Respiratory morbidity in wollastonite workers

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ABSTRACT Medical and environmental surveys were conducted at a wollastonite mine and mill in 1976 and in 1982. Health testing included chest radiography, spirometry, and a questionnaire. Workers at a nearby electronics plant were also examined in 1982 for a comparison of lung function and respiratory symptoms. Both wollastonite and control workers showed significant smoking effects for chronic respiratory symptoms, but differences between the groups were not detected. Pneumoconiosis was found in 3% (3/108) of the wollastonite workers in 1982, but none showed a significant progression from their 1976 radiographs. The lung function tests of the 108 wollastonite workers examined in 1982 showed dust related changes in FEV_1 , FEV_1/FVC ratio, and peak flow rate which were independent of age, height, and smoking habit ($p < 0.01$). For non-smokers alone, only the FEV_1/FVC ratio declined significantly with dust-years of exposure ($p < 0.01$). The comparison of lung function in 1982 between a high dust exposed subgroup of wollastonite workers and the control population showed a significantly lower FEV_1/FVC ratio and peak flow rate in the study group ($p < 0.05$). Analysis of 1976-82 changes in pulmonary function showed that wollastonite workers with higher dust exposure had a significantly greater decline in peak flow over the period than workers with lower exposures ($p < 0.01$). These data suggest that long term cumulative exposure to wollastonite may impair ventilatory capacity as reflected by changes in the FEV_1/FVC ratio and peak flow rate.

The adverse health effects that arise from exposure to asbestos has stimulated much research into the development of substitute materials.¹ One such substitute is the fibrous monocalcium silicate wollastonite. Wollastonite is used industrially as a filler and flux in wall tile and glass (ceramics), and in grinding wheels, refractory products, building blocks, acoustical tiles, wallboard, and paints. Reserves of this mineral are limited, however, and active mining takes place only in Finland and the United States.

In the United States underground and open pit mining occur at a single site located in the state of New York. The recovered ore is transported to an adjacent plant where garnet and diopside are removed and the relatively pure mineral is milled. In 1976 the National Institute for Occupational Safety and Health (NIOSH) performed a cross sectional environmental survey of this plant and examined workers with simple spirometry, chest radiography, and a respiratory questionnaire.^{2,3} Analysis of dust collected during this survey showed less than 2%

free silica, and fibrous particulates with a median diameter of $0.22 \mu\text{m}$ and a median length of $2.5 \mu\text{m}$. Airborne fibre counts by phase contrast microscopy showed 0.3 fibres/cc in the mine, and 23.3 fibres/cc in the mill. No significant respiratory abnormalities were found.

The workers were re-examined in 1982 by similar methods, and we report the results of this cross sectional and follow up survey. The purpose of the present study was to reassess respiratory morbidity based on accumulated environmental data. Findings are discussed in relation to dust exposure, type of ventilatory changes observed, and pulmonary responses to other fibrous mineral dusts.

Methods

The NIOSH surveys included an assessment of the respiratory health of the miners and mill workers, and an environmental assessment of workplace exposure. NIOSH industrial hygiene data are supplemented by dust measurements of the company and the Mine Safety and Health Administration (MSHA) obtained during the 1977-81 interstudy

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period. In addition, male workers at a nearby electronics component plant were studied in 1982 as a comparison group for lung function and respiratory symptoms.

ENVIRONMENTAL

The NIOSH surveys included personal breathing zone samples of respirable and total dust in the mine and mill occupations. These were obtained over full working shifts using portable pumps with cyclone preselectors (respirable dust samples only). Tared filters were subsequently collected, and dust concentrations were measured gravimetrically. The results are reported as eight hour time weighted averages.

MEDICAL

Health testing at each survey included administration of a modified British Medical Research Council questionnaire, spirometry, and chest radiography. Questionnaires were administered by experienced interviewers, and elicited data on smoking, respiratory symptomatology, and work history.

Spirometric testing conformed to criteria recommended by the American Thoracic Society,⁴ and consisted of at least five forced expiratory manoeuvres into an Ohio 840 rolling seal spirometer. Flow volume curves were recorded on FM analogue tape and later processed by a digital computer (LSI 11/23, Digital Equipment Corporation). From a minimum of three acceptable manoeuvres, the largest forced vital capacity (FVC), forced expiratory volume in the first second (FEV₁), and peak flow rate were selected regardless of the curve(s) on which they occurred.

