Asbestos-induced Pleural Fibrosis and Impaired Lung Function[1,2]

DAVID A. SCHWARTZ, LAURENCE J. FUORTES, JEFFREY R. GALVIN, LEON F. BURMEISTER, LYNN E. SCHMIDT, BRUCE N. LEISTIKOW, FRANK P. LAMARTE, and JAMES A. MERCHANT

SUMMARY To assess the clinical significance of asbestos-induced pleural fibrosis, we evaluated the relationship between radiographic evidence of pleural fibrosis and spirometric values in 1,211 sheet metal workers. Of those with pleural fibrosis (n = 334), 78% had circumscribed plaques and 22% had diffuse pleural thickening involving the costophrenic angle. Factors that were found to be associated with the presence and type of pleural fibrosis included increased age ($p < 0.001$), more years in the trade ($p < 0.0001$), more years since first exposure to asbestos ($p < 0.0001$), more pack-years of cigarette smoking ($p < 0.01$), and the presence and degree of interstitial fibrosis ($p < 0.0001$). After controlling for these potential confounders (age, years in the trade, latency, pack-years of smoking, and ILO profusion category), linear multivariate regression models demonstrated that both circumscribed plaques ($p = 0.007$) and diffuse pleural thickening ($p = 0.008$) were independently associated with decrements in FVC but not with decrements in the FEV_1/FVC ratio. Furthermore, our data indicate that the effect of diffuse pleural thickening on decrements in FVC is approximately twice as great as that seen with circumscribed pleural plaques. We conclude that the presence and type of pleural fibrosis among asbestos-exposed workers is independently associated with a pattern of spirometry that is suggestive of an underlying restrictive defect in lung function.

AM REV RESPIR DIS 1990; 141:321-326

Introduction

Between 1940 and 1979, 27.5 million persons in the United States were exposed to asbestos while at work (1). Among exposed workers, almost 19 million have had cumulative exposures that are considered to be potentially hazardous (1). These asbestos-exposed persons are at risk of developing pulmonary fibrosis, lung cancer, mesothelioma, and gastrointestinal malignancies (1-4). Although pleural fibrosis is a characteristic feature of asbestos exposure and occurs much more commonly than any of the other diseases, the potential association between pleural fibrosis and pulmonary impairment has not been adequately studied.

It has been suggested that asbestos-induced diffuse pleural thickening is associated with impairment in lung function (5-8). These case reports document reduced lung volumes (5-7) and abnormal responses to exercise (high minute ventilation and high V_D/V_T) (8) in asbestos-exposed subjects with diffuse pleural thickening. However, given the highly selected nature of the study subjects in these case reports, one is unsure whether unselected subjects with diffuse pleural thickening also have restrictive lung function. Moreover, none of these case reports (5-8) was able to adequately control for the presence and degree of interstitial fibrosis while examining the relationship between diffuse pleural thickening and lung function.

Recently, several investigators (9-16) have found that pleural plaques alone may account for reduced lung volumes. Of those studies that observed a relation between reduced lung volumes and pleural plaques (9-16), none examined this association in asbestos-exposed workers with and without radiographic fibrosis and also controlled for potentially important confounders such as age, exposure duration, smoking history, and degree of interstitial fibrosis. Because radiographically inapparent parenchymal fibrosis may confound the relationship that was observed between pleural fibrosis and reduced lung volumes, additional measures must be taken to assure that this relationship exists apart from the well-established association between parenchymal fibrosis and restrictive lung function. It is also recognized that a recent cross-sectional (17) and longitudinal (18) analysis of asbestos-exposed cement workers failed to demonstrate an association between pleural fibrosis and decrements in lung function.

Given the large number of exposed workers who are likely to have or to develop asbestos-induced pleural fibrosis, it is important to quantitatively determine the relationship between pleural fibrosis and pulmonary impairment in a large cohort of asbestos-exposed workers. Moreover, although previous reports have suggested that diffuse pleural thickening is likely to be associated with greater losses in lung volume than are circumscribed pleural plaques, none of the previous studies has directly investigated this hypothesis. We conducted this study to determine whether pleural fibrosis is associated with diminished lung volumes and, if so, whether the type of pleural fibrosis (circumscribed pleural plaques versus diffuse pleural thickening) is a determinant of the extent of pulmonary impairment.

