GRACE

Construction Products Division

July 9, 1984

TO: H. A. Eschenbach
R. C. Walsh
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FROM: A. N. Crawford

SUBJ: Article From The American Thoracic Society (ATS)

RE: "Pulmonary Changes After Exposure To Vermiculite Contaminated With Fibrous Tremolite"

The above referenced article is attached for your information.

I received this copy from the Vice President of Research@ KNAUF Fiberglass Co., Dr. John D. Koch, in Shelbeyville, Indiana. Dr. Koch received this in a packet of information sent to all members on the Medical & Scientific Committee of the Thermal Insulation Manufactures Association (TIMA).

Knauf is evaluating our new experimental vermiculite despersion and they are concerned about the potential exposure to tremolite.

Regards,

A. N. Crawford

ANC/dp

Pulmonary Changes after Exposure to Vermiculite Contaminated with Fibrous Tremolite[1-3]

J. E. LOCKEY, S. M. BROOKS, A. M. JARABEK, P. R. KHOURY, R. T. MCKAY, A. CARSON, J. A. MORRISON, J. F. WIOT, and H. B. SPITZ

SUMMARY Workers exposed to vermiculite contaminated with fibrous tremolite were surveyed for the presence of respiratory symptoms by questionnaire, and for pneumoconiosis by chest radiograph. Pulmonary function was measured by spirometry and single-breath carbon monoxide diffusing capacity ($DL_{CO}sb$). Fiber exposure indexes, expressed as fiber/ml-yr, were derived for each worker from available industrial hygiene data and work histories. The estimated cumulative exposure for the work force ranged from 0.01 to 39 fiber/ml-yr. Discriminant analysis demonstrated significant correlates with shortness of breath and pleuritic chest pain to cumulative fiber exposure. The radiographic changes were limited to pleural changes and involved 4.4% of the population. Parametric and discriminant analysis demonstrated a significant correlation with radiographic changes and cumulative fiber exposure. There were no correlations between spirometry or $DL_{CO}sb$ and fiber exposure. Exposure to vermiculite contaminated with fibrous tremolite can cause pleural changes in occupationally exposed workers. This is supported by the previously identified 12 cases of benign pleural effusions in this working population and the association of pleural radiographic changes and pleuritic chest symptoms with cumulative fiber exposure. The lack of significant parenchymal radiographic, spirometric, and $DL_{CO}sb$ changes most likely reflects the low cumulative fiber exposure. AM REV RESPIR DIS 1984; 129:952-958

Introduction

Vermiculite is the geological name given to a group of hydrated laminar aluminum-iron-magnesium silicates. It has the unique property of expanding as much as 12 times its original size with the application of heat between 427° and 1,093° C (1, 2). Unexpanded vermiculite is mined mainly in Montana, Virginia, and South Carolina in the United States, and in South Africa, and it is shipped to approximately 47 regional expander plants located in 30 states. The domestic uses of expanded vermiculite relate to its fire resistance, insulation, and ion exchange properties, but, additionally, it is used as a soil additive, animal feed bulking agent, and as a carrier for various chemicals, including herbicides, insecticides, fungicides, and fertilizers (2).

Investigations of some of the unexpanded vermiculite ore have demonstrated contamination of the ore with fibrous minerals (3). Montana ore contains a fibrous form of the amphibole tremolite. Virginia and South Carolina vermiculite ore contain a type of tremolite that, when milled, tends to form cleavage fragments that have fibrous characteristics with low length-to-width aspect ratios. South African ore is currently felt to be free of amphibole or cleavage fragment contamination (4).

A rurally located company that processed mainly Montana vermiculite ore to its expanded form for use as an inert carrier for herbicides and fertilizers reported a cluster of 12 cases of pleural effusions of unknown origin among their employees over a 12-yr period. Environmental sampling of work areas revealed airborne fibers believed to be tremolite. There was concern that the observed cluster of pleural effusion cases represented manifestations of exposure to the fibrous contamination of the vermiculite. The present study was undertaken to assess the respiratory status of current workers exposed to vermiculite contaminated with fibrous tremolite in this plant facility.