Radiography included standard 14 × 17 inch posteroanterior and lateral views of the chest. All chest films were independently interpreted by three certified pneumoconiosis readers using the 1980 ILO classification;⁵ the films were read without knowledge of worker occupation or exposures, and were considered positive for pneumoconiosis if at least two readers classified small opacity profusion as category 1/0 or greater. For those workers examined in 1976 and 1982, paired films were interpreted using the side by side method.

EXPOSURE INDEX

Based on NIOSH, MSHA, and company total dust data, the occupations of the wollastonite workers were grouped into five exposure categories (table 1). Since the mean dust concentrations from the three sources were similar, all were used to derive a mean concentration representative of each of the five categories. From these exposure estimates and each participant's work history, an index of lifetime

Table 1 Mean total dust concentrations* ($\pm$ SD) used in calculating dust-years by job category

Job category	NIOSH (1976 and 1982)	MSHA and company (1977-81)	All sources
All mining except crushing (n = 2)	0.90 (n = 2)	0.93 $\pm$ 1.94 (n = 9)	0.90 $\pm$ 2.16 (n = 11)
All administrative activities in mill (n = 2)	2.30 (n = 2)	—	2.30 (n = 2)
All milling and crushing (n = 11)	5.24 $\pm$ 1.95 (n = 11)	3.33 $\pm$ 1.40 (n = 15)	4.10 $\pm$ 1.90 (n = 26)
Labourer and beneficiator (n = 8)	11.65 $\pm$ 1.85 (n = 8)	6.88 $\pm$ 1.60 (n = 9)	8.71 $\pm$ 1.80 (n = 17)
Mill maintenance and packers (n = 26)	10.30 $\pm$ 1.93 (n = 26)	9.73 $\pm$ 1.99 (n = 15)	10.00 $\pm$ 1.94 (n = 41)

*Dust concentrations are reported in mg/M³ of air.

cumulative total dust exposure was calculated, where cumulative total dust exposure = $\sum (K_j \times T_j)$, and j = job category, T = time in years, and K = mean total dust concentration.

STATISTICAL

The analysis of the pulmonary function of the wollastonite workers uses a linear model fit of age, height, smoking status, and exposure expressed as total dust-years. Coefficients for each of these independent variables were derived from the model for FEV₁, FVC, FEV₁/FVC ratio, and peak flow rate, and were assessed for significance by a two-tailed *t* test at an alpha level of 0.05. The comparison of lung function between wollastonite and control workers uses a two tailed Student's *t* test for comparison of unpaired means.

Results

CROSS SECTIONAL STUDY (1982)

The study and comparison populations were composed entirely of white men. Participation rates were 89% among current workers, 25% among former workers, and 93% among comparison group workers (table 2). The mean age and tenure of par-

Table 2 Demographic characteristics of wollastonite and comparison workers by 1982 work status

	No (% total)	Mean age (y) (SD)	Mean tenure (y) (SD)
Wollastonite workers:			
Participants:			
Current workers	102 (89%)	36 (12)	10 (9)
Former workers	6 (25%)	47 (13)	11 (9)
Non-participants:			
Current workers	12 (11%)	36 (11)	7 (4)
Former workers	18 (75%)	56 (14)	13 (6)
Control workers	86 (93%)	42 (11)	—

Table 3 Prevalence of respiratory symptoms in wollastonite and control workers by smoking habit. (Percentages in parentheses)

Respiratory symptoms	Wollastonite			Control		
	NS	Ex	S	NS	Ex	S
Chronic cough, n	0 (0)	2 (7)	12 (24)*	0 (0)	3 (14)	16 (39)*
Chronic phlegm, n	1 (3)	2 (7)	14 (29)*	2 (8)	1 (5)	18 (44)*
Chronic bronchitis, n	0 (0)	0 (0)	10 (20)*	0 (0)	1 (5)	8 (20)*
Wheezing, n	5 (16)	3 (11)	15 (31)	6 (25)	5 (24)	15 (37)
Shortness of breath with wheezing, n	3 (9)	0 (0)	5 (10)	0 (0)	0 (0)	0 (0)
No	32	27	49	24	21	41
Mean age (y)	34	41	35	40	47	42

NS = Non-smokers; Ex = Ex-smokers; S = Current smoker.

