SPIROMETRIC ABNORMALITIES IN 2573 ASBESTOS INSULATORS WITH LONG TERM EXPOSURE: EFFECTS OF SMOKING HISTORY AND RADIOGRAPHIC ABNORMALITIES

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INTRODUCTION

The 2573 insulators who are the subjects of this report comprise one of the largest reported populations occupationally exposed to asbestos. They were selected on the basis of a long duration from onset of exposure (DURON; 87% were ≥ 30 years) in order to provide sufficient time for evolution of disease, whether it be pleuropulmonary fibrosis caused by asbestos or chronic airways obstruction attributable to smoking and perhaps to occupational dusts. This population is therefore well suited to provide information concerning:

1. The prevalence of the various pulmonary function impairments in a large well defined group occupationally exposed to asbestos.
2. The effect of such influences as radiographic abnormalities, DURON and smoking on pulmonary function. In this regard, the large number of lifetime nonsmokers (n = 506) allows characterization of the effects on pulmonary function of asbestos inhalation alone, unconfounded by cigarette smoking.

METHODS

Details concerning subject selection, medical evaluation and radiographic reading are given in a companion paper.[1] Subjects were studied in 19 cities in North America over a two year interval. Spirometric tests adhered to current guidelines;[2] at least 3 acceptable efforts were obtained on each subject, who was standing and wore a noseclip. A computerized rolling seal spirometer was used; efforts were monitored by maximum expiratory flow-volume curves recorded in real time and all data, including the flow volume arrays, were stored on digital tape.

Predicted values were those published by this laboratory using the same equipment in a random sample of the population of a large industrial state, adjusted for the effects of smoking in current smokers (which were significant on all tests except FVC).[3]

"Nonsmokers" (NS) smoked less than one cigarette a day, had smoked ≤ ten cigarettes a day for ≤ six months or smoked only cigars and pipes, which are not inhaled. Current smoker (SM) exceeded these limits. "Ex-smokers" (XS) exceeded these limits and had discontinued smoking ≥ two years previously.

Impairments were defined as follows:

Normal (Nl): Nl. FVC, FEV_1/FVC and MMF;

Restrictive (Rest): FVC <95% lower confidence interval (CI)

Restrictive (Rest): FVC <95% lower confidence interval (CI), ↓FEV_1/FVC nl (≥0.65 age ≥60, ≥0.70 age 30–59);

Overt Obstructive (Obs): FVC nl, FEV_1/FVC below limits defined above;

Small Airways Dysfunction (SAD): FVC nl, FEV_1 /FVC normal, $FET_{25\text{-}75\%}$ (also called mid-expiratory time) ≥0.78 sec;[5]

Combined, primarily restrictive (Comb Rest): Both FVC and FEV_1/FVC ↓ ; ↓ FVC ≥ ↓ FEV_1/FVC;

Combined, primarily obstructive (Comb Obs): ↓ FEV_1/FVC > ↓ FVC.

RESULTS

Mean Values

Table I shows mean demographic, exposure and pulmonary function variables for NS and those with a smoking history. There is no difference in age, DURON or years exposed. FVC and FEV_1 are reduced in the NS, but not FEV_1/FVC or the flows $FEF_{25\text{-}75\%}$ or $FEF_{75\%}$. FVC and FEV_1 are reduced to a greater extent in the smokers but FEV_1 /FVC and flows are only minimally reduced using smoking specific predicted values.

Prevalences of Functional Impairment

By Smoking History (Table II):

Of the 2573 workers studied, 506 (19.7%) were NS, 861 (33.5%) SM and 1206 (46.9%), XS. This last group, which includes only those who have discontinued smoking for at least 2 years, reflects the effect of educational efforts to discontinue smoking among asbestos workers.

Table I

Demographic, Exposure and Pulmonary Function Variables by Smoking History (Mean and SD)

	Nonsmokers (n = 506)	Current and Ex-Smokers (n = 2067)
Age (yrs)	58.6 (8.6)	57.3 (8.0)
Height (cm)	173.2 (6.9)	174.0 (6.6)
Duron (yrs)	36.3 (7.6)	34.9 (7.0)
Yrs exposed	32.0 (8.3)	31.6 (7.5)
Dur smoking (yrs)	0	31.6 (12.0)
Pack years	0	40.6 (26.1)
FVC (% pred)	86.5 (16.6)	82.0 (17.3)
FEV_1 (% pred)	85.5 (17.4)	82.3 (20.6)
$FEF_{25-75\%}$ (% pred)	96.6 (36.2)	86.6 (40.1)
$FEF_{75\%}$ (% pred)	101.2 (45.5)	97.7 (49.3)
FEV_1/FVC x 100	79.2 (7.6)	73.4 (10.5)
FEV_1/FVC (% pred)	100.6 (9.5)	97.1 (13.5)

