Influence of Cigarette Smoking on Bronchoalveolar Lavage Cellularity in Asbestos-induced Lung Disease[1-3]

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SUMMARY To investigate the influence of cigarette smoking on bronchoalveolar lavage (BAL) cellularity in asbestos-induced lung disease, we compared BAL cells in asbestos-exposed, nondiseased subjects (n = 20) with those with either asbestosis (n = 25) or asbestos-induced pleural fibrosis (n = 28). Patients with asbestosis (ILO ≥ 1/0) had higher concentrations of BAL macrophages (p = 0.04), neutrophils (p = 0.003), and eosinophils (p = 0.01), while patients with asbestos-induced pleural fibrosis (circumscribed plaques and diffuse pleural thickening) had higher concentrations of BAL lymphocytes (p = 0.02). Within our study population, however, cigarette smoking (smoking status or pack-years of smoking) was strongly associated with BAL macrophages, neutrophils, and eosinophils but was not associated with the concentration of BAL lymphocytes. Using multivariate analysis, we found that although asbestosis remained associated with higher concentrations of BAL macrophages, neutrophils, and eosinophils, cigarette smoking had a far greater contribution to the concentrations of BAL macrophages and eosinophils than did asbestosis. Although cigarette smoking accounted for 17 to 18% of the variance of BAL macrophages and eosinophils, asbestosis was associated with approximately 6% of the variance associated with these cells. In contrast, the concentration of BAL neutrophils remained associated with asbestosis and was not influenced by smoking behavior. We conclude that cigarette smoking strongly influences BAL cellularity (macrophages and eosinophils) in our patients with asbestosis but does not appear to affect the type or concentration of BAL cells in patients with asbestos-induced pleural fibrosis. Moreover, these findings indicate that cigarette smoking accounts for a substantial portion of the changes in BAL cells that have previously been attributed to the underlying interstitial process and may play a role in the pathogenesis of asbestosis.

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Introduction

Cigarette smoking appears to enhance the development of interstitial fibrosis in workers exposed to asbestos (1-6). In addition, other forms of interstitial fibrosis, such as idiopathic pulmonary fibrosis (7, 8), histiocytosis X (9), and rheumatoid arthritis associated with interstitial lung disease (10, 11), are epidemiologically associated with cigarette smoking. Potential mechanisms accounting for the development of interstitial fibrosis among cigarette smokers include altered regulation and abnormal function of inflammatory cells in the lung parenchyma (12-19), reduced clearance of inhaled agents (20), and enhanced permeability of airway epithelia (21). Recently we found that cigarette smoking influences the bronchoalveolar lavage (BAL) cellularity in patients with idiopathic pulmonary fibrosis (IPF) and accounts for at least a portion of the changes in BAL cells that have previously been ascribed to the underlying lung disease (22). These findings suggest that cigarette smoking may play a role in the pathogenesis of IPF and raise the possibility that the interaction between smoking behavior and inflammatory cells in BAL fluid may be generalizable to other types of pulmonary fibrosis.

Bronchoalveolar lavage studies in patients with asbestosis have identified an active alveolitis characterized by an excess number of activated macrophages and neutrophils (23-25). BAL cells from these patients spontaneously release increased amounts of neutrophil chemotactic factor (25), oxygen free radicals (23), fibronectin (23), growth factors (23), leukotriene B_4 (24), and interferon-γ (26). Interestingly, cigarette smoking can profoundly influence the cellularity in BAL fluid (12, 27) and can substantially alter the production and release of various mediators of inflammation (12-19). Because asbestosis is epidemiologically associated with cigarette smoking (1-6), it is logical to speculate that cigarette smoking significantly influences the inflammatory features of BAL cells and cell products that are known to be associated with asbestosis. Moreover, if our findings in idiopathic pulmonary fibrosis (22) are generalizable to other forms of interstitial fibrosis, then one could hypothesize that cigarette smoke acts as a cofactor in the development of interstitial lung disease.

The purpose of this investigation was to characterize the influence of cigarette smoking on bronchoalveolar lavage cellularity in asbestos-induced lung disease. *A priori*, we hypothesized that cigarette smoking behavior contributes to the amount and type of cells present in the BAL fluid. Our findings indicate that cigarette smoking strongly influences BAL cellularity (macrophages and eosinophils) in our patients with asbestosis but not in patients with asbestos-induced pleural fibrosis. Despite this association, asbestosis remained independently associated with the concentration of BAL macrophages, neutrophils, and eosinophils and asbestos-induced pleural fibrosis remained independently associated with higher concentrations of BAL lymphocytes.

