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Libby Amphibole Disease: Pulmonary Function and CT Abnormalities in Vermiculite Miners

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Abstract

Objective—This article describes radiologic and pulmonary function findings among miners exposed to Libby amphibole. Computed tomography permits the detection of the characteristic thin, lamellar pleural thickening (LPT).

Methods—Individuals who worked at the mine for a minimum of 6 months had chest CT and pulmonary function tests.

Results—Pleural thickening was noted in 223 (87%) of the 256 miners, parenchymal abnormalities in 49 (19%). LPT, found in 151 (68%), was associated with low values of forced vital capacity and diffusion capacity and significantly lower values in all pulmonary function tests when associated with parenchymal abnormalities.

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The remaining authors have no conflicts of interest to disclose.

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AM, JS, CWN, CIH, and JP significantly contributed to the drafting and writing of the manuscript.

BB, TM, LL and RF further contributed to review and edit the final draft. All these authors have critically revised the manuscript for important intellectual content.

AM, JS, CWN, CIH, JP, BB, DFY, TM, LL and RF significantly contributed to conception and/or design of the work, acquisition, analysis and interpretation of data.

CWN, CIH and RY performed the statistical and epidemiological analyses.

CIH, DFY, ML, YL, BB and JS read and reviewed the CT scans.

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Conclusions—Eighty-seven percent of miners exposed to Libby Amphibole had pleural abnormalities on CT. LPT alone, and more so with parenchymal abnormalities, resulted in decreased pulmonary function. The importance of this easily-missed LPT is demonstrated by its high frequency and significant functional effects.

Keywords

Libby Amphibole; Asbestos; Pleural Disease; Vermiculite Miners

INTRODUCTION

High rates of chest radiologic abnormalities have been reported in the population in and around Libby, MT, due to exposure to amphibole asbestos that contaminated the Libby vermiculite mine outside the town[1]. Morbidity and mortality from Libby Amphibole (LA) asbestos-related disease has been reported[1–7]. Sullivan reported that standardized mortality ratios for lung cancer, cancer of the pleura and asbestosis were 1.7, 23.3 and 165.8, respectively, when compared to the US white male population of the same age category[6]. Similar amphiboles have been detected in surface deposits in Nevada and Arizona[8]. A recent publication provided evidence that the increased incidence of mesothelioma in women and young individuals in southern Nevada may be linked to such environmental amphibole exposure[9]. In the Libby vermiculite-exposed population, we observed a different type of pleural disease in addition to the well-described circumscribed or diffuse pleural thickening, which are typically found in asbestos-exposed individuals. We called this different type of pleural disease “lamellar pleural thickening” (LPT)[7, 10].

We previously reported illustrative cases of patients who developed pulmonary disease after LA-exposure[10]. These patients presented rapidly progressing dyspnea, chest pain, worsening pleural radiological changes, a restrictive pattern in pulmonary function tests and rapid loss of pulmonary function. These findings are atypical when compared to classical asbestos-related disease. In a group of 189 volunteers who resided in Libby as children and adolescents but left before adulthood, 96 (48%) had pleural thickening on CT imaging with almost half of these being LPT. The severity of this LPT correlated with a decrease in pulmonary function[7]. LPT as found in Libby may be seen elsewhere but missed due to its non-traditional radiological features. In this report, we describe the radiologic and pulmonary function findings in former Libby miners who have been evaluated on repeated visits at the Center for Asbestos Related Disease (CARD) in Libby, MT, and who constitute the most heavily exposed group of the Libby population.

METHODS

During its 65 years of operation from the 1920s to 1990, 1862 individuals worked at the Libby vermiculite mine[11]. In July 2000, the CARD was established and has provided ongoing follow-up and imaging for the Libby exposed community. The CARD roster consists of approximately 5500 people; about 2000 of whom have been diagnosed with asbestos related disease (Black B, personal communication). This population includes former workers at the mine who have been evaluated on repeated clinical visits with

extensive information on their LA exposure, medical history, full pulmonary function tests (PFTs), and CT imaging.

Inclusion criteria

This report focuses on the 256 subjects who met the following entry criteria: a self-reported minimum six month history of working directly or as a contractor for the mine company, and had CT imaging at the time of inclusion. A total of 477 CARD patients initially identified themselves as miners. Seventy-two were removed as their work experience was less than six months, and an additional 18 were removed as they worked as contractors after the mine closed. Eighty-four of the remaining miners did not consent to participate, and 47 did not have CT imaging available at the time of inclusion. Figure 1 depicts the cohort. The research was performed under approval of the Institutional Review Board Spokane, WA.

All 256 subjects had completed standardized exposure questionnaires, including occupational, residential[12] and smoking histories, and physical examination prior to inclusion. Exposure histories were analyzed as described previously[12], and PFTs were performed at the CARD using American Thoracic Society criteria[13]. Static lung volumes were measured via plethysmography. Reference values for spirometry were from Hankinson[14], lung volumes were from Crapo[15] and DLco were from Miller[16]. Lower Limits of Normal (LLN), or upper limits of normal for residual volume, were used as criteria of abnormality.

CT imaging

Beginning in 2001, CT imaging was added to the radiologic testing performed at the CARD and it has provided a significant improvement in the detection of the pleural thickening frequently observed in the population[7, 10, 17]. Standard-dose chest CT scans were performed at the local hospital utilizing a 16 slice CT GE LightSpeed scanner (at 120 kVp and no more than 441 mAs) with 1-mm collimation. All identifiers were removed from the CT scan files, and readers were blind as to history and exposure status.

The most recent CT scan prior to date of inclusion was interpreted by consensus by academic thoracic radiologists with experience evaluating Libby disease (ML, YL, CH, DY), using lung (−500 level, 1400 width), mediastinal (40 level, 400 width), and extended-mediastinal windows (−200 level, 3500 width, with adjustments)[7]. Radiologists performed standard clinical interpretation and the International Classification of Occupational and Environmental Respiratory Disease scoring system (ICO-ERD)[18] as a CT-equivalent of the International Labour Organization Classification of x-rays for Pneumoconiosis[19]. In addition, radiologists were asked to differentiate between LPT[7, 10] and circumscribed pleural thickening (CPT). When both were identified on CT scans, radiologists further determined if the pleural thickening was predominantly CPT or predominantly LPT.

