Changing Patterns in Asbestos-Induced Lung Disease*

Jill Ohar, MD, FCCP; David A. Sterling, PhD; Eugene Bleecker, MD, FCCP; and James Donohue, MD, FCCP

Study objectives: To determine patterns in asbestos-induced lung diseases found in older, less exposed workers.

Design: Review of a database evaluating lung function, smoking status, form of asbestos-induced lung disease, and radiograph abnormalities.

Setting: Outpatient clinic.

Participants: A total of 3383 asbestos-exposed workers referred for independent medical evaluation, including control subjects who lacked asbestos-specific radiograph abnormalities (n = 243), subjects with low International Labor Organization (ILO) scores (n = 2,685), high ILO scores (n = 312), bronchogenic cancer (n = 63), and mesothelioma (n = 80). Of these, 3,327 workers have specific smoking status information and 3,312 workers have lung volume measures. Interventions: Chest radiographs were interpreted by a certified B-reader, and abnormalities were quantified according to the ILO scoring system. Spirometry and lung volume measurement were performed. Subjects completed a self-administered questionnaire that was reviewed at the time of examination. Control subjects were screened on two separate occasions at least 10 years apart to exclude subclinical or slowly progressive asbestos-induced lung disease.

Measurements and results: The mean age of the population was 65.1 ± 9.9 years, and the latency was 41.4 ± 10.1 years (± SD). Most subjects (41.8%) had normal pulmonary function. Obstruction was the most common pulmonary function abnormality (25.4%), followed by restriction (19.3%) and a mixed pattern (6.0%). Most subjects (79.4%) had low ILO scores. Benign pleural abnormalities were the only findings in 54% of subjects with low ILO score. Subjects with high ILO scores were older, smoked more, and had a longer latency than subjects with low ILO scores and control subjects. Smokers were younger, had a shorter latency, and had paradoxically greater ILO scores than nonsmokers. Subjects with bronchogenic cancer and mesothelioma had longer latencies than control subjects and subjects with benign asbestos-induced lung disease.

Conclusions: Asbestos-induced lung disease today is characterized by low ILO scores, long latencies, greater disease magnitude in smokers, and a normal or obstructive pattern of pulmonary function abnormality. Spirometric evaluation in the absence of lung volume measurements caused misclassification that resulted in overestimation of the presence of a restrictive pattern of pulmonary function.

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Key words: asbestosis; obstructive lung disease; occupational disease; pulmonary function test

Abbreviations: ILO = International Labor Organization; ± pp = with or without pleural plaque; RV = residual volume; TLC = total lung capacity

Between 1940 and 1979, it has been estimated that 40% of the workforce or almost 27 million individuals were exposed to asbestos. After 1980, industrial use of asbestos was curtailed in the United States by government-imposed exposure regulations. The development of asbestos-exposure induced lung disorders is associated with a latency period between

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Correspondence to: Jill Ohar, MD, FCCP, Wake Forest School of Medicine, Section of Pulmonary and Critical Care Medicine, Medical Center Boulevard, Winston-Salem, NC 27157-1054; e-mail: johar@wfubmc.edu

*From the Departments of Internal Medicine (Dr. Ohar) and Pediatrics (Dr. Bleecker), Wake Forest University School of Medicine, Winston-Salem, NC; School of Public Health, and Division of Pulmonary (Dr. Sterling), Critical Care and Occupational Medicine, Saint Louis University, St. Louis, MO; and Department of Internal Medicine (Dr. Donohue), University of North Carolina School of Medicine, Chapel Hill, NC. Dr. Ohar has served as an expert witness for both the defense and plaintiffs in judicial pleadings for compensation for asbestos-induced diseases.
date of first exposure and the time when the disease becomes clinically apparent. Typically, benign pleural effusions are the first manifestations of asbestos exposure, followed by pleural plaques, interstitial fibrosis, bronchogenic cancer, and mesothelioma. Any one of these asbestos-related lung diseases may be the first and only sequelae of asbestos exposure that a worker may acquire. Therefore, given a sufficient latency period, a worker may acquire mesothelioma as the initial and only result of asbestos exposure.