Methods

Study Population

In 1986, the Sheet Metal Workers' International Association initiated a nationwide, union-sponsored medical evaluation of all of its active and retired members who were employed for at least 25 yr. The University of Iowa, through its outreach program, Worksafe Iowa, provided the medical evaluation for sheet metal workers residing in the midwestern United States. Approximately 2,643 members of 12 union locals from the Sheet Metal Workers' International Association located in the Midwest were offered this evaluation, and 1,223 (46.3%) of the eligible sheet metal workers participated. The sheet metal

(Received in original form March 30, 1989 and in revised form July 14, 1989)

[1] From the Pulmonary Disease Division, the Department of Internal Medicine, the Division of Occupational and Environmental Health, the Department of Radiology, and the Department of Preventive Medicine, The University of Iowa, Iowa City, Iowa.

[2] Requests for reprints should be addressed to David A. Schwartz, M.D., M.P.H., Pulmonary Disease Division, Department of Internal Medicine, The University of Iowa College of Medicine, Iowa City, IA 52242.

TABLE 1

DEMOGRAPHIC CHARACTERISTICS OF SHEET METAL WORKERS*

	Study Population (n = 1,223)
Age, yr	57.1 ± 8.0
Male, %	100
White, %	99.7
Years in the trade	32.7 ± 6.7
Retired, %	27.8
Smoking history	
Never, %	20.3
Former, %	49.2
Current, %	30.5

* All values are expressed as the mean ± standard deviation or as a percentage of all sheet metal workers.

workers who participated in this evaluation were all male with extensive work experiences in the sheet metal trade, and almost all of them were Caucasian (table 1). The large proportion of retired workers (27.8%) is a distinguishing and beneficial feature of this study population (table 1). This older population allowed us to better assess the functional implications of asbestos-induced pleural fibrosis, which is known to have a latency period of 15 to 20 yr.

Health Evaluation and Assessment

All participants completed an occupational history and an American Thoracic Society (ATS) questionnaire (19). Pulmonary function tests were performed according to ATS standards (20) in the seated position without employing noseclips. Results were recorded on a Jones Datamite 3 (Model 1550) survey spirometer. The absolute FEV_1 and FVC were calculated by averaging the two largest measures of FEV_1 and FVC, respectively. Percent-predicted FEV_1 (%FEV_1) and FVC (%FVC) were calculated by applying the equations of Knudson and coworkers (21) to the average of the two largest acceptable measurements of FEV_1 and FVC. The FEV_1/FVC ratio was calculated by dividing the average of the two largest measures of the FEV_1 by the two largest measures of the FVC and multiplying by 100.

Rather than using ATS repeatability criteria (20) to determine spirometry acceptability, we examined the relationship between the two largest FVC measures and found that 18% of the study subjects had measures that differed by more than 5%. Moreover, those with spirometric measurements that would be considered unacceptable by ATS repeatability criteria tended to occur among study subjects with more work experience as sheet metal workers who were also more likely to be retired. In view of our study objectives and also the finding that those with spirometry measures that do not fulfill the repeatability criteria established by the ATS tend to have more respiratory disease than do those with acceptable tests (22, 23), we decided to include all subjects with spirometry measures. In total, 1,221 of our study subjects had spirometry performed and recorded.

Chest radiographs were performed in the posteroanterior projection and interpreted by one experienced reader (JAM), who used the International Labor Organization (ILO) 1980 Classification of radiographs of pneumoconioses (24). To evaluate the validity of the independent reader, 10% of these chest films were randomly sampled from each category of pleural and parenchymal fibrosis and independently reevaluated by two experienced readers (DAS and JRG) familiar with the ILO classification system. All readers were blinded to the specific exposure history and clinical data of the screened subjects. Two of the three readers agreed on the category of parenchymal profusion (0, 1, 2, and 3) on 74% of the films that were reread, and they were within one subcategory of profusion rating in 79% of the cases. Rates of agreement on pleural abnormalities were similar, with 68% agreement on circumscribed plaques and 86% agreement on diffuse pleural thickening. These figures compare favorably with other studies (25, 26) and indicate that the independent interpretation by the initial reader was valid and acceptable for the purposes of this investigation. Of 1,223 participants, 1,211 had both chest films and spirometry, and these subjects constitute the study population for this analysis.