CPT is defined as areas of pleural thickening with well-demarcated edges[20]. Diffuse pleural thickening on CT scan has been defined as a continuous sheet of pleural thickening more than 5 cm wide, more than 8 cm in cranio-caudal extent and more than 3 mm thick[21]. The 2000 International Labour Organization Classification of Radiographs of Pneumoconiosis defines diffuse pleural thickening as that “extending up the lateral chest wall … only in the

presence of, and in continuity with, an obliterated costophrenic angle"[19]. These types of pleural thickening are different from what we have termed as LPT (Figure 2). We describe LPT as a thin layer of pleural thickening seen on CT scans internal and parallel to the ribs, but distinguished from subpleural fat[7, 10, 22]. It progressively extends vertically and along the inner border of the chest wall[7, 10]. It may progress in thickness and may calcify, becoming easier to identify and confirming its earlier recognition[10].

Statistical Analysis

We calculated summary statistics of demographics, exposure estimates, and CT and PFT findings. Comparison between independent variables and categories of CT findings (i.e., CT groups) were evaluated by chi-square and analysis of variance. PFT percent predicted values, or ratio for FEV_1/FVC, were compared between CT groups in general linear models, adjusting for covariates. Associations between abnormal PFT findings (i.e., below LLN) and CT findings were evaluated with unconditional logistic regression models. Initially, we modeled associations separately for each CT finding adjusted for covariates of latency and history of smoking. To account for multiple CT findings within miners we further included all CT findings in the model. All data analyses were conducted using SAS v9.3 (Cary, NC).

RESULTS

Table 1 provides the descriptive data for the 256 miners: 243 (95%) were male and almost half were 65 years or older (115, 45%). Twenty seven percent lived in Lincoln County for 25 years or more prior to the closing of the mine, and the mean (standard deviation (SD)) occupational latency (i.e., years elapsed between first year of mine work and year of the CT used for the study) was 39 (8.2) years. Mean (SD) body mass index (BMI) was 31 (6.9) kg/m^2, and over half (52.5%) of the participants were obese (i.e., BMI ≥ 30). Among the 256 miners, 89 (34.8%) were never smokers, 43 (16.8%) were current smokers, 123 (48.1%) were former smokers, and 1 refused to provide the information. Sufficient information to calculate the pack-years of smoking was available on 146 (88%) of the 166 smokers and the mean (SD) was 30 (26). Mean (SD) quit time for the 123 former smokers was 26 years (14).

Table 2 shows the results of the CT interpretation for the 256 miners. No abnormalities could be identified on the CT scan in 30 (11.7%) of the miners, while 226 (88.3%) had some abnormality. Pleural thickening was the most frequent abnormality, noted in a total of 223 (87.1%). Among these 223 miners, 151 (67.7%) had only or predominantly LPT, and 72 (32.3%) had only or predominantly CPT. The 49 miners (19%) in whom parenchymal abnormalities were identified are reported in Table 2 using the ICO-ERD classification. These parenchymal abnormalities identified correspond to those seen in asbestosis (irregular opacities). Forty-seven of these had concomitant pleural thickening: 37 had LPT and the remaining 10 had CPT. Using clinical interpretation of the chest CT scan, two-thirds (33) of these 49 miners were also read as positive for "interstitial lung disease". Emphysema with no other parenchymal abnormalities was found in 57 (22.3%) miners, all but one had pleural thickening (56/57). Fifteen of the 256 miners (5.9%) had emphysema, pleural thickening and irregular opacities.

For subsequent comparisons with PFT findings, we grouped participants into eight mutually exclusive CT categories given in Table 3: CT negative (n = 30), CPT only (n = 35), LPT only (n = 52), both types but predominantly CPT (n = 11), both types but predominantly LPT (n = 37), CPT plus irregular opacities (n = 5), LPT plus irregular opacities (n = 27) and emphysema (n = 57). The two miners who had irregular opacities but no pleural thickening or emphysema were not included in these further analyses.

The participants' characteristics with respect to the above described eight mutually exclusive CT categories are given in Table 3. Miners with any type of pleural thickening were of similar age as those with no abnormalities on CT scan, while those miners who had parenchymal abnormalities were significantly older. The few females in the study were more likely to be in the CT-negative group. Mean BMI was similar across eight groups, except it was significantly lower for those with emphysema ($p < 0.05$). Smoking history was similar among the eight groups, except for the emphysema group which was significantly higher ($P< 0.01$). Years of working at the mine company, years of residence and total environmental exposure were not significantly different between the CT positive and the CT negative groups, except those with emphysema who had longer residency time in the Libby area.

PFT data were available for 241 (94%) of miners. To best describe pulmonary function relevant to imaging studies, we limited our analysis to those miners whose PFTs were done within one year of the date of CT. Fourteen records were removed by this exclusion, resulting in 227 records with FEV_1 and FVC data. Miners who were excluded from further PFT analysis (n=14) were not different from those included (n=227) with respect to percent male (93% versus 95%, respectively), percent overweight or obese (91% versus 88%, respectively) or percent current or former smokers (64% versus 65%, respectively). Fewer measures were available for DLco (n=158) and lung volumes (n=135). Mean PFT values by CT group are shown in Table 4 and all comparisons were adjusted for latency-years and smoking history. Those with both pleural thickening types were classified according to the predominant finding as identified by the radiologists, i.e., CPT or LPT. All the PFTs in the group with both LPT and parenchymal abnormalities were significantly lower than the CT negative group ($p<0.05$). DLco was lowest in the group with LPT and parenchymal abnormalities ($p<0.002$ compared to CT negative) and was lower in those with LPT than in those with CPT ($p=0.016$). The 57 miners with emphysema had lower values for FEV_1, FEV_1/FVC ratio and DLco compared to the CT negative (Table 4).