The development and severity of asbestos-induced lung disease is related to intensity of exposure (dose) and latency. Asbestos exposure for workers today is remote in time and more limited than described in previous studies. We hypothesized that the patterns of asbestos-induced lung disease found today may be different than those encountered in the past 2 decades. Changes in asbestos-induced lung disease characteristics may be due to improvement in life expectancy leading to an increased period of time for the development of asbestos-related pulmonary diseases. Workers have a 16-year life expectancy at the time of retirement at the age of 65 years compared with only 17 months 2 decades ago. Furthermore, because of a longer life expectancy, individuals already having a diagnosed asbestos-induced lung abnormality may progress to a more severe level or form of asbestos-induced lung disease such as asbestosis, bronchogenic cancer, or mesothelioma. An augmented number of new cases of asbestos-induced lung disease may therefore be anticipated in the next 2 decades because of the longer latency and the greater longevity enjoyed by retirees.

**Materials and Methods**

To test this hypothesis, we assessed patterns of asbestos-induced lung disease from a registry of asbestos-exposed workers (n = 3,383) established as the Selikoff registry. All patients were referred for independent medical evaluation. Entry criteria for an independent medical evaluation included documented workplace asbestos exposure, an elapsed time from date of first exposure (latency) of > 10 years, and an abnormal chest radiograph pattern consistent with the history of asbestos exposure. Referrals were drawn from trade unions, television, and newspaper advertisements. More than 99% of all referrals agreed to participate in the Selikoff registry. Subjects gave informed consent for their participation, and the protocol was approved by the Institutional Review Boards at Saint Louis University and Wake Forest University. As part of the referral process, a chest radiograph, pulmonary function tests, and an extensive questionnaire were obtained. Subjects were sent a detailed questionnaire for self-completion prior to their evaluation to obtain information on medical history, family medical history, and work exposure.

**B-readings and International Labor Organization Scores**

Chest radiographs were obtained and interpreted by a certified B-reader and reviewed by the physician investigator (J.O.) during the subject’s evaluation. Chest radiograph abnormalities were quantified according to the International Labor Organization (ILO) scoring system. The ILO score was expressed as a single digit to facilitate statistical evaluation (0/0 = 1, 0/1 = 2, 1/0 = 3, 1/1 = 4, etc.). Patients were grouped under one of three radiographic categories: those with asbestos exposure and no visible radiographic abnormality (control subjects), subjects with ILO scores ≥ 0/0 and < 1/1 with or without pleural plaque (≥ pp) [low ILO], and subjects with ILO scores ≥ 1/1 ± pp (high ILO). Pleural abnormalities were simply coded as present or absent. The subjects who were classified as control subjects due to lack of radiographic findings were recruited through the same mechanisms, worked in the same trades, and worked for the same duration as other subjects. Control subjects were screened on two separate occasions at least 10 years apart to exclude subclinical or slowly progressive asbestos-induced lung disease. To qualify as a control subject, the chest radiograph had to be completely free of asbestos-induced abnormalities on both occasions.

**Pulmonary Function Testing**

All pulmonary function testing was performed according to American Thoracic Society published standards. A small percentage of subjects, primarily those with a diagnosis of advanced lung cancer or mesothelioma, were unable to undergo pulmonary function testing. Lung volume measurements were obtained except when spirometric values were normal or consistent with obstruction with a normal FVC (FVC > 80% and FEV1/FVC < 70%). Subjects were grouped into four patterns of pulmonary function: normal, FVC > 80% predicted and FEV1/FVC ≥ 70%; obstruction, FVC > 80% and FEV1/FVC < 70%; restriction, FVC ≤ 80% and FEV1/FVC ≥ 70%; and mixed (obstruction with air trapping or coexistent restriction), FVC ≤ 80% predicted and a FEV1/FVC < 70%. The total lung capacity (TLC) was used to separate subjects with a mixed pattern into those with obstruction with an increased residual volume (RV) that defined air trapping, from subjects with obstruction and coexistent restriction.

**Asbestos Exposure and Health History Questionnaire**

The questionnaire detailed information about prior employment, smoking history, and personal and family health histories. The questionnaire was self-administered prior to evaluation, and the physician examiner reviewed answers at the time of examination. Subjects were asked to quantify their tobacco use behavior according to method of smoking (cigarette, cigar, or pipe), packs per day, and ages of initiation and cessation of tobacco use. Subjects were grouped according to smoking status as never smoked, currently smoking, and former smokers. Smoking status was also expressed in pack-years. Subjects were asked to list every job since finishing school (name of company, job title, and tasks performed). Other questions included the year of first exposure to asbestos, and whether they ever worked in trades or at locations known to be associated with asbestos exposure. Personal health history questions included a listing of all medications and hospitalizations, including date of confinement and diagnoses. The presence of dyspnea, chest pain, and cough were recorded. Also elicited were a personal history of other respiratory diseases and the occurrence of cancer. Subjects were grouped according to disease status in one of the following categories: bronchogenic cancer, mesothelioma, high ILO score, low ILO score, and control subjects. Each of the five disease-status groups was mutually exclusive. Subjects with isolated pleural plaque were included within the low ILO score group.