Methods

Study Population

The study population surveyed included all employees with a past history of vermiculite exposure and a control group of employees without such exposure. There were a total of 530 employees asked to participate in the study; 9 refused and 9 were not available because of vacation or illness, giving a total of 512 employees (97%) interviewed.

Medical Examination

All employees were interviewed by trained personnel using a modified American Thoracic Society (ATS) Respiratory Questionnaire (5). The major modifications of the questionnaire were the inclusion of questions pertaining to previous employment with asbestos and other fibrous mineral exposure, questions about time employed within various locations in the facility, and questions relating to pleuritic-type chest pain and illnesses with pleural manifestations.

A limited physical examination was performed on each employee for the presence of late inspiratory rales (crackles) in 4 different chest locations and for the presence of nail clubbing.

Spirometry was performed using an Ohio-Med 822 dry rolling seal spirometer (Ohio Instruments, Pine Brook, NJ) with a Spirotech 200 microprocessor (Spirotech, Inc., Atlanta, GA). Tests were accomplished according to ATS criteria using trained technicians (5). Employees were retested at a later date if they had had a respiratory infection within the preceding 3 wk.

Tests performed were forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), ratio of FEV_1 to FVC expressed as a percentage ($FEV_1/FVC\%$), and forced expiratory flow during the middle half of the FVC (FEF_{25-75}). All results were temperature corrected to BTPS. Results were expressed as measured values and as percentage of predicted using the normal values of Knudson and coworkers (6).

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[2] Presented in part at the Annual Meeting of the American Thoracic Society, Detroit, May 1981.

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Carbon Monoxide Diffusing Capacity

Single-breath carbon monoxide diffusing capacity ($D_{LCO}sb$), alveolar volume (V_A), and diffusing capacity per unit of lung volume (D_L/V_A) were obtained using a Collins Modular Lung Analyzer* (Warren E. Collins Co., Braintree, MA). All diffusion measurements were conducted according to ATS criteria using trained technicians (5). The diffusion carbon monoxide (CO) analyzer, helium meter, and Collins water seal spirometer were calibrated every 3 h during use. Employees were retested at a later date if they had had a respiratory infection within the preceding 3 wk or had smoked within 1 h prior to testing. Tests were accomplished in a seated position with a noseclip. Repeat tests were performed after a minimum wait of 5 min. Diffusion studies were accepted only if inspired volume (V_I) was within 10% of the best FVC (ATPS). Acceptable breath-holding time was between 8 to 12 s. Values of $D_{LCO}sb$ (ml CO [STPD]/min/mmHg) and D_L/V_A (ml CO [STPD]/min/mmHg/L [BTPS]) used were the means of 2 acceptable values within 7% of each other. The test results were expressed as measured values and as percentages of predicted using the normal values of Samet and coworkers (7).

Chest Radiographs

Chest radiographs taken in the postero-anterior projection were obtained on all employees. The radiographs were reviewed by 2 board-certified radiologists (B readers) using a modification of the ILO U/C 1971 International Classification for Pneumoconiosis. The modification includes the addition of grading criteria for radiographic changes associated with asbestos exposure. Radiographs were interpreted independently, with random interspersion of control films and without the radiologist's knowledge of the employee's work history. Any difference in interpretation was resolved by consensus reading by a third reader. Radiographs that could not be interpreted because of poor quality were repeated.

Environmental Measurements

The company first began using vermiculite in their facility in 1957. Industrial hygiene sampling for airborne fibers using membrane filters at a sampling rate of 2 L/min was initiated in 1972. Particles with a length greater than 5 μm, a diameter less than 3 μm, and an aspect ratio of 3:1 or greater were counted as fibers. Before 1976, sampling was accomplished by industrial hygiene personnel following an employee with a sampling device, but after 1976, fiber levels were obtained by industrial breathing zone sampling.

Exposure indexes expressed as fibers/ml were developed for each department, based on an 8-h time-weighted average (TWA). A separate index was developed before and up through 1973 and for the period beginning with and continuing after 1974. There was a substantial reduction in airborne fiber levels after the implementation of improved environmental controls in 1973 to 1974. The industrial hygiene values used to estimate the ≤ 1973 exposure index per department were mean fiber values for the years ≤ 1973 or the mean values from the year industrial hygiene values were first available. The ≥ 1974 exposure index was developed in a similar manner. The industrial hygiene measurements initiated in 1972 became more comprehensive in ensuing years. The ≤ 1973 exposure index most likely underestimates prior employee fiber exposure.