Table II

Spirometric Impairments in 2573 Asbestos Insulators ≥20 Years from Onset of Exposure (by Smoking History)

	NS (19.7%)*	SM (33.5%)	XS (46.9%)	All Smoking Categories
Normal pf	222 (43.9)*	146 (17.0)	376 (31.2)	744 (28.9)
Restrictive	156 (30.8)	270 (31.4)	413 (34.2)	839 (32.6)
Obstructive	17 (3.4)	144 (16.7)	92 (7.6)	253 (9.8)
Small Airways	98 (19.4)	145 (16.8)	204 (16.9)	447 (17.4)
Combined	13 (2.6)	156 (18.1)	121 (10.0)	290 (11.3)
Combined, rest	11 (2.2)	110 (12.8)	92 (7.6)	213 (8.3)
Combined, obst.	2 (0.4)	46 (5.3)	29 (2.4)	77 (3.0)
All Impsirments	506	861	1206	2573

* Percentages are shown in parentheses. Percentages after esch smoking category are of the total population (e.g., 19.7% of the population were NS). Percentages within each smoking category are of each impairment within that smoking category (e.g., 43.9% of NS had nl pf).

The prevalence of several impairments varies by smoking history. Normal pulmonary function was most likely in NS (43.9%) and least in SM (17.0%); XS were intermediate (31.2%). Overt obstruction was most likely in SM (16.7%) and least in NS (3.4%). While restrictive impairment by itself did not vary in frequency by smoking category, combined impairment was far more common in SM (18.1%), again with XS intermediate. Frequency of small airways dysfunction was similar in all smoking categories.

By radiographic abnormality (Table III):

Normal pulmonary function was most likely (43.4%) when the chest radiograph was normal and least likely (21.2%) when both parenchymal and pleural disease was present. While frequencies of small airways dysfunction did not vary by radiographic abnormality, restrictive and combined impairments were most common when parenchyma and pleura were both abnormal and obstruction was more likely when only the parenchyma was abnormal. Interestingly, when frequency of restriction was compared in *isolated parenchymal* vs. *isolated pleural* disease, it was greater in the latter (34.4% vs. 22.3%).

Despite the greater frequency of normal function when the radiograph was normal (43.3%), 21.3% of those with a normal film had restriction and 7.7% had combined impairment, meaning that 29% had a reduced FVC. Similarly, while a normal film was more likely when pulmonary function was normal (25.1%), 10.4 percent of workers with restriction had a normal film.

Table III

Spirometric Impairments in 2573 Asbestos Insulators ≥20 Years from Onset of Exposure (by Radiographic Abnormality)

	"Normal" (16%)*	Parenchymal Only (11.7%)	Both (Parpleu) (48.2%)	Pleural Only (24.1%)	All Radiograph Categoriea
Normal pf	187 (43.3)*	105 (34.9)	263 (21.2)	189 (30.5)	744 (28.9)
Restrictive	88 (21.3)	67 (22.3)	471 (38.0)	213 (34.4)	839 (32.6)
Obstructive	36 (8.7)	37 (12.3)	121 (9.8)	59 (9.5)	253 (9.8)
Small Airway	77 (18.6)	64 (21.3	202 (16.3)	104 (16.8)	447 (17.4)
Combined	25 (7.7)	28 (9.3)	182 (14.7)	55 (8.9)	290 (11.3)
All Impairments	413	301	1239	620	2573

* Percentages are shown in parentheses. Percentages after each radiographic abnormality are of the total population (e.g., 16% of the population had normal films). Percentages within each radiographic abnormality are of each impairment within that radiographic abnormality (e.g., 43.3% of subjects with normal films had normal pulmonary function).

The percentage of NS was relatively greater in subjects with normal pulmonary function no matter in which radiographic category they fell whereas the percentage of SM was increased in those with obstructive or combined impairments within each radiographic category.

By Duration from Onset of Exposure (Table IV): Frequency of normal pulmonary function fell with increased duration of exposure while frequency of restriction and of combined impairment increased. Small airways dysfunction did not change and obstruction actually decreased.