Subjects were asked the age and cause of death of their parents and siblings. A family history of cancer and respiratory and
cardiovascular diseases was elicited. At the time of the evaluation, all questionnaire responses were discussed and verified with the patient by the physician investigator (J.O.).

Statistical Analysis

The population was divided two different ways for most of the analyses performed. To assess the effects of cigarette smoking on pulmonary function and the development of asbestos-induced lung disorders, the population was divided according to smoking status into current, former, and never smokers. To evaluate other factors that may influence the development of asbestos-induced lung disorders, the population was divided according to disease status into five groups: control subjects, subjects with mesothelioma, subjects with bronchogenic cancer, and subjects with high and low ILO scores. Continuous variables were evaluated by analysis of variance. Fisher exact test was used for categorical two-by-two comparisons, and the Pearson test was used when more than four cells were compared. A regression model was used to identify the combined effects of multiple variables, such as latency, pulmonary function variables, age, and pack-years on ILO score. Post hoc analysis of variance used a Bonferroni correction; \( p < 0.05 \) was considered significant.

Results

Demographics

The mean age (± SD) of the study population was 65.1 ± 9.9 years (range, 28 to 93 years) [white race, 93%; male gender, 96%]. Six percent of the individuals were African Americans, and 1% characterized themselves as “other” race. Nearly two thirds of the workers could be classified with six job descriptors (Fig 1). A small number of subjects had a diagnosis of lung cancer (1.9%) or mesothelioma (2.4%). These individuals tended to be older than control subjects and subjects with nonmalignant asbestos-related radiographic abnormalities (Table 1).

ILO Scores

Among subjects with an identifiable asbestos-induced radiographic abnormality, 79.4% had an ILO score < 1/1 ± pp. Pleural abnormalities (plaque or diffuse pleural thickening) were the only abnormality in 54% of subjects with low ILO scores. Plaques were present in 80.8% of subjects with low ILO scores and 57% of subjects with high ILO scores. Pleural abnormalities were found in 63.3% of subjects with bronchogenic cancer. There was no significant difference in the distribution of ILO scores into high ILO and low ILO categories for subjects with mesothelioma (12% and 85%, respectively) or subjects with bronchogenic cancer (14% and 86%, respectively), compared with the population as a whole. Subjects with high ILO scores were significantly older, smoked more, and had a longer latency (\( p < 0.001 \)) than those with low ILO scores and control subjects (Table 1). The FEV\(_1\), FVC, and FEV\(_1\)/FVC were also lower in subjects with high ILO scores compared with subjects with low ILO scores and in subjects with low ILO scores compared to control subjects. ILO score did not correlate well with TLC (Table 1). Women were less likely to have a high ILO score than men (Table 1). In a regression model, latency corrected for age, percentage of predicted FEV\(_1\), and smoking history in packs-years predicted ILO score. FEV\(_1\)/FVC and percentage of predicted FVC were not significant in the ILO regression model.

Latency

The mean number of years since first exposure to asbestos (latency) for the entire population was

![Figure 1. Subjects stratified by trade.](http://publications.chestnet.org/pdfaccess.ashx?url=data/journals/chest/22005/ on 04/19/2017)
Table 1—Lung Volume, Smoking Status, Radiographic Measure, and Demographics By Disease Status*