Table 5 shows the association between frequency of abnormal PFTs and CT findings. A substantial proportion of miners had FEV_1 (35%), FVC (32%) and DLco (25%) below LLN. Adjusting only for latency and smoking history, we showed significantly elevated risk estimates for abnormal FEV_1 and FVC among those with LPT compared to no pleural findings. Risk estimates for these parameters among those with CPT were not different from those with no pleural thickening. When further adjusting for other CT findings, the odds ratio for abnormal FVC remained independently elevated among those with LPT compared to no pleural thickening (OR (95% CI) = 3.9 (1.1 – 14)). Presence of irregular opacities and presence of emphysema were consistently associated with frequency of abnormal PFTs. Additional modeling using years of work as a proxy for exposure did not appreciably change (< 5%) the risk estimates (data not shown). Because we had insufficient data to calculate

pack-years for a substantial portion of the observations (i.e., approximately 12% of the smokers with PFT data), we used a categorical variable for smoking history in our primary analysis. In sensitivity analyses, we used pack-years in place of the categorical variable; the effect estimates for CT findings and PFT abnormality were similar, but that had larger 95% confidence intervals. For example, OR (95% CI) for CPT and abnormal FVC was 3.6 (1.0 – 13).

LPT which cannot be identified on chest radiographs and is even difficult to recognize on CT scans until it has advanced or calcified, does lead to a decreased FEV_1, FVC, TLC and DLco as shown in Tables 4 and 5.

DISCUSSION

This report focuses on a population of individuals who were heavily exposed to LA as a result of their occupation at the mine. Prior reports using chest radiographs rather than CT scans have demonstrated that Libby miners had pleural thickening, parenchymal abnormalities and restrictive findings on spirometry[23].

Our investigation expands on previous studies by using the more sensitive and more accurate imaging modality of CT and the full spectrum of PFTs to evaluate the effect of pleural thickening and parenchymal abnormalities on pulmonary function findings. We found that 223 (87%) of the 256 miners had pleural thickening and among them, 47 (21%) had associated parenchymal abnormalities. Among the 223 with pleural thickening, 68% had LPT rather than the classical CPT. We have previously introduced the concept of LPT to describe a thin layer of pleural thickening internal and parallel to the ribs, distinguished from subpleural fat, seen on CT scans of LA exposed individuals[7, 10]. LPT is different from the traditional diffuse pleural thickening classified under the International Labour Organization (ILO) guidelines for reading x-rays of pneumoconiosis[19] and there is no specific category to describe it. While LPT is parietal in location, it does not fit the definition CPT since it lacks well-demarcated edges.

LPT cannot be identified on chest radiographs and is even difficult to recognize on CT scans until the pleural thickening becomes advanced or calcified. It does, however, lead to a decreased FEV_1, FVC, TLC and DLco as shown in Tables 4 and 5. Our study demonstrates that occupational exposure to LA leads to high frequencies of pleural thickening, of which the majority of cases are LPT. Lung function deficits are more frequently associated with LPT than with CPT, particularly in the presence of concurrent parenchymal abnormalities. The importance of pleural thickening from LA was demonstrated by our previous study of 198 subjects who had less intense environmental exposure only during childhood and adolescence, 96 (48%) of whom had pleural thickening. Of those with any pleural thickening, LPT was found in 47 (49%)[7].

Two recent papers have reported pulmonary function abnormalities associated with CT evaluation of LA exposure. Clark[24] found that 90% of 166 Libby vermiculite miners whose medical records between January 2000 and August 2012 were reviewed, presented pleural plaques, the majority of which were described as “bilateral and calcified”. Sixteen percent of

these workers had associated pulmonary fibrosis. No differences in PFT results were noted between those with only pleural plaques and those with no abnormalities on CT. Miners with both interstitial and pleural abnormalities had a significantly decreased TLC as compared to those with negative CT scans. Age, smoking and BMI were found to contribute to abnormal pulmonary function. While Clark did not differentiate CPT from LPT, we found similar percentages of overall pleural thickening in our group of miners (90% in Clark's study as compared to 87% in our study). Additionally, similar to Clark's findings, miners with both pleural thickening and parenchymal abnormalities in our study had significantly decreased PFTs. Our study, however, showed that presence of LPT among miners was independently associated with abnormal FVC after adjusting for presence of parenchymal abnormalities, thus showing that LPT alone contributes to impairment of pulmonary function.

Lockey and co-workers described CT findings in 191 workers with low exposure to LA working for a vermiculite expansion plant[25]. These authors found CT abnormalities in 55% of the workers: 53% had pleural thickening and 13% had parenchymal abnormalities. Localized pleural thickening, the description of which was that of plaques, was far more common and resulted in decreased FVC and FEV_1. Decreased FVC and FEV_1 were more marked in those who had pleural thickening and other abnormalities. Diffuse pleural thickening was described in only 8%, always in combination with localized thickening or parenchymal abnormalities, resulting in greater reduction in FVC. Our study found a higher incidence of pleural thickening among the Libby miners, which would be expected given that these miners had higher exposures. Similar to Lockey's findings, in our study, miners with CPT had decreased pulmonary function as compared to miners with no abnormalities in their chest CT. Again, no distinction was made between CPT and LPT by Lockey's group, and it is likely that many cases of LPT were not recognized. In a correspondence concerning their paper, Lockey reported results of additional PFTs showing that percent predicted TLC was decreased 3.6% and DLco was decreased 4.1% in those with limited pleural thickening only and much further in those with both pleural thickening and other findings[26].

Other studies using CT scans of asbestos-exposed workers have shown that CPT (plaques) is associated with decreased spirometry values[27] and diffuse thickening is additionally associated with decreased DLco[28]. A study of a large number (1584) of heavily exposed workers (long term insulators) using chest radiographs demonstrated that severity of CPT correlated with decreasing FVC and that diffuse thickening was associated with greater decrease in FVC irrespective of severity[29]. This distinction between the effects of different types of pleural thickening on pulmonary function is very similar to the differences observed in this current study between CPT and LPT.

