectable greater than 20 years after the end of exposure. McDonald et al. [1986b], studying workers exposed to Libby tremolite from the Grace mine in Libby, Montana, has previously demonstrated extensive pleural plaques and pleural thickening on chest radiographs. Previously, Lockey et al. [1984], was first to describe an association between benign pleural effusions as well as pleural plaques on exposure to Libby tremolite that had been processed at an expansion plant in Ohio to be used as a conditioner for fertilizer.

## CONCLUSIONS

This study demonstrates that pleural changes related to exposure to Libby tremolite are associated with progressive loss of pulmonary function in a group of patients exposed to tremolite from approximately 1950 to 1975. Progressive loss of lung function is continuing 40 years after last exposure in 76% of this group who are representative of the population of Libby, Montana. The studies quoted above document both interstitial disease and pleural disease, both radiographically and functionally, but none document the rapid progression of loss of pulmonary function in such a large group of patients with predominantly pleural disease. McDonald et al. [1999] speculated on tremolite's increased fibrogenicity, and it would appear that tremolite-actinolite-richterite-winchite amphibole found in Libby vermiculite has a propensity for causing pleural changes that result in a progressive restrictive pattern on pulmonary function testing. Pleural changes alone are unlikely to cause a decrease in DLCO. DLCO decreases are likely to be associated with interstitial disease not apparent clinically on either plain chest radiograph or HRCT.

Exposure histories for this group are complex, because for the most part there was continuous exposure throughout

this entire period that they lived in Libby, whether they were mine workers, family members of workers, or community members living near the vermiculite processing facilities.

This study demonstrates that the number of patients progressing is much higher than has previously been reported in studies with either chrysotile or amphibole asbestos exposure. Lincoln County, Montana, (where Libby is the county seat) has the highest mortality rate from asbestosis in the nation [DHHS/ATSDR CERCLIS No MT00090883840, 2000].

It is apparent from these data that the majority of the 1,500 persons who have radiologic changes of asbestos exposure are at increased risk for progressive loss of lung function from pleural changes alone or from potential future development of interstitial fibrosis. Assuming a latency period of between 20 and 30 years to significant disease, it is not unreasonable to expect that the people of Libby, Montana will have to be monitored over the next 30–40 years, because of the risk for loss of pulmonary function and other known diseases historically associated with asbestos exposure.

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