<table>
<thead>
<tr>
<th>Variables</th>
<th>Controls (Low ILO)</th>
<th>ILO ≥ 1/1 ± pp (High ILO)</th>
<th>Bronchogenic Cancer</th>
<th>Mesothelioma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>243 (7.2)</td>
<td>312 (9.2)</td>
<td>63 (19)</td>
<td>80 (2.3)</td>
</tr>
<tr>
<td>FEV1, L (% predicted)</td>
<td>2.8 ± 9 (89.1 ± 23.0)</td>
<td>2.3 ± 8 (71.4 ± 23.9)</td>
<td>1.9 ± 8 (59.6 ± 23.4)</td>
<td>2.2 ± 9 (67.4 ± 24.9)</td>
</tr>
<tr>
<td>FVC, L (% predicted)</td>
<td>3.8 ± 1.1 (94.5 ± 18.4)</td>
<td>3.3 ± 1.0 (76.6 ± 20.3)</td>
<td>2.9 ± 9 (70.7 ± 21.5)</td>
<td>2.9 ± 1.2 (67.7 ± 21.5)</td>
</tr>
<tr>
<td>FEV1/FVC</td>
<td>72.9 ± 11.3</td>
<td>68.7 ± 13.7</td>
<td>65.9 ± 16.4</td>
<td>75.5 ± 10.9</td>
</tr>
<tr>
<td>TLC, L (% predicted)</td>
<td>6.8 ± 2.3 (101.2 ± 45.6)</td>
<td>6.2 ± 2.9 (93.8 ± 41.1)</td>
<td>5.4 ± 1.3 (83.7 ± 19.1)</td>
<td>5.5 ± 1.8 (78.4 ± 25.6)</td>
</tr>
<tr>
<td>Numeric ILO score</td>
<td>1 ± 0</td>
<td>4.9 ± 1.6</td>
<td>2.4 ± 1.9</td>
<td>1.9 ± 1.6</td>
</tr>
<tr>
<td>Bronchogenic cancer</td>
<td>0</td>
<td>7 (14)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mesothelioma</td>
<td>0</td>
<td>3 (12)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Latency</td>
<td>39.8 ± 10.5</td>
<td>45.8 ± 9.5</td>
<td>45.8 ± 9.4</td>
<td>46.5 ± 12.1</td>
</tr>
<tr>
<td>Age, yr</td>
<td>62.9 ± 9.9</td>
<td>69.1 ± 9.1</td>
<td>67.6 ± 8.4</td>
<td>66.9 ± 11.3</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td>51 (21.3)</td>
<td>63 (20.5)</td>
<td>4 (65)</td>
<td>6 (8.1)</td>
</tr>
<tr>
<td>Former</td>
<td>107 (44.6)</td>
<td>198 (64.3)</td>
<td>57 (91.9)</td>
<td>49 (66.2)</td>
</tr>
<tr>
<td>Never</td>
<td>82 (34.2)</td>
<td>57 (15.5)</td>
<td>1 (1.6)</td>
<td>19 (25.7)</td>
</tr>
<tr>
<td>Pack-years</td>
<td>25.0 ± 22.5</td>
<td>46.1 ± 31.2</td>
<td>58.9 ± 36.4</td>
<td>36.4 ± 32.4</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>203 (83.5)</td>
<td>306 (98.1)</td>
<td>63 (100)</td>
<td>70 (87.5)</td>
</tr>
<tr>
<td>Female</td>
<td>40 (16.5)</td>
<td>6 (1.9)</td>
<td>0</td>
<td>10 (12.5)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>214 (88.1)</td>
<td>296 (94.9)</td>
<td>58 (92.1)</td>
<td>76 (95.0)</td>
</tr>
<tr>
<td>Black</td>
<td>26 (10.7)</td>
<td>15 (4.8)</td>
<td>4 (6.3)</td>
<td>3 (3.8)</td>
</tr>
<tr>
<td>Other</td>
<td>3 (1.2)</td>
<td>1 (0.3)</td>
<td>1 (1.6)</td>
<td></td>
</tr>
</tbody>
</table>

*Data are presented as mean ± SD or No. (%). Significance of differences among groups is reported within the text.
41.4 ± 10.1 years. Those with high ILO score had a longer latency than those with low ILO scores or control subjects (p < 0.001). However, the latency from first exposure to subjects with low ILO scores did not differ significantly from control subjects. Subjects with mesothelioma and bronchogenic cancer had a longer latency period than control subjects and subjects with low ILO scores (p < 0.001) but not subjects with high ILO scores.