Collection filters were analyzed by polarized light microscopy with dispersion staining. Additionally, fiber analysis was done by scanning electron microscopy with energy dispersive X-ray analysis and transmission electron microscopy with selected area electron diffraction.

After reviewing the industrial hygiene and manufacturing process data, it was apparent that the employees could be divided into 3 main exposure groups representing 9 departments. Group I, with limited or no exposure to airborne fibers, included workers in the chemical process, research, and management departments. Industrial hygiene measurements indicated their exposures were similar to background levels for the local community. Group II had low-level fiber exposure and included central maintenance, packaging, and the warehouse workers. Group III, with high-level fiber exposure, included vermiculite expanders, plant maintenance, and the pilot plant. The 8-h TWA exposure indexes are summarized in table 1.

The chemical processing facility that employs the majority of workers in the comparison group (Group I) was completed in 1969 and was located one-quarter mile from the vermiculite facility. Chemicals used in this facility were the same as those used in the vermiculite facility, except vermiculite was not used as an inert carrier. There was minimal rotation of job positions between the chemical and vermiculite facilities.

TABLE 1

DEPARTMENT FIBER EXPOSURE INDEXES BASED ON AN 8-HOUR TIME-WEIGHTED AVERAGE*

	≤ 1973 Exposure Index	≥ 1974 Exposure Index
Group I		
Chemical process	0.049	0.049
Research	0.049	0.049
Front office	0.049	0.049
Group II		
Central maintenance	0.415	0.131
Packaging	0.250	0.031
Warehouse	0.110	0.110
Group III		
Vermiculite expanders	1.511	0.375
Plant maintenance	1.264	0.212
Pilot plant	1.264	0.212

* Fiber exposure index for departments in study population. Group I are controls, Group II are low fiber exposure departments, and Group III are high fiber exposure departments. Values are fibers/ml.

The work areas with the highest airborne fiber exposure were the vermiculite expanders area and the vermiculite railroad car and truck unloading areas. Fiber levels increased when there were more vermiculite expanders in operation and when Montana vermiculite ore was used rather than vermiculite from other sources. Fiber levels in the unexpanded vermiculite ore unloading area were recorded as high as 103 fibers/ml for a 5-min sampling period. During unloading of the ore, high levels of fiber dust were generated, but the peak levels rapidly decreased to concentrations less than 5 fibers/ml by 15 to 20 min.

Exposure indexes were expressed in 3 ways: (*1*) cumulative fiber exposure (fiber/ml-yr), (*2*) time period from first exposure (latency), and (*3*) exposure groups, i.e., Groups I, II, and III. Cumulative fiber exposure for each individual employee was calculated from exposure values and length of employment in each particular department. The exposure index was based on an 8-h TWA and a maximum of a 365-day work year. Extensive overtime had been scheduled at the facility, but more precise estimates of past total work days per year were not available. Employees with a cumulative fiber exposure of less than 1 fiber/ml-yr were found to have fiber exposure equivalent to the community population exposed to ambient air. These employees acted as a comparison group for the exposed population.

Statistical Analysis

Discriminant analysis was performed on the results of the questionnaire, physical examination, and radiographic data. The discriminant analysis attempted to establish a relationship between a nominal dependent variable (radiographic results) and independent variables (cumulative fiber exposure, smoking in pack-years, and age). Spirometry and diffusion data were analyzed using analysis of covariance after adjusting for height and smoking in pack-years. The spirometry and diffusion data were also divided into smoking and exposure groups and reanalyzed in a similar manner. Mean difference between smoking groups and between exposure groups within smoking groups were analyzed after adjustment for age and height. The association between the radiographic data and cumulative fiber exposure was examined using a pair-matched analysis. Each employee with radiographic findings consistent with commercial asbestos fiber exposure was matched by age with a second employee with a normal radiograph. A paired *t* test and a nonparametric test, Wilcoxon's signed-rank test, were performed on the difference in cumulative fiber exposure.