The importance of CT evidence of pulmonary fibrosis is demonstrated in our study by the far greater decrease in all measures of pulmonary function in those miners with associated CT-detected parenchymal abnormalities. That the difference is most clearly seen with DLco is consistent with the sensitivity of this measurement for parenchymal lung involvement. That DLco is lower in LPT than CPT alone suggests that LPT may be associated with parenchymal inflammation or fibrosis that is not apparent on standard CT-window settings. A study in insulators using incremental exercise testing demonstrated evidence of

parenchymal involvement in those with pleural thickening only and no parenchymal abnormalities on chest radiographs[30].

Limitations of this study may include sample selection. The authors believe, however, that the sample is representative of the overall LA mining population, as it included all former miners and contractors who are patients of CARD, which is the local reference center for all individuals exposed to LA. In addition, CARD maintains a nation-wide screening program that targets those who now live elsewhere.

The asbestos-related benign and malignant consequences of LA are of national significance since vermiculite was shipped (in open rail cars) throughout North America for processing. The consequences of such exposure have been reported from processing sites[25, 31–37]. In addition to the Libby product, similar amphiboles have been found in surface sites in several states in sufficient air-concentrations to cause disease. The elevated rates of mesothelioma in women and in young persons in Southern Nevada are consistent with environmental exposure to asbestos[9]. Recognition of the unique radiologic presentation of LA pleural disease is therefore critically important to the diagnosis of individual patients and to the public health of communities.

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Abbreviation List

BMI	Body mass index
CARD	Center for Asbestos Related Disease
CT	Computed Tomography
CPT	Circumscribed Pleural Thickening
DLco	Carbon monoxide diffusing capacity of the lung

FEV1	Forced Expiratory Volume in 1st second
FVC	Forced Vital Capacity
ICO-ERD	International Classification of HRCT for Occupational and Environmental Respiratory Diseases
LA	Libby Amphibole
LLN	Lower Limits of Normal
LPT	Lamellar Pleural Thickening
PFT	Pulmonary Function Test
SD	Standard Deviation
TLC	Total Lung Capacity