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Methods

Patient Population

The subjects for this investigation were identified as part of an ongoing research program in interstitial and pleural occupational lung disease at our institution. Other clinical findings in this population are being published separately (28). All study subjects had been referred for evaluation of asbestos-related lung disease and were occupationally exposed to asbestos for at least 1 yr in a high-exposure setting. A minimum of 20 yr was required between first exposure to asbestos and entry into the study. In fact, the mean duration of occupational exposure to asbestos was 33 yr and the mean time from first exposure to asbestos and entry into the study was 38 yr. Although subjects with asbestos-induced parenchymal fibrosis and asbestos-induced pleural disease were preferentially invited to participate in this study, asbestos-exposed individuals without obvious lung disease were also included in the study population.

Chest Radiographs

Chest radiographs were performed in the posteroanterior projection and individually interpreted by three experienced readers (Schwartz, Galvin, and J. Merchant), who used the International Labor Organization (ILO) 1980 classification of radiographs of pneumoconioses (29). Each reader was blinded to the exposure history, clinical data, and the opinions of the other readers when interpreting the radiographs. At least two of the three readers agreed on the category of parenchymal profusion (0, 1, 2, and 3) on 99% of the films. Rates of three-way agreement on the presence of either pleural plaques or diffuse pleural thickening were similar, with 64% agreement on circumscribed plaques and 87% agreement on diffuse pleural thickening. Agreement between at least two of the three readers was required to identify either a parenchymal or a pleural abnormality. In the unusual case in which all three readers disagreed on the degree of parenchymal profusion, the median reading was chosen.

For the purposes of this study, we defined asbestosis as a profusion of 1/0 or greater. Because only three of the 25 subjects with asbestosis had an ILO Category 2 or 3 profusion, we analyzed the data categorizing subjects as having either normal parenchyma (ILO $\leq$ 0/1) or asbestosis (ILO $\geq$ 1/0). The ILO classification system (29) was used to identify the presence of pleural fibrosis and to define the type (circumscribed plaques versus diffuse pleural thickening) of 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 intra- and interreader variability (30) in distinguishing circumscribed plaques from diffuse pleural thickening. All pleural fibrosis that was not accompanied by obliteration of the costophrenic angle was considered circumscribed plaque. Approximately 27% of the study population had a normal chest radiograph; 34% had evidence of asbestosis (ILO profusion $\geq$ 1/0), and 38% had evidence of asbestos-induced pleural disease. Of the 25 patients with asbestosis, 14 also had asbestos-induced pleural fibrosis.

Pulmonary Function Testing

The pulmonary function tests consisted of standard spirometry, which was obtained with the use of a Medical Graphics 1070 system (St. Paul, MN) and lung volumes via body plethysmography Medical Graphics 1085 system (St. Paul, MN). A single-breath diffusing capacity was measured by using the Medical Graphics 1070 system. The measurements of lung function were performed with standard protocols, and the American Thoracic Society guidelines (31) were used to determine acceptability. The predicted normal values used were those of Morris and colleagues (32) for spirometry, Goldman and Becklake (33) for lung volumes, and Van Ganse and coworkers (34) for the diffusing capacity.

Bronchoalveolar Lavage

Bronchoscopic examination and lavage were performed on all study subjects using our standard method (35). Premedications included intramuscular atropine sulfate (0.8 mg), intramuscular meperidine hydrochloride (75 mg), and two inhalations of metaproterenol (total 1.3 mg) from a hand-held pressurized canister. The upper airway was anesthetized with Dyclone® gargle (Astra Pharmaceutical Products, Westborough, MA) and aerosolized 4% lidocaine. Lidocaine was also applied topically to the pyriform sinuses and vocal cords. The bronchoscope (Olympus Model BF 4B2; 4.9-mm diameter at the tip) was advanced into the airways and the tip was maintained in the wedged position in a subsegmental bronchus throughout the lavage procedure. In all cases two lavages were performed, and in most instances subsegments of the right middle lobe and lingula were lavaged. Each lavage consisted of 100 ml saline (five 20-ml aliquots).