Results

The mean age of all participants in the study was 37.5 yr (range, 19 to 66 yr). The ethnic distribution of participants was 496 (96.9%) white, 12 (2.3%) black, 2 (0.4%) Oriental, 1 (0.2%) American Indian, and 1 (0.2%) American-born Hispanics. There were 480 males and 32 females. The high fiber exposure group (Group III) tended to be older than the other 2 exposure groups ($p < 0.01$). Of the entire group, 44.4% were current smokers, 20.3% were ex-smokers, and 35.3% were never smokers. There was no significant difference in smoking history between exposure groups. Cumulative fiber exposure was significantly higher in Group III than in Groups I and II ($p < 0.01$). Years of employment were significantly greater in exposure Group III than in exposure Groups I and II ($p < 0.05$). These data are summarized in table 2.

TABLE 2

AGE, SMOKING HISTORY, CUMULATIVE FIBER EXPOSURE, AND YEARS OF EMPLOYMENT BY EXPOSURE GROUP

	Group I			Group II			Group III		
	NS	EX	CS	NS	EX	CS	NS	EX	CS
Number of Employees	49	22	41	63	36	107	69	46	79
Age, yr									
Mean	33.8	39.5	39.1	34.5	39.9	34.9	40.2	42.8	37.5
SE	1.7	2.5	1.8	1.5	2.0	1.1	1.4	1.7	1.3
Pack-years									
Mean	0	13.1	18.6	0	14.2	18.7	0	14.3	17.8
SE		2.9	2.1		2.3	1.3		2.0	1.5
Fiber/ml-yr									
Mean	0.35	0.57	0.50	1.15	1.56	0.97	6.51	7.55	6.05
SE	0.67	1.01	0.74	0.60	0.79	0.46	0.57	0.70	0.53
Years of employment									
Mean	6.6	11.3	10.5	8.4	13.3	8.9	12.2	13.0	10.7
SE	1.1	1.6	1.2	1.0	1.3	0.7	0.9	1.1	0.9

Definition of abbreviations: NS = never smoker, EX = ex-smoker, CS = current smoker.

Questionnaire Data

History of respiratory illness with time lost from work, chest injury or operation, phlegm production, wheezing with colds, and previous fibrous mineral exposures in industry or hobbies were not significantly related to age, smoking in pack-years, or cumulative fiber exposure. There was a significant association between history of pneumonia, confirmed by a physician, and age ($p < 0.05$). The prevalence of chronic cough, defined as cough 4 to 6 times/day, 4 or more days/week for 3 consecutive months for at least 2 yr, was significantly related to smoking in pack-years ($p < 0.05$). Apart from colds, wheezing or whistling present for at least 2 yr, and without associated shortness of breath with wheezing or current history of asthma confirmed by a physician, was significantly related to smoking in pack-years ($p < 0.05$). Chronic airway obstruction, defined as wheezing most days or nights and/or Grade 3 dyspnea (stop for breath when walking at your own pace on the level), and/or $FEV_1/FVC\%$ 60% or less, was significantly related to smoking in pack-years ($p < 0.05$). The prevalence of 2 or more attacks of shortness of breath with wheezing without a current history of asthma confirmed by a physician was significantly related to smoking in pack-years ($p < 0.05$) and strongly related to cumulative fiber exposure ($p < 0.1$).

Discriminant analyses indicated shortness of breath Grade I (shortness of breath when hurrying on the level or walking up a slight hill) and Grade II (walk slower than persons your own age on the level because of breathlessness) were significantly related ($p < 0.05$) to both smoking history in pack-years and cumulative fiber exposure. The prevalence of pleuritic chest pain lasting 6 h or more with physician evaluation (figure 1) was significantly related to cumulative fiber exposure ($p < 0.05$).

Physical Examination

The physical examination finding of crackles heard on auscultation of the chest was related to cigarette smoking in pack-years ($p < 0.05$), whereas clubbing of the nails was positively related to age ($p < 0.05$).