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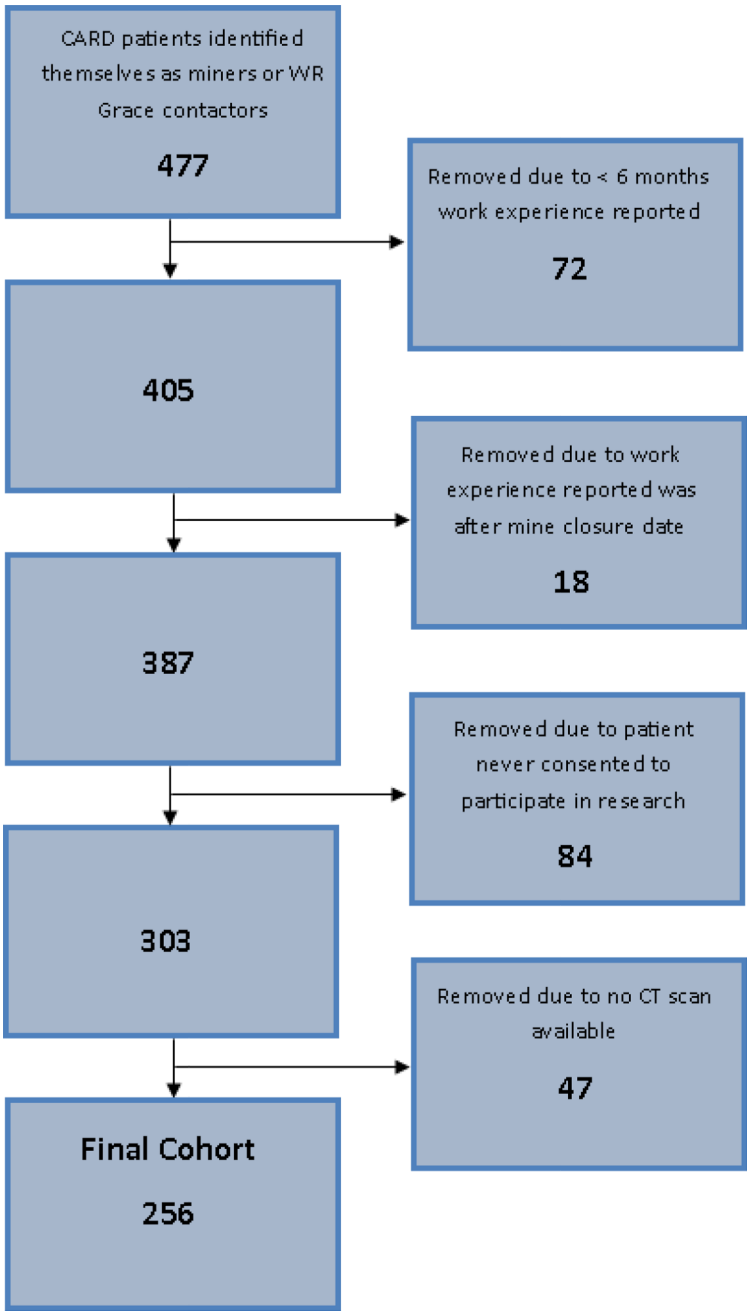
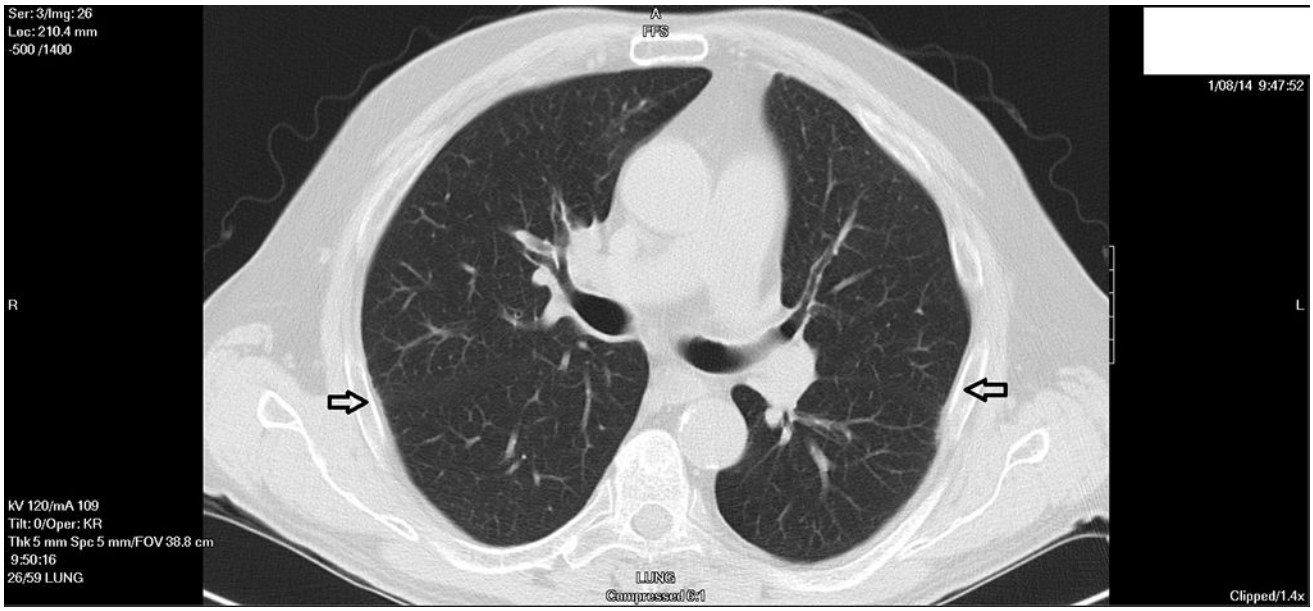