Outcome Measures

We used the ILO classification system (24) to grade the degree of radiographic fibrosis (profusion) and found that 17% of our study subjects had a profusion reading of at least 1/0, which represents an abnormal degree of profusion in the ILO classification. For the purposes of this analysis, we defined asbestosis as a profusion of 1/0 or greater; however, we also analyzed the data using the ILO profusion as a series of dummy variables (Categories 0, 1, 2, and 3) and as an ordinal measure with 0/0 assigned 0, 0/1 assigned 1, 1/0 assigned 2, and so on. Because none of our study subjects had a profusion rating greater than 2/3, Category 3 profusion will not be reported in our analyses.

The ILO classification system was used to identify the presence of pleural fibrosis and to define the type (circumscribed plaques versus diffuse pleural thickening) of the pleural abnormality. We defined diffuse pleural thickening as requiring obliteration of the costophrenic angle on the involved side. This modification of the ILO classification system was added to decrease the intrareader variability that has previously been reported (25) in distinguishing circumscribed plaques from diffuse pleural thickening. All pleural fibrosis that was not accompanied by obliteration of the costophrenic angle was considered to be circumscribed plaque. Of those with pleural fibrosis (n = 334), 260 (78%) had circumscribed plaques and 74 (22%) had diffuse pleural thickening involving the costophrenic angle.

Characterization of Smoking History

Participants were classified as "nonsmokers" (less than 20 packs of lifetime cigarettes and no cigarettes in the month prior to medical screening), "former smokers" (more than 20 lifetime packs of cigarettes but stopped more than 1 month before medical screening), and "current smokers" (smoked within 1 month of the medical screening).

Statistical Analysis

Univariate comparisons were made to determine whether demographic or clinical variables were associated with the presence and type of pleural fibrosis. A chi-square test with Yates correction factor was employed to test differences in the prevalence of categorical variables between sheet metal workers with normal pleura and those with either circumscribed plaques or diffuse pleural thickening, whereas an analysis of variance (ANOVA) was used to examine differences of means in continuous variables (27).

Variables that were found to be associated with the presence of circumscribed plaques and diffuse pleural thickening and spirometric measures of lung function were included in a linear multivariate analysis that examined the relationship between the presence and type of pleural disease and lung function (28). Dummy variables were established for smoking history (never smokers, former smokers, and current smokers) and for the ILO profusion grade (Categories 0, 1, and 2). After the models were established, clinically relevant and intuitively meaningful interactions of the independent variables were tested in a stepwise manner to determine if significant improvements in the model could be achieved by the inclusion of any one of these interactive terms.

Results

Sheet metal workers with pleural fibrosis, when compared with those with normal pleura, tended to be older, more often retired, and to have more work experience in the sheet metal trade (table 2). In addition, sheet metal workers with pleural fibrosis had a more extensive smoking history (i.e., more pack-years of smoking) than did those with normal pleura.

Sheet metal workers with either circumscribed plaques or diffuse pleural thickening were more likely to have asbestosis and higher ILO profusion grades than were workers with normal pleura (table 3). Sheet metal workers with circumscribed plaques had more extensive interstitial fibrosis than did those with normal pleura, and sheet metal workers with diffuse pleural thickening had more extensive interstitial fibrosis than did those with circumscribed plaques.

When compared with sheet metal workers with normal pleura, those with either circumscribed plaques or diffuse pleural thickening were found to have spirometry patterns that are suggestive

TABLE 2

DEMOGRAPHIC CHARACTERISTICS OF SHEET METAL WORKERS BY PRESENCE AND TYPE OF PLEURAL FIBROSIS*

	Normal Pleura (*n* = 877)	Circumscribed Plaques (*n* = 260)	Diffuse Pleural Thickening (*n* = 74)
Age, yr	56.1 ± 7.9	58.6 ± 7.5	63.4 ± 7.1
White, %	99.9	99.2	100
Years in the trade	32.1 ± 6.8	34.0 ± 6.0	35.8 ± 7.0
Retired, %	23.3	33.1	59.5
Smoking history			
Never, %	21.2	20.5	13.5
Former, %	47.6	49.4	56.8
Current, %	31.2	30.1	29.7
Pack-years	25.4 ± 29.5	29.9 ± 27.3	34.4 ± 32.3

* All values are expressed as the mean ± standard deviation or as a percentage of all sheet metal workers.