*p < 0.01 compared with never smokers in the same group.

Table 4 Coefficient estimates from regression analysis for lung function of wollastonite workers

	FEV ₁ (l)	FVC (l)	FEV ₁ /FVC	PFR (l/s)
<i>Total population (n = 108)</i>				
Intercept	- 1.2102	- 2.7407	0.9370	- 1.5000
Age (y)	- 0.0252**	- 0.0233**	- 0.0014	- 0.0326*
Height (cm)	- 0.0357**	- 0.0512**	- 0.0007	- 0.0700**
Smoking status:				
Smoker	0.0000	0.0000	0.0000	0.0000
Ex-smoker	- 0.1032	- 0.1023	- 0.0037	- 0.0433
Non-smoker	0.0600	0.2060	0.0525	0.2674
Dust-years†	- 0.0037*	- 0.0019	- 0.0005**	- 0.0088**
<i>Non-smokers (n = 32)</i>				
Intercept	- 2.9127	- 8.9240	1.6816	- 8.5478
Age (y)	- 0.0098	- 0.0240**	0.0022	- 0.0086
Height (cm)	- 0.0433**	- 0.0848**	- 0.0051**	- 0.1072**
Dust-years†	- 0.0060	0.0057	- 0.0022**	- 0.0052

*p < 0.02; **p < 0.01.

†(mg-y/MP).

ticipating current and former workers were not significantly different from those not examined. Comparison group workers were significantly older than the current worker group.

Chest radiography showed simple pneumoconiosis in 3% (3/108) of participating wollastonite workers. All three individuals had participated in the 1976 NIOSH survey, and had been considered then to have category 1 pneumoconiosis. Radiographic progression beyond category 1 was not observed in their 1982 chest x ray films. The workers with pneumoconiosis showed rounded opacities, had nine to 23 years of tenure, and a cumulative total dust exposure of 66 to 169 dust-years. By contrast, the entire study population averaged 10 years of tenure and 45 dust-years of exposure. Pleural abnormalities were not observed in the study group.

The prevalence of respiratory symptoms in the wollastonite workers was examined by smoking habit and total dust-years of exposure. Current smokers were found to have significantly higher prevalence rates of chronic cough, chronic phlegm, and chronic bronchitis than non-smokers ($p < 0.01$, table 3). To evaluate the effect of wollastonite exposure, workers were divided into groups accord-

ing to their cumulative dust-years of exposure. After stratification by smoking habit, no significant differences were observed between the various exposure categories. A comparison of the prevalence of symptoms between the wollastonite and control plant workers also failed to show any significant differences when adjusted for smoking habit.

The analysis of pulmonary function in the wollastonite workers used multiple regression techniques, and the results are summarised in table 4. After allowing for the effects of age, height, and smoking FEV₁, FEV₁/FVC ratio, and peak flow rate declined with increasing total dust-years of exposure and the dust-years' coefficients for these lung function tests were significantly different from zero ($p < 0.01$). To avoid a potential interaction between smoking and exposure index, the results are also reported for non-smokers alone. For this group only the FEV₁/FVC ratio showed a significant decline with total dust-years of exposure ($p < 0.01$).

As lung function decrements may result from long term dust exposure, the lung function data were also examined for the comparison population and wollastonite workers with more than 30 dust-years of exposure (table 5). Both groups were similar in age,

Table 5 Lung function and related data of control plant and wollastonite workers with over 30 dust-years of exposure

	Control workers	Wollastonite workers (> 30 dust-years)
No	86	52
Mean age (y) (SD)	42 ± 11	41 ± 12
Mean height (cm) (SD)	173 ± 6	173 ± 6
Smoking status:		
% Non-smokers	28	25
% Ex-smokers	24	33
% Current smokers	48	42
Mean peak-years (SD)	18 ± 18	20 ± 18
FEV ₁ (l), SD	3.68 ± 0.69	3.56 ± 0.73
FVC (l), SD	4.73 ± 0.68	4.87 ± 0.67
FEV ₁ /FVC, SD	0.78 ± 0.08	0.73 ± 0.09**
Peak flow (l/s), SD	9.30 ± 1.89	8.59 ± 1.76*

*p < 0.05; **p < 0.01.