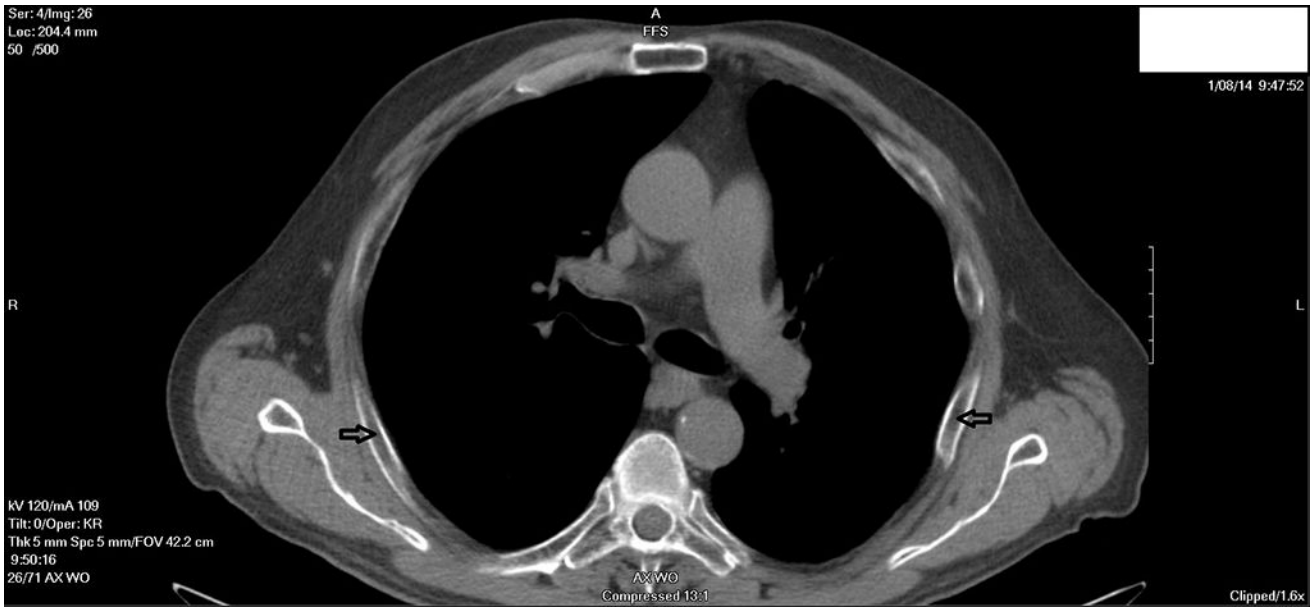
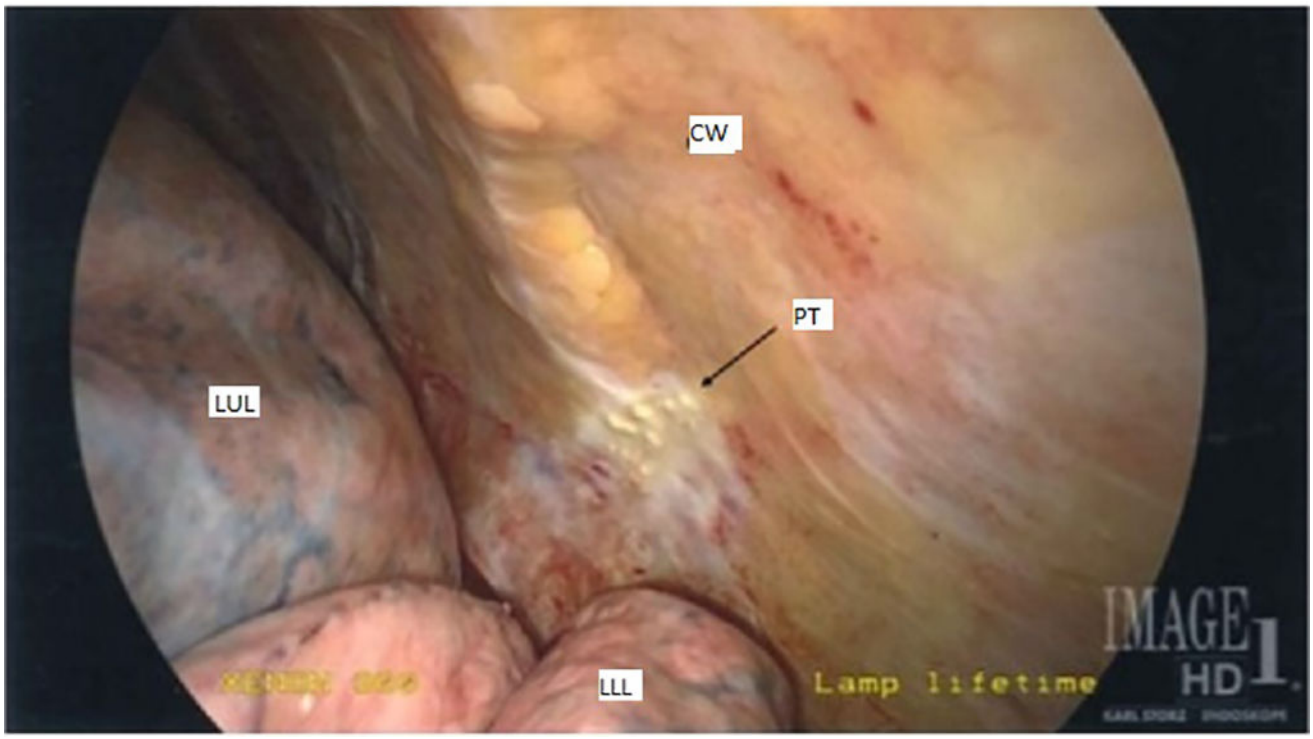
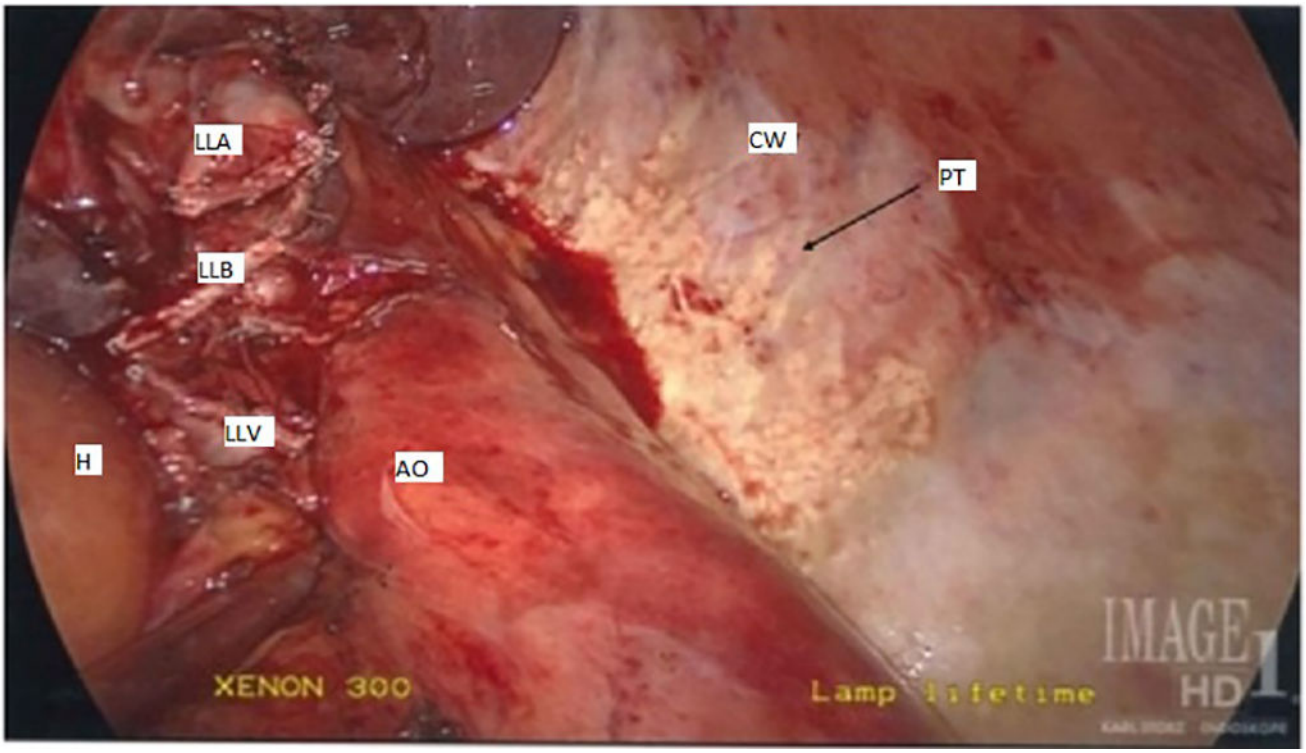