TABLE 3

COMPARISON OF ROENTGENOGRAPHIC FIBROSIS BY PRESENCE AND TYPE OF PLEURAL FIBROSIS*

	Normal Pleura (*n* = 877)	Circumscribed Plaques (*n* = 260)	Diffuse Pleural Thickening (*n* = 74)
Asbestosis ⩾ 1/0, %	9	31†	62†
ILO profusion grade, %			
0/0	68	36	11
0/1	23	32	27
1/0	6	22	29
1/1	2	8	15
1/2	1	1	10
⩾ 2/1	0	1	8

* p values were computed by comparing sheet metal workers with circumscribed plaques to those with normal pleura and comparing sheet metal workers with diffuse pleural thickening to those with normal pleura.
† $p < 0.0001$.

TABLE 4

RELATIONSHIP BETWEEN CATEGORICAL VARIABLES AND SPIROMETRIC MEASURES OF LUNG FUNCTION IN SHEET METAL WORKERS*

	FEV_1		FVC		FEV_1/FVC Ratio	
Pleural fibrosis						
Normal pleura, n = 877	3.08 ± 0.82	‡	4.09 ± 0.91	‡	74.9 ± 9.5	†
Circumscribed plaque, n = 258	2.83 ± 0.71		3.75 ± 0.77		75.4 ± 8.9	
Diffuse thickening, n = 74	2.24 ± 0.73		3.16 ± 0.83		70.4 ± 11.5	
Race						
Caucasian, n = 1,140	2.97 ± 0.83		3.96 ± 0.91		74.6 ± 9.6	
Other, n = 3	2.52 ± 0.55		3.23 ± 0.44		78.3 ± 5.1	
Smoking history						
Never, n = 247	3.43 ± 0.68	‡	4.29 ± 0.87	‡	80.2 ± 5.2	‡
Former, n = 587	2.91 ± 0.85		3.89 ± 0.94		74.3 ± 10.0	
Current, n = 373	2.77 ± 0.75		3.85 ± 0.85		71.9 ± 9.6	
ILO profusion grade						
0/0, n = 696	3.13 ± 0.82	‡	4.17 ± 0.90	‡	74.8 ± 9.1	†
0/1, n = 309	2.95 ± 0.72		3.89 ± 0.79		76.1 ± 9.8	
1/0, n = 133	2.56 ± 0.74		3.50 ± 0.84		72.6 ± 9.8	
1/1, n = 47	2.41 ± 0.72		3.28 ± 0.84		72.9 ± 8.5	
1/2, n = 14	2.56 ± 0.64		3.33 ± 0.58		76.9 ± 12.1	
⩾ 2/1, n = 9	1.77 ± 0.65		2.48 ± 0.70		69.8 ± 9.7	
ILO profusion category						
0, n = 1,005	3.08 ± 0.80	‡	4.08 ± 0.88	‡	75.2 ± 9.3	†
1, n = 194	2.52 ± 0.73		3.43 ± 0.83		73.0 ± 9.7	
2, n = 9	1.77 ± 0.65		2.48 ± 0.70		69.8 ± 9.7	

* Values are mean ± SD; p values were computed by using an analysis of variance (ANOVA) to compare the mean values of lung function.
† $p < 0.005$.
‡ $p < 0.0001$.

of an underlying restrictive defect in lung function (table 4). Both forms of pleural fibrosis were associated with pronounced decrements in the absolute FEV_1 and FVC, but only diffuse pleural thickening was associated with modest decrements in the FEV_1/FVC ratio. Decrements in lung function were also associated with increasing grades of interstitial fibrosis, cigarette smoking, increasing age, more work experience in the sheet metal trade, and a longer latency period from first exposure to asbestos (tables 4 and 5). Height was directly related to FEV_1 and FVC values and was not significantly associated with the FEV_1/FVC ratio.