Immediately after the lavage, the lavage fluid was strained through two layers of surgical 4 × 4 inch gauze into 50-ml conical tubes. The tubes were centrifuged for 5 min at 200 × *g*, and the residual pellet of cells was resuspended and washed twice in Hanks' balanced salt solution (without Ca^{2+} or Mg^{2+}). After the second wash, a small aliquot of the sample was removed for a cell count with the use of a hemocytometer. The cells were then washed once more and resuspended in RPMI 1640 medium so that the final concentration was 1×10^7 cells/ml. The cells present in 10 to 12 µl of the 1×10^7 cells/ml suspension were spun onto a glass slide with the use of a filter card and a cytocentrifuge (Cytospin® 2; Shanden Southern, Sewickley, PA). Three drops of fetal calf serum was added to the cell suspension to help the cells stick to the slide. After drying for 2 min, staining of the cells was accomplished by using a Diff-Quik® stain set (Harleco, Gibbstown, NJ). The cells were counted and classified only after the cytocentrifuge preparation was thought to be satisfactory by the following criteria: negligible staining artefact, uniform dispersal of cells without clumping, essentially no disruption of cells, and < 3% airway epithelial cells.

Statistical Analysis

Univariate comparisons were made to determine whether demographic or clinical variables were associated with the amount or type of cells in the BAL fluid. Because we recently demonstrated that BAL cellularity is not normally distributed (RK Merchant and colleagues, unpublished findings), we used nonparametric statistics to evaluate all our comparisons. The Mann-Whitney U test and Kruskal-Wallis one-way analysis of variance were used to evaluate the relationship between categorical variables and BAL cellularity, and Spearman's correlation coefficient was used to evaluate the relationship between continuous variables and BAL cellularity (36).

We used a multivariate linear regression model (37) to identify the independent determinants of BAL cellularity in patients with asbestos-induced lung disease. A linear model was generated that incorporated all potential confounders and determined the relative strength of the relationship between BAL cellularity and cigarette smoking behavior. Dummy variables were established to test whether former or current smoking status was related to our dependent variables. We used a logarithmic transformation (base 10) of the BAL cell concentrations to account for the underlying distribution of these measures. After a linear model was established, all possible two-way interactions were tested in a stepwise manner to determine if significant improvements could be achieved by inclusion of any of the interactive terms. Conditional R^2 (37) was used to assess the relative contribution of each term in the multivariate equation.

Results

Our study population consisted of 73 asbestos-exposed workers who were on average 60 yr of age and had extensive occupational exposure to asbestos. Subjects with pleural fibrosis and asbestosis were more often retired from their trade than asbestos-exposed study subjects with normal chest X-rays (table 1). In addition, subjects with asbestosis had more extensive smoking histories than those with normal chest films. Otherwise, study subjects, regardless of radiographic evidence of asbestos-induced lung disease, were comparable regarding their age and asbestos exposure histories.

The relationship between the bronchoalveolar lavage cellularity and as-

TABLE 1

DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF STUDY POPULATION BY TYPE OF ASBESTOS-INDUCED LUNG DISEASE*

	Normal CXR (N = 20)	Pleural Fibrosis (N = 28)	Asbestosis† (N = 25)
Age	57.1 ± 9.4	63.3 ± 8.8‡	59.4 ± 8.3
Male (%)	20 (100)	28 (100)	25 (100)
White	20 (100)	28 (100)	25 (100)
Retired	3 (15)	14 (50)‡	12 (48)‡
Asbestos exposure			
Duration	34.7 ± 6.4	33.2 ± 9.7	30.9 ± 12.8
Time since first exposure	37.1 ± 6.3	37.4 ± 11.0	38.2 ± 9.1
Smoking history (%)			
Never	5 (25)	7 (25)	1 (4)‡
Former	13 (65)	20 (71)	17 (68)‡
Current	2 (10)	1 (4)	7 (28)‡
Pack-years of smoking	28.1 ± 23.9	20.5 ± 18.6	42.2 ± 23.4‡

* Values are expressed as the mean ± standard deviation for continuous variables and the frequency and percentage for categorical variables.

† Study subjects with asbestosis (ILO ⩾ 1/0) had either normal pleura (N = 11) or pleural fibrosis (N = 14).

‡ $p < 0.05$. p values were computed by comparing subjects with either pleural fibrosis or asbestosis to asbestos-exposed subjects with normal chest radiographs.