Figure 1. Libby Vermiculite Miners cohort









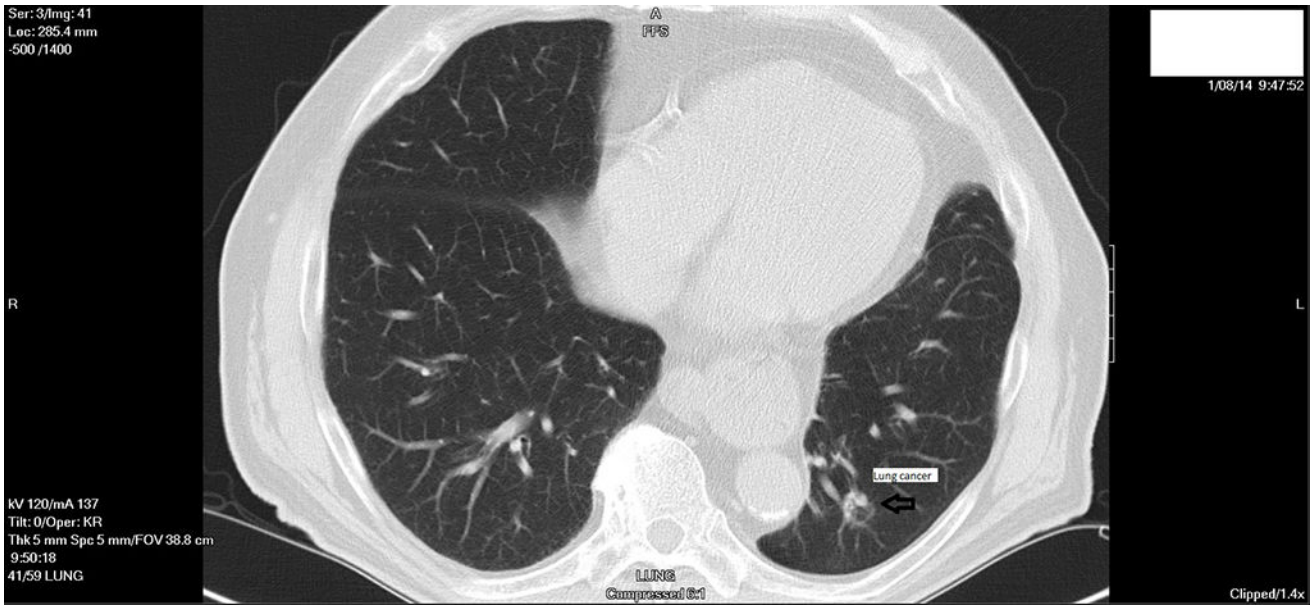


Figure 2. Lamellar Pleural Thickening

Figure 2*A* illustrates side-by-side chest CT images in extended lung windows and mediastinal windows of a miner with lamellar PT who is included in the present series. Lung window shows the characteristic thin layer of pleural thickening extending internal and parallel to the ribs, that has been characterized by the authors as lamellar thickening (arrows). This thickening can best be seen on the lung windows due to technical factors that make it less visible on mediastinal windows (Figure 2*B*, arrows). Figures 2*C1* and *2C2* show two surgical images of the parietal pleura of this same patient during a thoracotomy for a lung cancer (Figure 2*D*, arrow). A thin layer of parietal pleural thickening that corresponds to the chest CT scan image of lamellar PT is clearly visible (black arrows), the remainder of the pleura is opaque.

AO = aorta; CW = parietal chest wall; H = heart; LUL = left upper lobe; LLL = left lower lobe; LLA = left lower lobe artery; LLB = left lower lobe bronchus; LLV = left lower lobe vein; PT = pleural thickening.

(Surgical photos courtesy of Dr. Steven J. Nisco, MD, Thoracic Surgeon, Providence Spokane Heart Institute, Spokane, WA)

Table 1

Demographic characteristics, smoking history and exposure history of miners

	N (%)
Gender	
Female	13 (5.1)
Male	243 (94.9)
Age group	
30 – 54 years	37 (14.5)
55 – 64 years	104 (40.6)
65 + years	115 (44.9)
Body Mass Index Category (BMI data missing for 33)	
Normal (< 25 kg/m^2)	26 (11.7)
Overweight (25–29.9 kg/m^2)	80 (35.9)
Obese (>= 30 kg/m^2)	117 (52.5)
Smoking History	
Never	89 (34.8)
Current	43 (16.8)
Former	123 (48.1)
Missing/Refused	1 (0.4)
Latency (years since first worked at or contracted for WR Grace)	
21–33	65 (25.4)
34–38	65 (25.4)
39–43	60 (23.4)
44–69	66 (25.8)
Years lived in Lincoln County prior to 1990	
< 7 years	61 (23.8)
7 – 16 years	66 (25.8)
17 – 24 years	60 (23.4)
25 + years	69 (27.0)
Years worked at WRG	
0.6 to 1.5 years	87 (34.0)
1.6 to 5 years	84 (32.8)
5.1 to 40 years	85 (33.2)

Table 2

CT findings (Mutually exclusive)

CT Findings	Number	Percent
Normal	30	11.7
Pleural Thickening with no other findings		
CPT only	35	13.7
Both types, but predominantly CPT	11	4.3
LPT only	52	20.3
Both types but predominantly LPT	37	14.5
Pleural Thickening + irregular opacities[a]		
CPT[b] + irregular opacities	5	2.0
LPT[c] + irregular opacities	27	10.6
Pleural Thickening + emphysema		
CPT[b] + emphysema	16	6.3
LPT[c] + emphysema	25	9.8
Pleural Thickening + irregular opacities + emphysema		
CPT[b] + irregular opacities + emphysema	5	2.0
LPT[c] + irregular opacities + emphysema	10	3.9
Irregular opacities only	2	0.8
Emphysema only	1	0.4
Total	**256**	**100**

[a] Irregular opacities include intra (including subpleural curvilinear opacities, 3 cases), interlobular opacities (45 cases) and honeycombing (1 case). Location of these abnormalities was predominantly in the middle and lower lobes in all cases.

[b] Includes those with CPT and those with both types, but predominantly CPT.

[c] Includes those with LPT and those with both types, but predominantly LPT.

Table 3

Demographic characteristics, smoking history and exposure history of miners according to CT findings.