Table 6 Regression analysis of change in pulmonary function for 57 wollastonite workers examined in 1976 and 1982

	FEV ₁ (l)	FVC (l)	FEV ₁ /FVC	PFR (l/s)
Intercept	1.1135	1.2216	0.0316	6.9140
Age (y)	-0.0034	-0.0100	0.0005	-0.0237
Height (cm)	-0.0079	-0.0070	-0.0004	-0.0369
Smoking status:				
Smoker	0.0000	0.0000	0.0000	0.0000
Ex-smoker	0.0323	0.1264	-0.0143	-0.1061
Non-smoker	0.1240	0.1191	0.0079	0.1984
Dust-years†	-0.0003	0.0001	0.0001	-0.0053*

†(mg-y/MP).

*p < 0.02.

height, and smoking habit. This high exposure subgroup of wollastonite workers had significantly lower mean values of the FEV₁/FVC ratio and peak flow rate than the non-exposed population (p < 0.05).

FOLLOW UP STUDY

Sixty one of the 82 workers included in the 1976 NIOSH survey were re-examined in 1982. Since the 1976 pulmonary function data of three workers, and the 1982 data of one worker, were technically unsatisfactory, the follow up study was limited to 57 workers, representing 71% of the 80 men still alive in 1982. A comparison of the mean age, mean tenure, and 1976 lung function data of the workers tested in 1976 only versus those examined in 1976 and in 1982 showed no significant differences between the groups.

The mean annual decrement in FEV₁ for workers participating in both surveys was 49 ml for never smokers, and 75 ml for current smokers. For FVC, the mean annual decrements were 47 ml for never smokers, and 73 ml for current smokers. Linear modelling on age, height, smoking habit, and total dust-years was also performed for the 1976-82 changes in spirometry (table 6). This analysis showed a significant relation between the decline in

peak flow rate and total dust-years of exposure (p < 0.02).

Discussion

Respiratory morbidity from the inhalation of fibrous mineral dusts has been the subject of several recent reviews.⁶⁻⁸ Exposure to asbestos minerals has been associated with pleural disease, diffuse interstitial pulmonary fibrosis, and malignancies of the respiratory tract.⁹ Knowledge of the pulmonary disease which might result from exposure to acicular non-asbestos minerals is scanty and limited to a few isolated reports of radiographic findings in select populations often with mixed exposures.

Pleural and parenchymal lung fibrosis have been described in a Turkish population with exposure to fibrous zeolite minerals from soil and building materials.¹⁰ Of 312 persons examined in one village, 17% were found to have calcified pleural plaques, 10.5% pleural thickening, and 12% pulmonary fibrosis. Chest x ray films in 95 inhabitants of a second village without zeolites in the environment had no pulmonary abnormalities. Malignant pleural mesotheliomas have also been described in zeolite exposed Turkish communities^{10 11} and benign pleural effusions have been noted in a group of

workers exposed to vermiculite contaminated with amphibole asbestos fibres.¹² Baris and co-workers obtained chest x ray films from 63 workers employed as trimmers of the clay mineral sepiolite,¹³ ten of whom were observed to have pneumoconiosis and to reside in homes that had been finished with a tremolite (asbestos) containing stucco. Attapulgite, another fibrous clay mineral, has been implicated in lung fibrosis in a single case report.¹⁴

This study presents data on respiratory morbidity in a small population of wollastonite miners and mill workers. In the 1982 survey a significant smoking effect was observed in both the wollastonite and the comparison populations for chronic cough, chronic phlegm, and chronic bronchitis ($p < 0.01$, table 3). No influence of wollastonite dust exposure on the prevalence rates of these symptoms was found in the exposed population. Similar findings have been reported in Finnish wollastonite workers.¹⁵ Both studies, however, contained small numbers of exposed workers and substantial proportions of cigarette smokers.