To further examine the relationship between pleural fibrosis and lung function while controlling for potential confounders (age, height, duration and latency of exposure, smoking history, pack-years of smoking, and degree of interstitial fibrosis), we developed a linear multivariate model. We controlled for the degree of interstitial fibrosis by using the ILO profusion classification to create a series of indicator or dummy variables (Categories 0, 1, and 2). This approach was chosen to allow independent weighting of higher grades of interstitial fibrosis. Alternative approaches such as simply classifying parenchyma as normal and abnormal or using the ILO profusion grade as an ordinal scale were considered but rejected. The former approach appeared to simplify the relationship between the ILO profusion grade and measures of spirometric function, whereas the latter approach imposed assumptions regarding linearity that were not entirely supported by our univariate analysis (table 4).

Our multivariate analyses (tables 6, 7, and 8) indicate that both circumscribed pleural plaques and diffuse pleural thickening are independently associated with decrements in FVC but not with decrements in the FEV_1/FVC ratio. Although diffuse pleural thickening was associated with significant decrements in FEV_1 (table 6), the FEV_1/FVC ratio (table 8) was not significantly related to the presence of diffuse pleural thickening. Therefore, the reduction in FEV_1 in those with diffuse pleural thickening appears to be largely a result of restricted physiology rather than airflow obstruction. Moreover, sheet metal workers with circumscribed pleural plaques were found to have modest but significant increases in the FEV_1/FVC ratio (table 8). These analyses indicate that both circumscribed plaques and diffuse pleural thickening are

TABLE 5

CORRELATION COEFFICIENTS FOR RELATIONSHIP BETWEEN CONTINUOUS VARIABLES AND SPIROMETRIC MEASURES OF LUNG FUNCTION IN SHEET METAL WORKERS

	FEV_1	FVC	FEV_1/FVC Ratio
Age, yr	−0.53*	−0.53*	−0.25*
Height, cm	0.33*	0.42*	−0.03
Pack-years of smoking	−0.32*	−0.26*	−0.24*
Years in sheet metal trade	−0.31*	−0.31*	−0.13*
Years since first employed in sheet metal trade (latency)	−0.43*	−0.44*	−0.19*

* $p < 0.0001$.

TABLE 6

MULTIVARIATE LINEAR REGRESSION FOR RELATIONSHIP BETWEEN TYPE OF PLEURAL FIBROSIS AND FEV_1

	Circumscribed Plaque versus Normal Pleura		Diffuse Thickening versus Normal Pleura	
	Coefficient (SE)	p Value	Coefficient (SE)	p Value
Pleural fibrosis	−0.08 (0.05)	0.12	−0.24 (0.09)	0.009
Age, yr	−0.04 (0.004)	0.0001	−0.04 (0.004)	0.0001
Height, cm	0.08 (0.007)	0.0001	0.07 (0.008)	0.0001
ILO profusion category				
1	−0.21 (0.06)	0.0005	−0.21 (0.07)	0.005
2	−0.63 (0.36)	0.08	−0.66 (0.27)	0.01
Latency, yr	−0.01 (0.004)	0.003	−0.01 (0.004)	0.007
Current smoker	−0.48 (0.06)	0.0001	−0.51 (0.07)	0.0001
Former smoker	−0.20 (0.05)	0.0002	−0.24 (0.06)	0.0001
Pack-years	−0.003 (0.0001)	0.0002	−0.003 (0.0001)	0.0006
Constant	0.62 (0.58)	0.29	1.11 (0.65)	0.09
Model R^2	0.43		0.46	
F (df)	82.1 (9,988)		78.9 (9,829)	