	Normal[b]	Pleural thickening with no other findings				Pleural thickening + irregular opacities[a]		Emphysema + (Pleural thickening and/or irregular opacities)[c]
		CPT only	Both types, predominantly CPT	LPT only	Both types, predominantly LPT	CPT[e] + irregular opacities	LPT[f] + irregular opacities	
Total, n	30	35	11	52	37	5	27	57
Age, years	62 (8.2)	63 (8.2)	66 (6.2)	59 (8.9)	63 (8.6)	72 (7.3)*	72 (8.7)**	68 (7.0)**
Gender, % male	76.7%	97.1%*	90.9%	100%**	97.3%*	100%	100%*	94.7%*
Body mass index (BMI, kg/m^2)[d]	31 (7.2)	32 (9.0)	33 (4.9)	32 (7.2)	32 (4.8)	27 (1.8)	31 (6.7)	28 (6.1)*
Smoking history, % current or former	56.7%	54.3%	54.6%	51.9%	73.0%	20.0%	63.0%	91.1**
Latency (years since first worked at WRG)	35 (6.1)	39 (8.1)*	43 (6.6)**	36 (7.3)	40 (8.2)*	41 (6.1)	44 (11)**	40 (7.4)**
Years worked at WRG	5.1 (5.9)	4.1 (6.1)	5.8 (6.4)	7.6 (8.9)	6.7 (6.8)	4.6 (3.8)	8.8 (8.8)	6.6 (7.5)
Years of residence	13 (9.4)	18 (12)	20 (10)	18 (13)	19 (13)	13 (11)	18 (17)	19 (13)*
Total environment exposure, weighted years	2.7 (4.5)	3.1 (5.6)	2.2 (2.4)	3.6 (4.4)	2.7 (3.6)	1.8 (2.2)	2.8 (2.9)	2.0 (2.8)

[a] Table excludes those with irregular opacity findings only (n=2).

[b] No pleural or parenchymal findings.

[c] Includes one observation with emphysema findings only.

[d] Missing BMI data for 33.

[e] Includes those with CPT and those with both types, but predominantly CPT.

[f] Includes those with LPT and those with both types, but predominantly LPT.

* $p < 0.05$;

** $p < 0.01$ comparing to Normal group.

Table 4

Mean (SD) percent predicted[a] pulmonary function measures with respect to CT findings

CT grouping[b]	FEV_1 (n = 226)	FVC (n = 226)	FEV_1/FVC (n = 226)	TLC (n = 134)	RV (n = 134)	DLco (n = 157)
Normal[c]	95.7 (14.1)	93.6 (13.5)	0.78 (0.07)	97.2 (14.5)	110 (34.5)	95.7 (15.5)
Pleural thickening[d] *with no other findings*						
CPT	89.4 (18.2)	90.1 (17.6)	0.75 (0.08)	93.8 (17.9)	105 (30.4)	102 (21.1)
LPT	87.3 (15.9)	89.0 (15.0)	0.75 (0.08)	94.1 (14.2)	112 (24.9)	91.5 (20.1)
Pleural thickening[d] *with irregular opacities*						
CPT + irregular opacities	82.2 (22.2)	84.0 (20.8)	0.73 (0.09)	95.5 (9.8)	113 (7.1)	110 (10.5)
LPT + irregular opacities	71.7 (19.9)*	73.3 (17.5)*	0.72 (0.10)*	73.9 (13.1)*	83.0 (19.2)*	67.3 (19.2)*
Emphysema + (pleural thickening and/or irregular opacities)	74.7 (20.7)*	83.9 (16.0)*	0.66 (0.12)*	92.7 (17.8)	113 (29.9)	71.1 (18.9)*

FEV_1 First second forced expiratory volume; FVC: Forced vital capacity; TLC = Total lung capacity; RV = Residual volume; DLco: Carbon monoxide diffusing capacity; CPT = circumscribed pleural thickening; LPT = lamellar pleural thickening

[a] Ratio for FEV_1/FVC.

[b] Excludes one CT with irregular opacities only and one CT with emphysema only.

[c] No pleural or parenchymal findings.

[d] CT findings with both pleural thickening were classified according to the predominant finding as identified by the radiologists.

* Least squares means different from Normal group ($p < 0.05$), adjusted for latency and smoking history.

Table 5

Odds ratios (and 95% confidence interval (CI)) for abnormal[a] pulmonary function measures with respect to CT findings

CT findings[b]	FEV_1			FVC			DLco		
	No. abnormal (%)	Model 1[c] OR (95% CI)	Model 2[d] OR (95% CI)	No. abnormal (%)	Model 1[c] OR (95% CI)	Model 2[d] OR (95% CI)	No. abnormal (%)	Model 1[c] OR (95% CI)	Model 2[d] OR (95% CI)
Pleural thickening[e]									
No	4 (14)	1.0	1.0	3 (10)	1.0	1.0	2 (13)	1.0	1.0
CPT	18 (29)	0.7 (0.3 – 1.3)	1.7 (0.5 – 5.9)	17 (27)	0.7 (0.4 – 1.4)	2.6 (0.7–10)	8 (21)	0.7 (0.3 – 1.8)	0.9 (0.1 – 6.1)
LPT	57 (42)	2.2 (1.2 – 4.1)	2.7 (0.9–8.7)	83 (61)	2.1 (1.2 – 3.9)	3.9 (1.1 – 14)	30 (29)	1.6 (0.7 – 3.9)	1.3 (0.2 – 7.2)
Irregular opacities									
No	54(29)	1.0	1.0	51 (27)	1.0	1.0	23 (18)	1.0	1.0
Yes	21 (61)	5.0 (2.2 – 11)	4.2 (1.8 – 9.5)	22 (54)	2.9 (1.4 – 6.0)	2.5 (1.2 – 5.3)	17 (61)	6.9 (2.6 – 18)	6.6 (2.4 – 18)
Emphysema									
No	50 (28)	1.0	1.0	55 (31)	1.0	1.0	25 (20)	1.0	1.0
Yes	19 (40)	3.0 (1.5 – 6.0)	2.7 (1.3 – 5.8)	18 (38)	1.3 (0.6 – 2.6)	1.1 (0.5 – 2.3)	15 (48)	3.0 (1.3 – 7.3)	3.0 (1.2 – 7.7)

FEV_1 First second forced expiratory volume; FVC: Forced vital capacity; DLco: Carbon monoxide diffusing capacity; CPT = circumscribed pleural thickening; LPT = lamellar pleural thickening

[a] Below lower limit of normal (LLN).

[b] Presence/absence of a given CT finding irrespective of concurrent CT findings.

[c] Model 1: Adjusted for latency (years since first worked at the mine) and smoking history (current/former versus never).

[d] Model 2: Adjusted for latency, smoking history and concurrent CT findings.

[e] CT findings with both pleural thickening types were classified according to the predominant finding as identified by the radiologists.