**Smoking Behavior**

The majority of the study population (78.2%) smoked at some point in their life; however, only 19% of the population were current smokers at the time of evaluation. Most of the subjects who had ever smoked (73.9%) quit during the 1970s. Current smokers were significantly younger and had a shorter time from first exposure to asbestos until manifestation of disease (latency) than did former and non-smokers (Table 2). Despite the shorter latency, current smokers had a significantly greater numeric ILO score than did nonsmokers. TLC values were paradoxically higher for current smokers than for former or never smokers despite the greater ILO score in current smokers (p < 0.001). Nonsmokers had a significantly greater FEV1 and FEV1/FVC ratio than former or current smokers, and a greater FVC than former smokers but not current smokers (p < 0.001). The FEV1 and FEV1/FVC ratio did not significantly differ between current and former smokers. Subjects with bronchogenic cancer smoked significantly more than control subjects (p < 0.001), subjects with mesothelioma (p < 0.001), subjects with high ILO scores (p < 0.05), and subjects with low ILO scores (p < 0.001) [Table 1]. Subjects with high ILO scores smoked significantly more than those with low ILO scores (p < 0.001) [Table 1]. Subjects with mesothelioma smoked less than subjects with bronchogenic cancer (p < 0.001).

**Pulmonary Function**

Most of the subjects had normal pulmonary function (Fig 2). When spirometry was used to assess pulmonary function in the absence of lung volume measurements, a purely restrictive pattern (FVC ≤ 80% predicted and FEV1/FVC ≤ 70%) was present in 23.8% of the asbestos-exposed population overall. Airflow obstruction was present in 16%, and a mixed pattern of obstruction with restriction was present in 18.4%. A clear separation was apparent when subjects were classified into restrictive and nonrestrictive pulmonary function patterns on the basis of percentage of predicted FVC (using > 80% predicted as the norm). The mean FVC predicted percentage for the restrictive group was 66.2 ± 11.5% and 96.5 ± 11.4% for the nonrestrictive group (Fig 2). This separation was maintained even when subjects were classified according to smoking status (Fig 3).

Spirometric evaluation without lung volume mea-

### Table 2—Lung Volume, Radiographic Measure, and Demographics by Smoking Status*

<table>
<thead>
<tr>
<th>Variables</th>
<th>Nonsmoker</th>
<th>Former Smoker</th>
<th>Current Smoker</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>725 (21.8)</td>
<td>1,971 (59.3)</td>
<td>631 (19.9)</td>
<td></td>
</tr>
<tr>
<td>FEV1, L (% predicted)</td>
<td>2.9 ± .9</td>
<td>2.6 ± .9</td>
<td>2.5 ± .8</td>
<td>&lt; 0.001†</td>
</tr>
<tr>
<td>FVC, L (% predicted)</td>
<td>3.7 ± 1.0</td>
<td>3.5 ± .9</td>
<td>3.6 ± .9</td>
<td>&lt; 0.001†</td>
</tr>
<tr>
<td>FEV1/FVC</td>
<td>76.8 ± 8.9</td>
<td>71.0 ± 12.3</td>
<td>68.7 ± 12.7</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>TLC, L (% predicted)</td>
<td>6.2 ± 1.5</td>
<td>6.2 ± 1.6</td>
<td>6.6 ± 2.3</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Numeric ILO score</td>
<td>1.8 ± 1.3</td>
<td>2.1 ± 1.4</td>
<td>2.2 ± 1.3</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Bronchogenic cancer†</td>
<td>1 (1.6)</td>
<td>57 (91.9)</td>
<td>4 (6.5)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Mesothelioma†</td>
<td>19 (25.7)</td>
<td>49 (66.2)</td>
<td>6 (8.1)</td>
<td>0.048</td>
</tr>
<tr>
<td>Latency</td>
<td>41.2 ± 11.2</td>
<td>42.8 ± 10.2</td>
<td>37.2 ± 8.9</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Age, yr</td>
<td>64.9 ± 10.8</td>
<td>66.3 ± 9.6</td>
<td>60.3 ± 5.7</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Pack-years</td>
<td>0</td>
<td>35.7 ± 28.7</td>
<td>52.3 ± 31.3</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>666 (91.9)</td>
<td>1,915 (97.2)</td>
<td>604 (95.7)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Female</td>
<td>69 (8.1)</td>
<td>56 (2.8)</td>
<td>27 (4.3)</td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>676 (93.2)</td>
<td>1,829 (92.8)</td>
<td>580 (91.9)</td>
<td>0.618</td>
</tr>
<tr>
<td>Black</td>
<td>41 (5.7)</td>
<td>124 (6.3)</td>
<td>47 (7.4)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>8 (1.1)</td>
<td>18 (0.9)</td>
<td>4 (0.6)</td>
<td></td>
</tr>
</tbody>
</table>