The prevalence rate of pneumoconiosis among wollastonite workers was 3% (3/108). The small opacities in each case were rounded, and pleural abnormalities were not detected. By contrast, chest radiographs of 46 Finnish wollastonite workers are described as exhibiting pneumoconiosis with small irregular opacities in 30%, and bilateral pleural thickening in 28%. These findings may reflect differences in the nature of exposure and the time since initial exposure between the two wollastonite populations. Dust exposure in the current population has been described in terms of dose (total dust), elemental composition, crystalline silica content ($< 2\%$), and lack of contamination by asbestos fibres^{2,3}; these data have not been reported for the Finnish cohort. It is clear, moreover, that the Finnish group had a longer time since first exposure, all workers having had 10 or more years of tenure, and perhaps also a larger dose, than the current population whose mean tenure was under 10 years. Use of magnified chest films in the Finnish study and differences in the mechanism for handling disparate interpretations may also contribute to these divergent observations. Complete occupational histories in both studies suggest that previous exposure to noxious dusts is an unlikely explanation for the observed differences in radiographic findings.

The analysis of pulmonary function was based on linear modelling techniques using a total dust-years index of exposure, and a comparison of mean spirometric values between a high dust exposed subgroup and the control population. Total dust was used as the exposure variable since most data were

available for this measurement. In the initial NIOSH survey of 1976 few data were obtained for respirable dust, and airborne fibre concentrations were not available for the interstudy period. The consistency of sample results from independent sources for total dust (NIOSH, MSHA, and company) suggested, moreover, a greater reliability in this measurement.

Lung function in the 1982 survey was found to be affected by exposure to wollastonite dust. FEV₁, FEV₁/FVC ratio, and peak flow rate were all associated with total dust-years of exposure independent of age, height, and smoking habit ($p < 0.02$, table 4). Regression analysis for non-smoking wollastonite workers confirmed the significance of these results for the FEV₁/FVC ratio ($p < 0.01$). While potential interactions between age, smoking habit, and dust-years cannot be fully eliminated by regression techniques, the strength of the association for at least the FEV₁/FVC ratio is supported by the results of the comparison of pulmonary function between the non-exposed population and wollastonite workers with more than 30 dust-years of exposure (table 5).

Analysis of longitudinal changes in pulmonary function showed an association between cumulative dust exposure and a decline in peak flow rate (table 6). No such effect was demonstrable for FEV₁, FVC, or their ratio. The annual rates of decline in FEV₁ and FVC derived from the two surveys are difficult to interpret since a non-exposed population was not examined in 1976. Serial lung function testing in several studies has shown annual rates of decline in FEV₁ ranging from 20 ml to 60 ml in non-exposed workers.¹⁶⁻²¹ Nevertheless, these populations have differed in age, smoking habit, and on exposure to general air pollutants, as well as frequency of examination and duration of follow up. While the decline in FEV₁ (49-75 ml a year) and FVC (47-73 ml a year) observed in our study are somewhat greater than those reported, the only appropriate comparison requires longitudinal examination of a suitable control population.²² Prospective study of the comparison group examined in 1982 will provide such a reference group for future surveys.

The lung function data indicate an obstructive ventilatory effect from wollastonite dust exposure. The observed decrement in peak flow rate suggests that at a minimum large airways are affected. Although forced expiratory flows at low lung volumes were examined and found not to be significantly affected, the greater variability of these measurements is well known.²³ Coupled with the relative insensitivity of spirometry to small airway dysfunction²⁴ and the small size of our population, these data are insufficient to discard an effect on

small airways.

Wollastonite's potential as an industrial exposure is restricted by the paucity of commercially exploitable deposits. Exposure will probably be limited to miners, millers, and workers in the few industries using the milled product. The current study suggests, however, that wollastonite dust may not be an entirely innocuous exposure.