TABLE 7

MULTIVARIATE LINEAR REGRESSION FOR RELATIONSHIP BETWEEN TYPE OF PLEURAL FIBROSIS AND FVC

	Circumscribed Plaque versus Normal Pleura		Diffuse Thickening versus Normal Pleura	
	Coefficient (SE)	p Value	Coefficient (SE)	p Value
Pleural fibrosis	−0.14 (0.05)	0.007	−0.27 (0.10)	0.008
Age, yr	−0.04 (0.004)	0.0001	−0.04 (0.005)	0.0001
Height, cm	0.12 (0.01)	0.0001	0.12 (0.01)	0.0001
ILO profusion category				
1	−0.28 (0.07)	0.0001	−0.28 (0.08)	0.0006
2	−0.87 (0.39)	0.03	−1.02 (0.30)	0.0008
Latency, yr	−0.01 (0.005)	0.006	−0.01 (0.005)	0.01
Current smoker	−0.15 (0.05)	0.0002	−0.17 (0.06)	0.003
Pack-years	−0.003 (0.001)	0.0001	−0.004 (0.001)	0.0001
Constant	−1.67 (0.64)	0.009	−1.17 (0.72)	0.10
Model R^2	0.44		0.46	
F (df)	95.5 (8,989)		88.1 (8,830)	

associated with spirometry patterns consistent with restrictive lung function that appears to be independent of the degree of interstitial fibrosis. Furthermore, the mean decline in the FVC (table 7) for those with diffuse pleural thickening (270 ml) was approximately twice as large as was observed among those with circumscribed plaques (140 ml).

Although potential interactions between pleural fibrosis and other factors associated with changes in lung function were examined, none was found to significantly contribute to the noninteractive multivariate models or substantially alter the relationship between pleural fibrosis and spirometric measures of lung function. To assure ourselves that we had adequately controlled for the degree of interstitial fibrosis, we investigated the relationship between pleural fibrosis and FVC while using other approaches to control for the degree of interstitial fibrosis. Regardless of the method employed (normal versus asbestosis, ILO perfusion category, or ILO as an ordinal scale), both forms of pleural fibrosis were significantly associated with decrements in FVC, and the decline in FVC for those with diffuse pleural thickening was approximately twice as large as was observed among those with circumscribed pleural plaques.

To further illustrate the relationship between pleural fibrosis and interstitial fibrosis on lung function, we displayed the cumulative effect of these two factors on the %FVC (table 9). For each category of pleural fibrosis (none, circumscribed plaques, and diffuse pleural thickening), the FVC was lower for those with interstitial fibrosis than for those with normal parenchyma. However, within each stratum of interstitial fibrosis, we observed a consistent decline in the %FVC that was significantly associated with the type of pleural fibrosis.

Because our univariate analysis suggested that the presence and type of pleural fibrosis might be associated with cigarette smoking (table 2), we investigated the association between pleural fibrosis and cigarette smoking while controlling for age. A multivariate logistic regression analysis controlling for age indicated that smoking behavior and pack-years of smoking are not significantly related to the presence or type of pleural fibrosis (data not shown).

Discussion

We conclude that pleural fibrosis among asbestos-exposed persons is an independent predictor of spirometry patterns consistent with restrictive lung function. Moreover, our data indicate that both circumscribed plaques and diffuse pleural thickening are independently associated with decrements in FVC, and the effect of diffuse pleural thickening is approximately twice as great as that observed among persons with circumscribed pleural plaques. Asbestos-exposed workers with normal parenchyma as well as those with interstitial fibrosis were found to have a similar relationship between the presence and type of pleural fibrosis and decrements in FVC.

Our finding that circumscribed plaques are an independent predictor of decrements in FVC even among those with interstitial fibrosis supports and extends the observations of other investi-

TABLE 8

MULTIVARIATE LINEAR REGRESSION FOR RELATIONSHIP BETWEEN TYPE OF PLEURAL FIBROSIS AND FEV_1/FVC

	Circumscribed Plaque versus Normal Pleura		Diffuse Thickening versus Normal Pleura	
	Coefficient (SE)	p Value	Coefficient (SE)	p Value
Pleural fibrosis	1.34 (0.62)	0.03	−1.67 (1.11)	0.13
Age, yr	−0.30 (0.03)	0.0001	−0.33 (0.04)	0.0001
Current smoker	−7.96 (0.73)	0.0001	−8.15 (0.82)	0.0001
Former smoker	−4.39 (0.68)	0.0001	−5.00 (0.77)	0.0001
Constant	96.39 (1.93)	0.0001	98.53 (2.16)	0.0001
Model R^2	0.154		0.173	
F (df)	51.1 (4, 1123)		49.2 (4,940)	