*Data are presented as mean ± SD or No. (%).
†Percentages given are out of total number of bronchogenic cancers (n = 62) or mesotheliomas (n = 74) with smoking data.
‡Nonsmoker against former and current.
§Nonsmoker against former, former against current.
||Nonsmoker against current, former against current.
Measurements overestimated the number of subjects with restriction and underestimated those with obstruction. When subjects were classified according to smoking status, airways obstruction was the most common pattern of pulmonary function abnormality by spirometric assessment in current smokers. Restriction predominated in nonsmokers and former smokers (Fig 4). However, when pulmonary function was assessed by lung volume measurement in conjunction with spirometric evaluation, obstruction was the most common pattern in both current and former smokers (Fig 5). As anticipated, the RV and RV/TLC ratio were increased in most subjects who had a mixed pattern on spirometric evaluation. Only 27% of cigarette smokers with airways obstruction and a reduced FVC had coexistent restriction (TLC/FEV$_1$ < 80% predicted).

When subjects were classified according to disease status and evaluated by spirometry and lung volume measurements, airways obstruction was the most common pattern of pulmonary function abnormality found in all groups (low ILO, high ILO, and bronchogenic cancer). The only exception was found in subjects with mesothelioma (Fig 6). Restriction was more common in subjects with high ILO scores (25.0%) than those with low ILO scores (17.8%); however, obstruction was the most common abnormality in both. Among smokers, there was no significant difference in the degree of airways obstruction, measured by FEV$_1$/FVC and percentage of predicted FEV$_1$, when subjects were classified according to disease status (ie, mesothelioma, lung cancer, high ILO scores, low ILO scores, or control subjects) despite significant differences among these groups in tobacco exposure measured in pack-years. Among nonsmokers, the only disease state where FEV$_1$/FVC significantly differed (p = 0.025 with Bonferroni correction), was subjects with high ILO scores (72.8 ± 15.2%) compared to those with low ILO scores (76.2 ± 9.2%). In a regression model, latency was a weak predictor of FEV$_1$/FVC after controlling for age and smoking history in packs-years.

**Discussion**

In this study, we found that most subjects had normal pulmonary function. When pulmonary function abnormalities were present, the dominant finding was airways obstruction. Spirometric evaluation in the absence of lung volume measurements caused misclassification of subjects who had obstruction with coexistent airtrapping as part of the mixed-pattern group. This misclassification resulted in overestimation of the presence of a restrictive pattern of pulmonary function by attributing causation of the reduced FVC to obstruction mixed with restriction instead of obstruction with airtrapping.
Therefore, when a reduced FVC was present, in most subjects, it was caused by an increase in RV (hyperinflation) that was probably due to airway collapse. Hyperinflation, quantified by an increased RV and RV/TLC ratio, accounted for the reduced FVC in 83% of smokers and 71% of nonsmokers with obstruction and a reduced FVC. These findings confirm an earlier report by Harber and colleagues.14

Most subjects evaluated for asbestos-related lung disease had either low ILO scores or pleural plaques with no parenchymal abnormalities. Smokers were younger, had a shorter latency and, paradoxically, greater ILO scores than nonsmokers. These results confirm an earlier report by Harber and colleagues.14

Subjects with bronchogenic cancer and mesothelioma had longer latencies than control subjects and subjects with high and low ILO scores. When patients were classified according to disease state, a restrictive pattern of pulmonary function abnormality was found only in subjects with mesothelioma. An obstructive pattern was the major finding in subjects with bronchogenic cancer and subjects with both high and low ILO scores. Control subjects demonstrated a low frequency of both obstruction (11.8%) and restriction (11.8%).

The presence of a restrictive pattern has been reported in the literature, for asbestosis5,7,8,17,19–24 as well as for diffuse pleural thickening in the absence of asbestos-induced parenchymal abnormalities.25 Many of these reports, however, evaluated small numbers of subjects and failed to measure lung volumes; one large study5 failed to report FEV1 in nearly half of the patients analyzed. Workers evaluated in these reports had greater intensity and duration of exposures to asbestos, shorter latencies, were younger, and smoked more than the subjects in this study. Latency in previous reports4,6,10,14,16,20,21,26–34 ranged between 15 years and 35 years. The subjects’ mean ages in these studies 6,16,20,21,29,30,35–39 were between 34 years and 62 years, and the frequency of current smokers was 21 to 73%. In contrast to these reports, the mean latency in this study was 41.4 years, the mean age was 65.1 years, and the frequency of current smokers was 19%.