Regression Analysis of Pulmonary Function

FVC (analyzed as percent predicted, to adjust for age and height) and the actual ratio FEV_1/FVC were analyzed for the contributions of such independent variables as radiographic category (any par, any pleu and parpleu interaction), DURON and pack years (Table V). Parenchymal involvement was not significant for FVC, although pleural and combined parenchymal-pleural involvements were. Pleural involvement (alone or combined) was not significant for FEV_1/FVC: The predominant influence on FEV_1/FVC was pack years, each pack year diminishing the FEV_1/FVC (x 100) by 0.11 so that 41 pack years (the mean of all subjects with a positive smoking history) would diminish the FEV_1/FVC (x 100) by 4.5. By contrast, DURON 35 years (the mean of all subjects in the study) would diminish FEV_1/FVC (x 100) by two-thirds of the smoking effect (2.9) and the presence of parenchymal disease on chest film would diminish the ratio negligibly (0.013).

Each year from onset diminished the FVC by 0.436 percent of predicted, so that DURON 35 years would diminish FVC by 15.3 percent of predicted, whereas each pack year diminished FVC by 0.096 percent of predicted. Cumulative decrement for 41 pack years was 3.9 per cent of predicted or 25% of the effect of DURON. The presence of pleural involvement on radiography diminished the value by 4.7 percent of predicted and the presence of parenchymal plus pleural involvement diminished the value by 7.8 percent of predicted.

DISCUSSION

The 2573 asbestos insulators are a large enough group to allow analysis of the effects on lung function of such independent variables as years from onset of exposure, cigarette smoking (pack years) and radiographic abnormalities. We used percent predicted FVC, the most easily and universally measured single test of pulmonary function, as our index of restrictive impairment. The largest effect was that of DURON, followed by combined pleuropulmonary involvement, smoking and isolated pleural involvement. As expected, smoking was the predominant influence on FEV_1/FVC, used as an index of airways obstruction. The effect of DURON is probably attributable to aging (which obviously parallels duration) since the FEV_1/FVC ratio is not adjusted for age as is percent predicted FVC.

In computing the prevalence of impaired pulmonary function, common practice has been to use as the numerator the number of subjects with abnormal values for *any* of the major pulmonary function parameters, e.g., FVC or FEV_1. This tends to obscure differences in the types of impairments and the relationship of these impairments to various exposures, e.g., asbestos vs. cigarette smoking. A reduced FVC is not necessarily indicative of restriction (airways obstruction with air trapping and an elevated RV may reduce

Table IV

Spirometric Impairments in 2573 Asbestos Insulators ≥20 Years from Onset of Exposure (by Duration from Onset of Exposure)

	≤ 29 Yrs. n = 331 (12.9%)	30-39 Yrs. n = 1593 (61.9%)	≥ 40 Yrs. n = 649 (25.2%)
Normal	127 (38.4)	470 (29.5)	147 (22.7)
Restrictive	84 (25.4)	487 (30.6)	268 (40.3)
Obstructive	39 (11.8)	171 (10.7)	43 (6.6)
Small Airways	56 (16.9)	287 (18.0)	104 (16.0)
Combined	25 (7.6)	178 (11.2)	87 (13.4)

Table VA

Regression Analysis of Percent Predicted FVC

Percent Predicted FVC (n = 2667)

Intercept	106.19
Duron	-0.436 (p0.0001, F 92.4)
Pack Yrs.	-0.096 (p0.0001, F 74.2)
Any pleu	-4.676 (p0.0001, F 28.1)
Parpleu interact	-3.091 (p0.0001, F 14.8)
Any par	NS
R^2	11.7

Table VB

Regression Analysis of FEV_1/FVC

$FEV_1/FVC \times 100$ (n = 2573)

Intercept	81.949
Pack Yr.	-0.111 (p0.0001, F 265.8)
Any par	-0.013 (p0.0018, F 9.73)
Duron	-0.084 (p0.002, F 9.56)
Any pleu	NS
Parpleu interact	NS
R^2	11.1

the FVC as well) nor are reduced FEV_1 and flow rates specific for obstruction (restrictive disease will generally result in a reduction in FEV_1 and flow rates proportional to the reduction in FVC).

Instead, a mutually exclusive classification of impairments based on a *combination* of spirometric measurements, including the FEV_1/FVC ratio, was employed. We have published the prevalence of these impairments in 351 patients with chronic pulmonary sarcoidosis.[4] Preliminary results from our sampling of the population of the state of Michigan[5] show far lesser frequencies of restriction (7% NS, 9% XS, 12% CS) and combined impairment (0% NS, 5% XS, 5% CS) but similar or greater frequencies of obstruction (13% NS, 17% XS, 21% CS).