TABLE 9

THE INDIVIDUAL AND CUMULATIVE EFFECTS OF PLEURAL FIBROSIS AND INTERSTITIAL FIBROSIS ON THE PERCENT PREDICTED FVC

Interstitial Fibrosis	Pleural Fibrosis	N	% FVC (mean ± SD)	p Value*
No	No	797	94.7 ± 16.8	
No	Circumscribed	178	90.3 ± 13.4	0.0002
No	Diffuse	28	85.7 ± 19.2	
Yes	No	80	83.3 ± 16.9	
Yes	Circumscribed	80	80.1 ± 15.8	0.009
Yes	Diffuse	46	73.6 ± 18.2	

* p value calculated by comparing the %FVC across categories of pleural fibrosis within each stratum of interstitial fibrosis. Analysis of variance was used to calculate the p value.

gators (9–16). Although several reports document, in the absence of radiographically evident interstitial fibrosis, that asbestos-induced circumscribed pleural plaques may independently account for reduced lung volumes (9–15), only one study (16) examined this relationship across grades of interstitial fibrosis. Unfortunately, too few study subjects (16) permitted these investigators to control for potential confounders such as the duration of exposure and the use of cigarettes when examining the relationship between the type of pleural fibrosis and lung function.

Although diffuse pleural thickening has been reported to impair lung function (5–8, 16), concerns regarding selection of study subjects and potential confounding by interstitial fibrosis and other factors have compromised the general acceptance of these conclusions. McGavin and Sheers (7) found that dockyard workers with diffuse pleural thickening and no evidence of interstitial fibrosis had reduced lung volumes that were directly related to the extent of pleural fibrosis. Unfortunately, these investigators were unable to control for important variables such as exposure duration and cigarette smoking, which are likely to confound the relationship between diffuse pleural thickening and decrements in lung function. Our cohort of sheet metal workers allowed us to control for these factors and also permitted confirmation of a previous report (16) that suggested that diffuse pleural thickening will result in a greater reduction in FVC than circumscribed plaques.

Our findings raise several questions regarding the physiology and pathogenesis of restrictive lung function among persons with pleural fibrosis. Because asbestos-exposed workers with pleural fibrosis have more extensive exposure histories than do those with normal pleura, it is quite possible that they are also more likely to have parenchymal fibrosis. Although we attempted to control for this possibility by examining the relationship between pleural fibrosis and lung function while controlling for the degree of interstitial fibrosis, it is possible that for each ILO grade of radiographic fibrosis, those with pleural fibrosis have more parenchymal fibrosis than do those with normal pleura. More detailed measures of parenchymal fibrosis (such as high resolution CT scans or histologic specimens) would be needed to pursue this hypothesis. Alternatively, the presence of pleural fibrosis may impair chest wall motion. In the extreme case, extensive diffuse pleural thickening has been reported to encase the lung and clearly restrict lung expansion (5, 6). Despite these reports, it is difficult to conceive that pleural plaques, in and of themselves, result in the abnormal chest wall motion that accounts for the observed decrements in FVC. We are therefore led to speculate that subclinical alveolitis or interstitial fibrosis not detected by routine chest radiograms is responsible for the development of restrictive lung function among those with asbestos-induced pleural fibrosis. Given the large number of workers who are expected to develop asbestos-induced pleural fibrosis (1), more detailed studies are warranted to identify the underlying mechanisms responsible for the loss of lung function that appears to be associated with this pleural abnormality.