Pulmonary Function Tests

There were no differences in mean spirometry values or percent predicted values in relation to cumulative fiber exposure, time since first exposure, or exposure group. Predicted values for blacks were considered to be normally 10% lower than a corresponding white population. The prevalence of "restrictive lung defect" defined as FEV_1/FVC ratio of equal to or greater than 70% and FVC less than 80% predicted was not shown to be significantly related to cumulative fiber exposure. The FEV_1, $FEV_1/FVC\%$, and FEF_{25-75} showed significant differences only between smoking categories ($p < 0.01$). No significant difference in FVC was found for the various smoking categories.

There were no differences in mean D_{LCOSB} or D_L/V_A values or predicted values in relationship to cumulative fiber exposure, time since first exposure, or job category. A significantly low D_{LCOSB} was noted in smokers ($p < 0.01$).

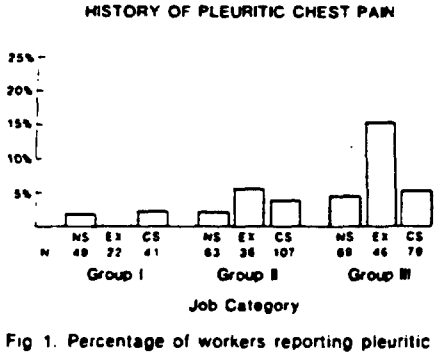

Fig 1. Percentage of workers reporting pleuritic chest pain by exposure group and by cigarette smoking history. Discriminant analysis indicates a significant association between cumulative fiber exposure and history of chest pain ($p < 0.05$). For definition of groups, see table 1

Chest Radiographs

The results of the radiographic survey included all employees with available interpretable films; 501 of 512 (97.9%) employees were reviewed. There were 479 (95.6%) with no significant radiographic changes, 11 (2.2%) with costophrenic angle blunting only, 10 (2%) with significant pleural changes (thickening, plaques, and/or calcifications), and 1 (0.2%) individual showed parenchymal changes of bilateral, small, irregular opacities (table 3). The mean cumulative fiber exposure for the latter 11 employees (10 with pleural and 1 with parenchymal change) was 12.07 (range, 0.01 to 39.9 fiber/ml-yr). The

TABLE 3

CHEST RADIOGRAPH CHANGES

Type	Grade*
Costophrenic angle blunting only, 11 employees	
Pleural changes, 10 employees	
Bilateral pleural thickening	A/1
Bilateral pleural plaques	1/1
Bilateral pleural thickening	C/2
Left pleural thickening	A/1
Bilateral pleural thickening	B/1
Bilateral pleural plaques	1/1
Bilateral pleural thickening	B/2
Left pleural plaque	1/1
Left pleural thickening	A/1
Left pleural plaque	0/1
Right pleural thickening	C/1
Right pleural plaque	1/1
Unilateral pleural thickening	A/1
Left pleural calcification	Grade 1
Bilateral pleural thickening	B/1
Bilateral pleural plaques	1/1
Right diaphragm calcification	Grade 2
Parenchymal changes	
Bilateral small, irregular opacities Type s	Perfusion 1/1

* Grade of pleural thickening width: A, < 5 mm; B, 6-10 mm; C, > 10 mm at widest part of pleural shadow. Grade of pleural thickening by extent: 1 = definite pleural thickening in one or more places, such that the total length do not exceed one half of the projection of one lateral wall; 2 = pleural thickening greater than Grade 1. Certainty of plaque: 0/1, possible present; 1/0, probably present; 1/1, definitely present. Grade of pleural calcification by total length: Grade 1 = < 20 mm, Grade 2 = 20-100 mm; Grade 3 = > 100 mm.