Other investigators1,6,10,14,18,31,40–43 have also reported an obstructive pulmonary function pattern as the dominant finding in asbestos-related lung dis-
ease. The results of these studies, however, have been disputed because of small numbers of subjects evaluated.\(^40\)–\(^42\) Furthermore, a standardized definition of obstruction has not been universally applied for each of these investigations. Some investigators\(^3,8,16,33,34,42,44\) have defined airways obstruction on the basis of FEV\(_1\) or its ratio to FVC, others by terminal flow rates, mid-expiratory flow rates, or specific airway conductance. Several factors have fueled the controversy as to whether asbestos-related lung disease causes restriction or airways obstruction.\(^43\)–\(^45\) These factors include the use of different tests to assess obstruction with different levels of specificity and sensitivity as well as confusion in terminology, failure to measure lung volumes, differences in demographics of subjects, and small numbers of patients evaluated in previous studies.

In this analysis of 3,383 subjects, we have shown that airways obstruction is more common than restriction in asbestos-exposed individuals currently undergoing evaluation. These results confirm the findings of Kilburn and colleagues\(^31,39,40,43\) and supports published clinical pathologic correlates. Churg et al\(^46\) have shown that asbestos exposure results in small airways disease. Furthermore, Begin et al\(^41,47\) demonstrated mononuclear peribronchiolar inflammation in a sheep model of early asbestosis, a precursor to the peribronchiolar fibrosis of the respiratory bronchioles seen by Churg et al\(^46\) in humans; they support the hypothesis that asbestos fibers impact on small airway carinae. Fibers are phagocytosed by macrophages initiating an inflammatory response that results initially in bronchitis and subsequently to peribronchial fibrosis. In some cases, this inflammatory response extends to the pulmonary parenchyma to cause interstitial fibrosis (asbestosis). Cigarette smoking-induced chronic bronchitis is in many ways similar to asbestos-induced bronchitis, and in this study the effects of exposure to both cigarette smoke and asbestos acted additively to induce airways obstruction. An animal model\(^48\) demonstrates synergy between cigarette smoke and asbestos exposure in the causation of airway and parenchymal lung disease, possibly through cigarette smoke-induced reduction of mucociliary clearance of asbestos fibers. The synergistic effects of exposure to both cigarette smoke and asbestos in the induction of lung cancer are well known. Given the mechanistic and demographic overlap in the induction of both lung cancer and chronic bronchitis, the observed synergy in this study could be anticipated.

The fact that subjects were recruited from legal cases based on the presence of a radiographic abnormality observed in subjects with bronchogenic cancer and both high and low ILO scores. The most common pulmonary function abnormality in subjects with mesothelioma was restriction.
radiographic progression to an asbestos-induced pulmonary disease. Since the presence of asbestos-induced radiographic abnormalities has been shown to correlate with evidence of asbestos exposure, the presence of asbestos-induced radiographic abnormalities narrows the population under study to those with a higher likelihood of asbestos exposure and the ability to respond to the exposure with measurable pulmonary disease. Furthermore, the fact that subjects had litigation pending enhanced selection bias from nonparticipation. While the study is descriptive, it provides a foundation to illustrate the clinical characteristics of asbestos-induced lung disease in the United States today. It also permits us to ask important mechanistic questions about asbestos-induced lung disease and its overlap with airways obstruction. Demographic evidence of disease overlap fosters the question of overlapping genetic susceptibility. Areas yet to be explored include the potential for overlapping genetic susceptibility for COPD and asbestos-related lung disease.

REFERENCES


24 Wright GW. Functional abnormalities of industrial pulmonary fibrosis. Arch Ind Health 1955; 11:196–203
35 Wang X, Yano E, Nonaka K, et al. Respiratory impairments due to dust exposure: a comparative study among workers
exposed to silica, asbestos, and coal mine dust. Am J Ind Med 1997; 31:495–502
43 Kilburn KH, Warshaw RH. Airways obstruction from asbestos exposure. Chest 1994; 106:1061–1070