TABLE 2

RELATIONSHIP BETWEEN BRONCHOALVEOLAR LAVAGE CELLULARITY AND ASBESTOS-INDUCED LUNG DISEASE*

	Bronchoalveolar Lavage Cellularity (Cells × 10^4/ml)			
	Macrophages	Lymphocytes	Neutrophils	Eosinophils
Interstitial fibrosis (N)				
ILO ⩽ 0/1 (48)	18.9 ± 20.9	1.8 ± 2.5	0.3 ± 0.5	0.1 ± 0.5
ILO ⩾ 1/0 (25)	41.4 ± 41.1†	3.3 ± 5.5	0.9 ± 1.1†	0.2 ± 0.4‡
Pleural fibrosis (N)				
Normal pleura (31)	27.1 ± 31.4	1.3 ± 1.9	0.5 ± 0.8	0.1 ± 0.4
Circumscribed plaque (27)	22.8 ± 23.4	3.2 ± 5.7‡	0.4 ± 0.8	0.1 ± 0.2
Diffuse thickening (15)	32.6 ± 41.9	2.6 ± 2.2‡	0.7 ± 1.1	0.3 ± 0.6

* Values represent the mean ± standard deviation. P values were calculated using the Mann-Whitney U test to compare those with interstitial fibrosis with those with normal parenchyma and to individually compare those with circumscribed plaques or diffuse pleural thickening with those with normal pleura.

† $p < 0.005$.

‡ $p < 0.05$.

TABLE 3

RELATIONSHIP BETWEEN BRONCHOALVEOLAR LAVAGE CELLULARITY AND CIGARETTE SMOKING BEHAVIOR*

	Bronchoalveolar Lavage Cellularity (Cells × 10^4/ml)			
	Macrophages	Lymphocytes	Neutrophils	Eosinophils
Smoking history (N)				
Never (13)	13.7 ± 5.6	3.0 ± 7.0	0.1 ± 0.2	0.1 ± 0.2
Former (50)	21.9 ± 23.5	2.1 ± 2.8	0.5 ± 0.8	0.1 ± 0.4
Current (10)	67.1 ± 49.7†	2.4 ± 3.1	1.2 ± 1.1†	0.6 ± 0.7‡
Pack-years of smoking	0.29‡	−0.07	0.31‡	0.09

* Values represent the mean ± standard deviation for the smoking history and Spearman's correlation coefficient for the pack-years of cigarette smoking. p values for smoking status were calculated using the Mann-Whitney U test to individually compare former and current smokers with never smokers. Spearman's correlation coefficient was used to test the relationship between pack-years of smoking and the concentration of BAL cells.

† $p < 0.005$.

‡ $p < 0.05$.

bestos-induced lung disease is presented in table 2. Subjects with asbestosis had higher concentrations of alveolar macrophages, neutrophils, and eosinophils, and study subjects with asbestos-induced pleural fibrosis had higher concentrations of BAL lymphocytes. Although 14 of the 42 subjects with pleural fibrosis had asbestosis, the observed increase in BAL lymphocytes associated with pleural disease was still present when we limited our analysis to subjects with normal parenchyma.

However, within our study population BAL cellularity was also influenced by cigarette smoking (table 3). Current cigarette smokers had higher concentrations of BAL macrophages, neutrophils, and eosinophils compared to never smokers. In addition, pack-years of cigarette smoking was directly related to the concentration of alveolar macrophages ($r = 0.29$, $p = 0.01$) and neutrophils ($r = 0.32$, $p = 0.007$). Interestingly, the same BAL cells (alveolar macrophages, neutrophils, and eosinophils) that appeared to be associated with asbestosis were also associated with cigarette smoking. This was not so for asbestos-induced pleural disease, however, which was found to be associated only with BAL lymphocytes. Therefore, the remaining analyses in this study focus on the influence of cigarette smoking on the relationship between asbestosis and the concentration of BAL macrophages, neutrophils, and eosinophils.