TABLE 5

RADIOGRAPHIC CHANGES BY EXPOSURE GROUP*†

Results	Group I (n)	Group I (%)	Group I Age*	Group II (n)	Group II (%)	Group II Age*	Group III (n)	Group III (%)	Group III Age*
Normal	104	97.2	36.4 ± 10.8	196	96.1	34.9 ± 11.9	179	94.2	39.1 ± 12.0
Costophrenic angle blunting only	1	1.0	55.5	5	2.5	49.7 ± 13.0	5	2.6	41.0 ± 8.2
Pleural/parenchymal changes‡	2	1.9	48.7 ± 8.3	3	1.5	52.5 ± 3.8	6	3.2	55.1 ± 4.0
Combined changes	3	2.8	51.0	8	3.9	50.7	11	5.8	48.7
Total	107			204			190		

* I = control group, II = low fiber exposure group, III = high fiber exposure group.
† Values are mean ± SD
‡ One employee with bilateral small irregular s-type opacities. This employee was in exposure Group III.

mean cumulative fiber exposure for employees with costophrenic angle blunting was 5.4 (range, 0.2 to 27.5 fiber/ml-yr).

There was an increased prevalence of radiographic changes in employees with 1 to 10 and greater than 10 fiber/ml-yr cumulative exposure in comparison with the control group. Of 48 employees with greater than 10 fiber/ml-yr exposure, 12.5% had costophrenic angle blunting or pleural/parenchymal changes (table 4). Employees with greater than 10 yr of employment from initial employment in exposure Groups II or III had an increased prevalence of radiographic changes. Of 48 employees with 20 yr or more of employment, 11.1% had costophrenic angle blunting or pleural/parenchymal changes. Employees ever employed in the low (Group II) or high (Group III) fiber exposure groups had a higher prevalence of radiographic changes than did the control group (table 5). The employees with radiographic changes showing costophrenic angle change only or pleural changes were older ($p < 0.01$) than employees with normal radiographs. Because age could act as a confounding factor in the observed radiographic changes, an age-matched control study was conducted. Each of 22 employees with an abnormal chest radiograph was matched by age to an employee with a normal chest radiograph. A significant difference in cumulative fiber exposure (table 6) was noted between the 22 employees with abnormal radiographs and the control group ($p < 0.041$). The results of the nonparametric analysis (Wilcoxon's sign-rank test) indicated a strong trend toward an association between cumulative fiber exposure and significant pleural/parenchymal abnormalities ($p < 0.098$). An association was noted using discriminate analysis between cumulative fiber exposure ($p < 0.05$), smoking in pack-years ($p < 0.05$), and radiographic changes.

TABLE 4

RADIOGRAPHIC CHANGES BY CUMULATIVE FIBER EXPOSURE

Results	Control* (n)	Control* (%)	Fiber/ml-yr 1-10 (n)	Fiber/ml-yr 1-10 (%)	Fiber/ml-yr > 10 (n)	Fiber/ml-yr > 10 (%)
Normal	247	97.6	190	95.0	42	87.5
Costophrenic angle blunting only	4	1.6	5	2.5	2	4.2
Pleural/parenchymal changes†	2	0.9	5	2.5	4	8.4
Combined changes	6	2.4	10	5.0	6	12.5
Total	253		200		48	

* Less than 1 fiber/ml-yr total exposure
† One employee with bilateral small irregular s-type opacities. This employee's cumulative exposure was 39 fiber/ml-yr

Discussion

This cross-sectional epidemiologic study revealed a number of findings showing a significant association with cumulative fiber exposure: dyspnea on exertion, pleuritic chest pain, and pleural changes on chest radiograph. Furthermore, an apparent dose-response relationship between cumulative fiber exposure and radiographic changes was suggested.

The occurrence of dyspnea among workers occupationally exposed to asbestos has been documented in previous studies (8-10). The presence of dyspnea on exertion was associated with cumulative tremolite fiber exposure. This is in the face of a relatively low cumulative fiber exposure and a relatively short latency period for the work force. The association among cigarette smoking and the presence of chronic cough, wheezing, and spirometric evidence of air-flow obstruction is expected and provides validation of the questionnaire.