References

1. Nicholson WJ, Perkel G, Selikoff IJ. Occupational exposure to asbestos: population at risk and projected mortality—1980–2030. Am J Ind Med 1982; 3:259–311.
2. Walker AM, Loughlin JE, Friedlander EF, Rothman KJ, Dreyer NA. Projections of asbestos-related disease 1980–2009. J Occup Med 1983; 25:409–25.
3. Hughes JM, Weill H. Asbestos exposure: quantitative assessment of risk. Am Rev Respir Dis 1986; 133:5–13.
4. Lilienfeld DE, Mandel JS, Coin P, Schuman LM. Projection of asbestos related diseases in the United States, 1985–2009. I. Cancer. Br J Ind Med 1988; 45:283–91.
5. Wright PH, Hanson A, Kreel L, Capel LH. Respiratory function changes after asbestos pleurisy. Thorax 1980; 35:31–6.
6. Miller A, Teirstein AS, Selikoff IJ. Ventilatory failure due to asbestos pleurisy. Am J Med 1983; 75:911–9.
7. McGavin CR, Sheers G. Diffuse pleural thickening in asbestos workers: disability and lung function abnormalities. Thorax 1984; 39:604–7.
8. Picado C, Laporta D, Grassino A, Cosio M, Thibodeau M, Becklake MR. Mechanisms affecting exercise performance in subjects with asbestos-related pleural fibrosis. Lung 1987; 165:45–7.
9. Baker EL, Dagg T, Greene RE. Respiratory illness in the construction trades. I. The significance of asbestos-associated pleural disease among sheet metal workers. J Occup Med 1985; 27:483–9.
10. Jarvholm B, Larsson S. Do pleural plaques produce symptoms? A brief report. J Occup Med 1988; 30:345–7.
11. Oliver LC, Eisen EA, Greene R, Sprince NL. Asbestos-related pleural plaques and lung function. Am J Ind Med 1988; 14:649–56.
12. Jarvholm B, Sanden A. Pleural plaques and respiratory function. Am J Ind Med 1986; 10: 419–26.
13. Fridricksson HV, Hedenstrom H, Hillerdal G, Malmberg P. Increased lung stiffness in persons with pleural plaques. Eur J Respir Dis 1981; 62: 412–24.
14. Jones RN, Diem JE, Glindmeyer H, Weill H, Gilson JC. Progression of asbestos radiographic abnormalities: relationship to estimates of dust exposure and annual decline in lung function. IARC Sci Publ 1980; 30:537–43.
15. Hedenstierna G, Alexandersson R, Kolmodin-Hedman B, Szamosi A, Tollqvist J. Pleural plaques

and lung function in construction workers exposed to asbestos. Eur J Respir Dis 1981; 62:111–22.
16. Rosenstock L, Barnhart S, Heyer NJ, Pierson DJ, Hudson LD. The relation among pulmonary function, chest roentgenographic abnormalities, and smoking status in an asbestos-exposed cohort. Am Rev Respir Dis 1988; 138:272–7.
17. Ohlson CG, Rydman T, Sundell T, Bodin L, Hogstedt C. Decreased lung function in long-term asbestos cement workers: a cross-sectional study. Am J Ind Med 1984; 3:359–66.
18. Ohlson CG, Bodin L, Rydman T, Hogstedt C. Ventilatory decrements in former asbestos cement workers: a four year follow-up. Br J Ind Med 1985; 42:612–6.
19. Ferris BG Jr. Epidemiology standardization project. Am Rev Respir Dis 1978; 118:55–88.
20. American Thoracic Society. Snowbird workshop on standardization of spirometry. Am Rev Respir Dis 1972; 119:831–8.
21. Knudson RJ, Lebowitz MD, Holberg CJ, Burrows B. Changes in the normal maximal expiratory flow-volume curve with growth and aging. Am Rev Respir Dis 1983; 127:725–34.
22. Eisen EA, Robins JM, Greaves IA, Wegman DH. Selection effects of repeatability criteria applied to lung spirometry. Am J Epidemiol 1984; 120:734–42.
23. Eisen EA, Oliver LC, Christiani DC, Robins JM, Wegman DH. Effects of spirometry standards in two occupational cohorts. Am Rev Respir Dis 1985; 132:120–4.
24. Guidelines for the use of International Labor Organization (ILO). International Classification of radiographs of pneumoconioses. Geneva; International Labor Office, 1980.
25. Bourbeau J, Ernst P. Between- and within-reader variability in the assessment of pleural abnormality using the ILO 1980 international classification of pneumoconioses. Am J Ind Med 1988; 14:537–43.
26. Rossiter CE, Browne K, Gilson JC. International classification trial of AIA set of 100 radiographs of asbestos workers. Br J Ind Med 1988; 45:538–43.
27. Colton T. Statistics in medicine. Boston: Little Brown, 1974.
28. Kleinbaum DG, Kupper LL. Applied regression analysis and other multivariable methods. Boston: Duxbury Press, 1978.