Not surprisingly, normal pulmonary function was most likely in NS (44%) and least likely in SM (17%) while obstruction was most likely in SM (17%) and least in NS (3%). FREQUENCY OF RESTRICTIVE IMPAIRMENT DID NOT VARY BY SMOKING HISTORY, consistent with the predominant effects on FVC of asbestos exposure (measured as years from onset) and radiographic evidence of pleuropulmonary or pleural fibrosis. However, combined impairment was far more frequent in SM (18%) than NS (2.6%), with XS intermediate. This pattern results from the addition of obstruction (attributable to smoking) to the restriction of pleuropulmonary fibrosis. Such combined impairment is frequently seen in advanced sarcoidosis, bronchiectasis, cystic fibrosis or silicosis (progressive massive fibrosis).[6,7]

It is of interest that the most common impairment in both SM and XS (as well as NS) was restriction. It is recognized that what we call combined impairment can also result from reduction in FVC secondary to air trapping in severe obstruction. True combined impairment and air trapping can be distinguished only by full lung volumes. These obviously cannot be measured using physiologic methods on such large numbers of subjects under survey conditions. (We hope to measure full lung volumes using a planimetric method[8] on the posteroanterior and lateral chest films of these workers). We attempted to separate combined impairments into "predominant restrictive," and "predominant obstructive" by the relative decreases in FVC vs. FEV_1/FVC.

RESTRICTION WAS IDENTIFIED AS THE PREDOMINANT ELEMENT IN THE COMBINED IMPAIRMENT IN ALL SMOKING CATEGORIES (Table II)

The large number of NS in our study permits us to characterize the pulmonary function patterns attributable to inhalation of asbestos fibers alone. The 3 percent prevalences each of overt obstruction and of combined impairment do not provide strong evidence for obstructive impairment resulting from such inhalation (Table II). Half of the patients with these impairments (14 of 30) did not show radiographic evidence of pulmonary fibrosis. These 30 (of 506) NS may well have an independent cause of obstruction (e.g., asthma).

The decrease in frequency of obstruction with increasing

duration of exposure is the reciprocal of the increase in combined impairment, resulting from the superimposition of restriction in subjects with obstruction.

The greater contribution of radiographically identified pleural fibrosis (by itself) than of interstitial fibrosis (by itself) to restrictive impairment is seen in the regression analysis (Table V) and in the higher frequency of restrictive and combined impairments in those with isolated pleural vs. isolated parenchymal involvement (Table III). These findings concerning pulmonary function are similar to those concerning dyspnea in this population[1,9] and demonstrate the important effect of pleural fibrosis on lung function. These conclusions concerning pleural vs. parenchymal fibrosis may not be generalizable to other exposed populations for the following reasons:

1. This population was selected for long duration from onset and for heavy occupational exposure.
2. It is to a certain extent a survivor population in which those with the most severe interstitial fibrosis may have died (either of respiratory insufficiency or of bronchogenic carcinoma).
3. The largest proportion of subjects (48.2% of all subjects and 52.4% of those with abnormal films) had pleuropulmonary disease.

However, pleural disease is more prominent than interstitial fibrosis in many occupations with less intense exposure, and in family exposures. The important effect of pleural disease on lung function may be relevant to these groups.

Pulmonary function tests are used not only to *quantify* and *characterize* impairment in asbestos-related disease but to *detect* evidence of disease which is not apparent clinically or radiologically. In this regard, it is noteworthy that 21.3% of those with a normal film had restriction and an additional 7.7% had combined impairment and that of those with only pleural disease, 34.4% had restriction and an additional 8.9% had combined impairment. Further testing, especially of gas exchange (D_L, V_D/V_T) would undoubtedly uncover additional individuals with intrinsic lung disease despite normal lung fields on chest radiograph.

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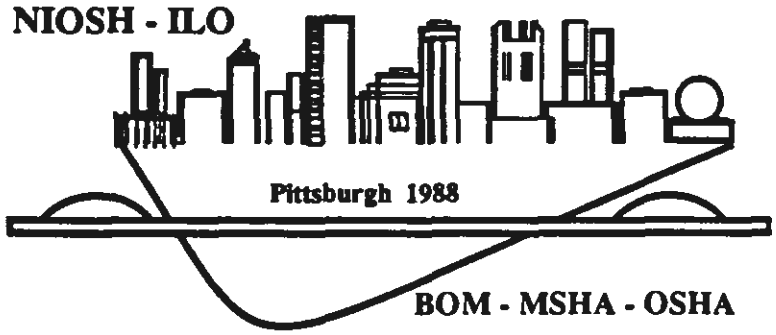

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