To assess which other factors might influence the relationship between asbestosis and the concentration of BAL macrophages, neutrophils, and eosinophils, we examined the relationship between a variety of demographic and clinical variables and the concentration of BAL cells (table 4). The concentration of BAL macrophages was inversely related to age ($r = -0.28$, $p = 0.02$), time since first exposure to asbestos ($r = -0.24$, $p = 0.07$), and D_{LCO} ($r = -0.31$, $p = 0.007$) and positively associated with the $AaPo_2$ difference ($r = 0.25$, $p = 0.04$). The concentration of BAL neutrophils was inversely related to the D_{LCO} ($r = -0.45$, $p = 0.0001$) and directly related to the $AaPo_2$ difference ($r = 0.32$, $p = 0.006$). The concentration of BAL eosinophils was inversely related to residual volume (V_R) ($r = -0.25$, $p = 0.04$) and D_{LCO} ($r = -0.40$, $p = 0.0001$). Thus, these factors that were found to be associated with BAL cellularity (age, time since first exposure to asbestos, residual volume, D_{LCO}, and $AaPo_2$ difference) need to be accounted for while examining the influence of cigarette smoking on BAL cellularity in persons with asbestosis.

Next, we utilized multivariate linear regression to assess the independent influence of cigarette smoking (either smoking history or pack-years) on the observed relationship between asbestosis and the concentration of BAL macrophages, neutrophils, and eosinophils. For each of our measures of BAL cellularity, we performed a logarithmic transformation to account for the nonnormal distribution of these measures. These multivariate analyses (table 5) indicate that

TABLE 4

RELATIONSHIP BETWEEN BRONCHOALVEOLAR LAVAGE CELLULARITY AND BOTH DEMOGRAPHIC AND CLINICAL VARIABLES*

	Bronchoalveolar Lavage Cellularity (Cells × 10^4/ml)		
	Macrophages	Neutrophils	Eosinophils
Retired (N)			
No (43)	34.6 ± 38.2	0.5 ± 0.8	0.2 ± 0.5
Yes (29)	15.5 ± 6.8	0.6 ± 0.9	0.1 ± 0.3
Age	−0.28†	−0.02	0.03
Asbestos exposure			
Duration	−0.22	−0.03	−0.20
Time since first exposure	−0.24†	0.12	−0.02
Pulmonary function‡			
FEV_1	−0.07	−0.18	−0.06
FVC	−0.03	−0.12	−0.01
FEV_1/FVC ratio	0.01	−0.11	−0.04
TLC	−0.11	−0.17	−0.18
VR	−0.07	−0.14	−0.25*
DLCO	−0.31†	−0.45§	−0.40§
$AaPO_2$	0.25†	0.32†	0.19

* Values represent the mean ± standard deviation for categorical variables and Spearman's correlation coefficient for continuous variables.
† $p < 0.05$.
‡ Measures of pulmonary function were assessed using the percentage predicted values for FEV_1, FVC, TLC, VR, and DLCO. The absolute values are used for the FEV_1/FVC ratio and the $AaPO_2$ difference.
§ $p < 0.005$.

TABLE 5

MULTIVARIATE LINEAR REGRESSION FOR RELATIONSHIP BETWEEN BAL CELLULARITY AND BOTH ASBESTOSIS AND CIGARETTE SMOKING BEHAVIOR WHILE ACCOUNTING FOR PERTINENT CLINICAL VARIABLES*

	Macrophages	Neutrophils	Eosinophils
Asbestosis	0.29 (0.13)†	0.24 (0.10)†	0.40 (0.18)†
Current smoker	0.45 (0.15)‡	—	0.32 (0.11)‡
DLCO	—	−0.009 (0.002)‡	−0.005 (0.002)†
Model R^2	0.25	0.30	0.31

* Values in table represent the regression coefficient and the standard error of the regression coefficient in parentheses.
† $p < 0.05$.
‡ $p < 0.005$.

TABLE 6

DETERMINANTS OF THE VARIANCE IN BAL CELLULARITY AS ASSESSED BY CONDITIONAL R^2 GENERATED FROM MULTIVARIATE LINEAR REGRESSION MODELS

	BAL Cellularity (%)		
	Macrophages	Neutrophils	Eosinophils
Asbestosis	7	6	6
Cigarette smoking	19	—	17

subjects with asbestosis are more likely to have higher concentrations of BAL macrophages, neutrophils, and eosinophils, and current cigarette smokers are more likely to have higher concentrations of macrophages and eosinophils. After accounting for the presence of asbestosis and current smoking status, pack-years of cigarette smoking and former cigarette smoking status were no longer related to any of the dependent variables; the only other factor that remained related to BAL cellularity was the DLCO. The model R^2 indicates that these variables (asbestosis, current cigarette smoker, and DLCO) account for 25 to 31% of the variance of BAL macrophages, neutrophils, and eosinophils. Additional multivariate models failed to identify interactive terms that significantly contributed to the multivariate models.