The observed association between the presence of pleuritic chest pain and cumulative tremolite fiber exposure is an interesting finding. The presence of

TABLE 6

DIFFERENCES IN EXPOSURE (FIBER/ML-YR) PAIR-MATCHED ANALYSIS (NORMAL VERSUS ABNORMAL RADIOGRAPH) AND PARAMETRIC ANALYSIS (PAIRED *t* TEST)*

	Exposure Fiber/ml-yr		
	Costophrenic Angle Blunting Only (*n* = 11 pairs)	Pleural/Parenchymal Change† (*n* = 11 pairs)	Both (*n* = 22 pairs)
Mean difference	3.0	8.6	5.8
SD	9.7	14.7	12.5
p	0.232	0.082	0.041

* Cases were each matched by age with employees who had normal radiographs
† One employee with bilateral small irregular s-type opacities

pleuritic chest pain was documented if the employee was evaluated by a physician, and no specific medical or surgical cause for chest pain was identified. Pleuritic chest pain was examined because it can be a clinical manifestation of inflammation involving the parietal pleura. Irritation of pleura surface by inhaled fibers is a postulated mechanism for the occurrence of pleural effusion and plaque formation. A recent hypothesis suggests that the fibers reach the parietal pleura by lymphatic drainage. Macrophages within the parietal pleural engulf fibers and stimulate submesothelial fibroblasts with subsequent pleura plaque formation (11, 12). In either case, the resulting inflammation from pleural irritation may cause pleuritic chest pain, possible bloody pleural effusions and, eventually, pleural thickening or pleural plaque formation.

The pleural changes noted on chest radiographs of workers exposed to airborne fibrous tremolite are consistent with the pleural changes seen with commercial asbestos exposure (11, 13-16). In the present study, the prevalence of these pleural changes increased with duration of exposure, time since initial exposure, and high exposure group, and were dose related. The absence of significant parenchymal changes (i.e., asbestosis-fibrosis) and a higher percentage of pleural changes most likely reflect the short interval since initial exposure and the low cumulative fiber exposure. In any event, the presence of a greater prevalence of pleural disease among the population exposed to vermiculite contaminated with fibrous tremolite is supported by the following observations: (*1*) cluster of 12 cases of benign pleural effusion, (*2*) higher prevalence of pleural changes on chest radiographs, (*3*) age-matched control study revealing greater tremolite fiber exposure among workers with pleural changes on chest radiographs, and (*4*) higher prevalence of pleuritic chest pain in exposed employees.

The lack of association between simple spirometric and D_{LCOSB} measurements and fiber exposure most likely reflects the low cumulative fiber exposure and short interval period. Simple spirometric measurements have been shown to be sensitive indicators of the toxic effects of cumulative asbestos exposure. The D_{LCOSB} changes are not asbestos-dose related and are less sensitive than spirometry (17-19). The level of cumulative fiber exposure needed to cause a change in spirometric values is greater than the exposure levels reported in the present study. Weill and colleagues (18) reported decrease in lung function after 100 mppcf-year dust exposure, while Becklake and colleagues (19) showed an effect at a cumulative dust exposure index of 10 to 100 mppcf-year. Berry and Lewinsohn demonstrated a 12.1% reduction for FEV, and 10.6% reduction for FVC per 100 fiber/cc-years (20).

The cumulative fiber exposure in this study was low compared with that in other studies. Only 9.6% of the employees had greater than 10 fiber/ml-yr exposure; 10.7% had been employed 20 yr or more since initial exposure. The highest cumulative fiber exposure for any employee was 39 fiber/ml-yr. It is likely that the exposure level reported in this study underestimates the actual cumulative fiber exposure. No industrial hygiene data were available before 1972; the lower fiber values after 1974 reflect improved environmental controls within the facility. Additionally, personal sampling, which more adequately reflects individual exposure, was not introduced until 1976.

Nonmalignant pleural changes associated with asbestos exposure include pleural plaques with or without calcification, bilateral pleural thickening, progressive pleural fibrosis (21-23), pleural effusions, and pleural thickening, with costophrenic angle involvement or costophrenic angle blunting alone as residual findings of a previous pleural effusion (15, 24). The prevalence of pleural changes commonly exceeds that of asbestos-related interstitial fibrosis (25, 26). The prevalence of pleural plaques, calcification, and thickening is related to duration of asbestos exposure, time since onset of exposure (10, 17, 27-29), and possible cumulative fiber exposure (30, 31). The occurrence of pleural effusions may be an early manifestation of asbestos exposure (15, 32).