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References

- ¹ National workshop on substitutes for asbestos. Washington: EPA, 1980. (Publication No EPA-560/4-80-001.)
- ² Zumwalde R. *Industrial hygiene study of the Interpace Corporation, Willsboro, New York. Division of surveillance, hazard evaluation, and field studies.* Morgantown, West Virginia: NIOSH, 1976.
- ³ Shasby DM, Peterson MR, Hodous TK, Boehlecke BA, Merchant JA. Respiratory morbidity of workers exposed to wollastonite through mining and milling. In: Lemen P, Dement JM, eds. *Dust and disease.* Illinois: Pathotox Publishers Inc. 1979:251-6.
- ⁴ American Thoracic Society. Standardization of spirometry. *Am Rev Respir Dis* 1979; **119**:831-9.
- ⁵ International Labour Organisation. *Guidelines for use of the ILO classification of radiographs of pneumoconioses.* Geneva: ILO, 1980.
- ⁶ Craighead JE, Mossman BT. The pathogenesis of asbestos-associated diseases. *N Eng J Med* 1982; **306**:1446-55.
- ⁷ Becklake MR. Asbestos-related diseases of the lungs and other organs: their epidemiology and implications for clinical practice. *Am Rev Respir Dis* 1976; **114**:187-227.
- ⁸ Lockey JE. Nonasbestos fibrous minerals. *Clin Chest Med* 1981; **2**:203-18.
- ⁹ New York Academy of Sciences. Health hazards of asbestos exposure. *Ann NY Acad Sci* 1979; **330**:1-814.
- ¹⁰ Artvinli M, Baris YI. Malignant mesotheliomas in a small village in the Anatolian region of Turkey: an epidemiologic study. *JNCI* 1979; **63**:17-20.
- ¹¹ Baris YI, Artvinli M, Sahin AA. Environmental mesothelioma in Turkey. *Ann NY Acad Sci* 1979; **330**:423-32.
- ¹² Lockey JE, Brooks SM, Jarabek AM, et al. Pulmonary changes after exposure to vermiculite contaminated with fibrous tremolite. *Am Rev Respir Dis* 1984; **129**:952-8.
- ¹³ Baris YI, Sahin AA, Erkan ML. Clinical and radiological study in sepiolite workers. *Arch Environ Health* 1980; **35**:343-6.
- ¹⁴ Sors H, Gaudichet A, Sebastien P, Bignon J, Even P. Lung fibrosis after inhalation of fibrous attapulgite. *Thorax* 1979; **34**:695.
- ¹⁵ Huuskonen MS, Tossavainen A, Koskinen H, et al. Respiratory morbidity of quarry workers exposed to wollastonite. In: Gee JBL, Morgan WKC, Brooks SM, eds. *Occupational lung disease.* New York: Raven Press, 1984: 245.
- ¹⁶ Berry G, McKerrow CB, Molyneux MKB, Rossiter CE, Toblenson YBL. A study of the acute and chronic changes in ventilatory capacity of workers in Lancashire cotton mills. *Br J Ind Med* 1973; **30**:25-36.
- ¹⁷ Ashley F, Kannel WB, Sorlie PD, Masson R. Pulmonary function: relation to aging, cigarette habit and mortality. The Frammingham study. *Ann Intern Med* 1975; **82**:739-45.
- ¹⁸ Kauffmann F, Drouet D, Lellouch J, Brille D. Occupational exposure and 12-year spirometric changes among Paris area workers. *Br J Ind Med* 1982; **39**:221-32.
- ¹⁹ Fletcher C, Peto R, Tinker C, Speizer FE. *The natural history of chronic bronchitis and emphysema.* New York: Oxford University Press, 1976.
- ²⁰ Sparrow D, Bosse R, Rosner B, Weiss ST. The effect of occupational exposure on pulmonary function: a longitudinal evaluation of fire fighters and nonfirefighters. *Am Rev Respir Dis* 1982; **125**:319-22.
- ²¹ Van der Lende R, Kok TJ, Peset Reig R, Quanjer PH, Shouten JP, Orie NGM. Decreases in VC and FEV₁ with time: indicators for effects of smoking and air pollution. *Bull Europ Physiopath Respir* 1981; **17**:775-92.
- ²² Glindmeyer HW, Diem JE, Jones RN, Weill H. Noncomparability of longitudinally and cross-sectionally determined annual change in spirometry. *Am Rev Respir Dis* 1982; **125**:544-8.
- ²³ Pennock BE, Rogert RM, McCaffree DR. Changes in measured spirometric indices. *Chest* 1981; **80**:97-9.
- ²⁴ Macklem PT. Obstruction in small airways—a challenge to medicine. *Am J Med* 1972; **57**:721-4.