To assess the relative contribution of asbestosis and cigarette smoking on the cellular content of BAL fluid, we reexamined the multivariate models and used the conditional R^2 to quantify the relative importance of each independent variable in the model (table 6). These analyses indicate that cigarette smoking accounts for 17 to 18% of the variance of BAL macrophages and eosinophils and asbestosis is associated with approximately 6 to 7% of the variance in BAL macrophages, neutrophils, and eosinophils. The conditional R^2 was estimated by first fitting asbestosis and then cigarette smoking behavior; however, the order did not appreciably alter the estimated R^2.

Discussion

Our findings indicate that cigarette smoking strongly influences BAL cellular content in patients with asbestosis but not among patients with asbestos-induced pleural disease. Patients with asbestosis had elevated concentrations of BAL macrophages, neutrophils, and eosinophils, and patients with asbestos-induced pleural disease had excess BAL lymphocytes. Importantly, cigarette smoking independently influenced the concentration of BAL macrophages and eosinophils even after accounting for the effect of asbestosis. In fact, although cigarette smoking accounted for 17 to 18% of the variance of BAL macrophages and eosinophils, asbestosis was responsible for 6 to 7% of the variance of BAL macrophages, neutrophils, and eosinophils. We conclude that cigarette smoking strongly influences BAL cellularity in patients with asbestosis but not in patients with asbestos-induced pleural fibrosis.

Our findings suggest that cigarette smoking may influence the pathogenesis of asbestosis. Several epidemiologic studies have identified cigarette smoking as a potential risk factor in the development of asbestosis (1–6). In fact, Blanc and colleagues (4) found that among those with extensive smoking histories, there appears to be a 13-fold excess risk of having asbestosis. Although potential mechanisms for the development of asbestosis in cigarette smokers include reduced clearance of asbestos fibers (20) and increased permeability of airway

epithelia (21), cigarette smoke may enhance the development of asbestosis by altering the constituents and function of inflammatory cells in the alveoli. In addition to excess macrophages and neutrophils (38, 39), BAL cells and fluid from cigarette smokers have clear defects in phagocytic ability (12), the metabolism of arachidonic acid (13), the balance of protease-antiprotease enzymes (14–16), the regulation of immunoglobulin production (17, 18), and the ability to regulate the production of fibronectin (19). Similarly, among patients with asbestosis, excess macrophages and neutrophils are found in BAL fluid (23–25). Moreover, BAL cells from these patients release increased amounts of neutrophil chemotactic factor (25), oxygen free radicals (23), fibronectin (23), growth factors (23), leukotriene B_4 (24), and interferon-γ (26). Although the inflammatory changes in the alveoli are clearly different in individuals who smoke cigarettes and patients with asbestosis, there exists enough overlap to suggest that exposure to cigarette smoke may play a role in initiating or "fueling" the chronic inflammatory process of asbestosis. Moreover, our similar findings in patients with idiopathic pulmonary fibrosis (22) suggest that this observation may be generalized to other forms of interstitial lung disease.

We (40) and others (41) have found that individuals with asbestos-induced pleural fibrosis and no evidence of interstitial lung disease have an elevated number and percentage of lymphocytes in the BAL fluid. Our current observations support this finding and indicate that this "lymphocytic alveolitis" is unrelated to cigarette smoking. In this context, it is interesting to note that for patients with IPF, BAL neutrophils and eosinophils are associated with a poor prognosis (42–46) and BAL lymphocytes are associated with a beneficial outcome (42, 43, 45). Among patients with IPF, these findings suggest that the lymphocytic component of the alveolitis is indicative of a reversible parenchymal process, and the neutrophil- and eosinophil-associated component signifies an established, progressive process in the lung parenchyma. If these findings in IPF are applicable to asbestos-induced lung disease, the lymphocytic alveolitis observed in asbestos-exposed individuals with pleural fibrosis may represent an early, potentially reversible stage of asbestos-induced parenchymal inflammation. Moreover, the associated parenchymal changes on high-resolution chest computed tomography scan (40) may represent reversible inflammatory rather than fixed, fibrotic lesions. Further prospective studies are clearly needed to determine whether this hypothesis is valid. However, these observations indicate that intervention trials (restriction from further asbestos exposure, smoking cessation, and antiinflammatory pharmacologic agents) aimed at preventing the development and/or progression of asbestosis may best be directed toward asbestos-exposed subjects with a lymphocytic alveolitis.

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