The majority of asbestos-related pleural changes have a latency period of more than 20 yr from initial exposure (28). However, pleural changes are seen in workers with short durations of asbestos exposure. Studies of asbestos insulation workers (21), Navy shipyard workers (26), household contacts of amosite asbestos workers (10), and Quebec chrysotile mine and mill workers (24) support this observation.

Benign asbestos-related pleural effusions are now recognized to cause pleural change including greater than 50% rate of residual pleural thickening and greater than 90% of residual costophrenic angle blunting. The occurrence of asbestos-induced pleural effusion appears to be dose related and represents, in one study, the most common manifestation of asbestos exposure in the initial 20 yr since first exposure (15). In the current study, 7 employees were still employed with previously documented benign pleural effusions. Of these 7, four had residual pleural changes, including 2 with unilateral costophrenic angle blunting, 1 with bilateral costophrenic angle blunting, and 1 with bilateral pleural thickening and pleural plaques. These 4 were included in the total of 22 employees with pleural changes noted in chest radiographs.

The prevalence of pleural thickening and pleural calcification in a rural population of midwestern dairy farmers without occupational exposure to fibrogenic dust was found to be 0.9% and 0.0%, respectively. The prevalence in a New Jersey urban population was 1.2% for pleural thickening and 0.0%

or pleural calcification (21). The predictive value for bilateral pleural thickening as an indicator of previous possible asbestos exposure with exclusion of known medical or surgical etiologies was recently found to be 81% (23).

A careful review of all chemical and physical agents used at the plant facility failed to identify any substance known to be associated with pleural radiographic changes. A few of the chemicals could cause acute pulmonary injury after exposure to high concentrations. The study and control populations were evenly matched for exposure history, except for the presence or absence of exposure to vermiculite contaminated with tremolite.

There are over 150 minerals that exist in fibrous form and that are generally expected to contain fibrous minerals (3). The amphibole tremolite is a silicate mineral found in commercial talc deposits from New York state and in vermiculite deposits within the United States (4, 33). The size and shape of tremolite after undergoing crushing and grinding in a milling process is largely dependent on the original crystalline structure of the mineral. Tremolite can occur in a fibrous form with high aspect ratios identical to commercial asbestos fibers or as cleavage fragments with lower aspect ratios (34, 35). The commercial talc deposits in New York state contain varying amounts of tremolite and anthophyllite, both as cleavage fragments and as true fibers (33). The vermiculite deposits from Montana contain a fibrous form of tremolite, while the vermiculite deposits in Virginia and South Carolina contain a type of tremolite that forms predominantly cleavage fragments when milled (4). Vermiculite itself does not exist in a fibrous form, but plates of vermiculite can roll up on themselves as a scroll and resemble fibers (36).

Tremolite is not mined or used as a commercial asbestos. Therefore, no working populations were exposed only to tremolite. On the other hand, natural exposure to tremolite does occur in certain rural populations. Pleural changes, including plaques and calcifications, have been reported in rural populations of Czechoslovakia, Bulgaria, Finland, and Greece. These changes have been attributed to tremolite and anthophyllite fibers deposited in the local soil (37, 38). A recent epidemiologic report on 7,000 inhabitants around the town of Cermik in southeast Turkey, where local deposits of minerals containing fibrous tremolite are used to make whitewash and stucco, revealed an increased prevalence of pleural thickening and calcification and interstitial pulmonary fibrosis (39).

Animal studies in rats with fibrous tremolite administered by intraperitoneal injection have shown it to be both fibrogenic and tumorgenic (40). Although reported animal studies with vermiculite are limited, 2 studies on the use of South African vermiculite (generally believed to be free of tremolite) did not show fibrogenic or tumorgenic changes after intrapleural or intratracheal injection (41, 42).

Exposure to fibrous tremolite that contaminates certain vermiculite ores can cause pulmonary abnormalities. Identification of other minerals that have similar fiber contamination and recognition of the potential health implications are critical issues in occupational and pulmonary medicine. Just as important is the recognition that not all amphiboles exist in fibrous forms. The biologic activity of tremolite that forms cleavage fragments with low aspect ratios may be different from fibrous tremolite with high aspect ratios. There are enormous health, economic, and regulatory implications at stake in these issues.

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