PULMONARY FIBROSIS AS A DETERMINANT OF ASBESTOS-INDUCED LUNG CANCER IN A POPULATION OF ASBESTOS CEMENT WORKERS

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INTRODUCTION

It has long been recognized that workers exposed to asbestos are at increased risk of both asbestosis and lung cancer (as well as mesothelioma), and that these effects are dose-related. It is not clear, however, if these two lung diseases are separate, independent consequences of exposure or if asbestos is a lung carcinogen because of its fibrogenicity. Some authors have concluded that, although the evidence is not conclusive, asbestos-induced lung cancer may, in fact, be a complication of asbestosis.[12,2] Others have questioned the plausibility of this view.[5]

Evidence in support of fibrosis being a precursor to asbestos-induced lung cancer includes two studies[9,11] of lung cancer cases among asbestos workers which found high percentages (100% and 90%) to have histologic evidence of fibrosis; one of these studies found 82% to have X-ray evidence.[9] If asbestosis and lung cancer are unrelated processes, then some of the asbestos-related, as well as the smoking-related, cases would be expected to be free of fibrosis.

Elevated lung cancer risk could be the non-specific result of lung fibrosis in general, a view supported by the observation of a considerable lung cancer excess among patients with other fibrotic diseases such as cryptogenic fibrosing alveolitis and pulmonary systemic sclerosis.[13]

Possibly the most important evidence suggesting a relationship between asbestos-induced lung cancer and fibrosis are several studies demonstrating that asbestos workers with lung fibrosis were at increased risk of lung cancer relative to a comparison population.[10,1,6,4,3] The difficulty in making this interpretation, however, is that the asbestotics have generally had greater asbestos exposure than the comparison groups, so that the elevated lung cancer risk may have been due to the exposure; the occurrence of asbestosis may have been a separate, unrelated condition serving primarily to identify a group with substantial asbestos exposure.

The purpose of this study was, therefore, to compare the mortality experience of asbestos workers with and without fibrosis, while accounting for asbestos exposure.

DESCRIPTION OF THE STUDY POPULATION

In 1969, chest X-rays and interviews were obtained on 908 workers in two New Orleans asbestos cement plants.[14] In the current, follow-up study, the 36 women, the 32 men who had retired prior to 1968, and the one man with an unreadable chest film have been excluded, leaving a study population of 839 men. All were employed in 1969 or recently retired.

Exposure information for these two plants has been described elsewhere.[8] Although chrysotile was the primary type of asbestos used in both plants, most of the workers in the current study were also exposed to crocidolite; many of those from Plant 1 were also likely to have had some amosite exposure. Job histories were available and an estimated asbestos profile calculated for each worker.

Mean age for workers from both plants was approximately 45 years, ranging from 21 to 68. Approximately 52% were current cigarette smokers in 1969, 26% ex, and 22% never. The prevalence of cigarette smoking was very similar to the 55% reported for all male U.S. blue-collar workers aged 20–64 in 1970.[7]

X-RAY FINDINGS

Chest films were read in 1972 by three experienced readers using the ILO U/C International Classification for the Pneumoconioses (1971). Median readings were used to classify each film into one of several mutually exclusive X-ray categories (Table I). Films for 79 workers had no large opacities, but had profusion of small opacities of Category 1 or higher (61 Category 1, 18 Category 2 or 3). For 89 workers, the profusion of small opacities was 0/1. A total of 72 workers had no large or small opacities, but had pleural plaques, diffuse pleural thickening or costophrenic angle obliteration (see Table I). Because of the small number, the four workers with large opacities will be excluded from analyses.

Using multiple logistic regression, presence of small opacities (of any profusion level) was found to be related to age (p < .001) and cigarette smoking (either pack-years [p < .001] or ever/never [p = .01]); after accounting for these variables, plant was also a significant factor (a higher prevalence in Plant 2 than in Plant 1, p < .01). After these variables, estimated cumulative asbestos exposure was also significant (p < .001). The same results were found when analyses were restricted to workers with at least 20 years of follow-up since hire.

Table I

Distribution of Workers by X-ray Category (Median Reading)

Category	Number (%)
No Abnormalities	595 (71%)
Unilateral Costophrenic Angle or Diffuse Pleural Thickening	27 (3%)
Bilateral Costophrenic Angle or Diffuse Pleural Thickening	10 (1%)
Pleural Plaque	35 (4%)
Small Opacities 0/1	89 (11%)
Small Opacities ≥1/0	79 (9%)
Large Opacities	4 (0.5%)
	839 (100%)

MORTALITY RESULTS

The mortality experience of this population was first compared to that expected on the basis of Louisiana death rates, using the usual person-years approach. In order to allow for 20 years' latency, each worker began contributing person-years in June, 1970, or 20 years from his hire date, whichever was later.

There were 646 workers with follow-up 20 or more years from hire. Among these, there were 135 deaths, including 26 lung cancers, eight mesotheliomas (another mesothelioma occurred in 1984, after the end of follow-up), and six with asbestosis. All of those with lung cancer were either current or ex-smokers in 1969. Four of these workers had large opacities (including one of the lung cancers), and will not be included in the following analyses. A description of these workers by X-ray category appears in Table II; those with plaques, diffuse pleural thickening and costophrenic angle obliteration have been combined into one group. Differences between those with small opacities and the other workers are as expected based on the X-ray findings reported above. In particular, the 77 with small opacities ≤1/0 were slightly older than the 421 with no abnormalities (median ages of 53 and 47, respectively), with a slightly lower percentage of never-smokers, and higher pack-years of smoking. Concerning exposure indices, median years employed were similar, but there was a lower percentage employed for less than 18 years among those with small opacities. Estimated cumulative asbestos exposure, as well as average concentration of exposure, were also somewhat higher.

The ratios of the observed to expected deaths for selected causes for these X-ray groups appear in Table III. Among those with no abnormalities, there was no excess of all malignancies combined or of respiratory cancer, although there were five mesotheliomas. By contrast, among those with small opacities ≥1/0, there was a significant excess of cancer, all of it from lung cancer (9 observed, 2.1 expected).

Those with no abnormalities were subdivided into two groups: 244 workers employed less than 22 years (the approximate median duration for this category) and 177 employed at least 22 years. There was no significant excess lung cancer in either group: 5 observed versus 4.5 expected, and 5 observed versus 5.3 expected, respectively. The median estimated cumulative asbestos exposure in the second group was 140 mppcf-yrs, making this group comparable in exposure estimates to those with small opacities ≥1/0.

There was a small excess of lung cancer among those with small opacities 0/1 (4 observed, 2.3 expected), but a significant excess of "other" cancers (4 observed, 0.6 expected). Three of these cases (all current or ex-smokers in 1969) listed only cancer as the cause of death, without specification of site; the remaining case, a non-smoker, listed the cause as "generalized abdominal carcinoma," raising the possibility of a mesothelioma.

Since age-specific rates were used to calculate expected numbers, the substantial difference in the lung cancer experience of workers with small opacities ≥1/0 and those without abnormalities could not be due to age differences.

371

Table II

Description of Workers* with Follow-up ≥20 Years, by X-ray Category in 1969

	No Abnormalities	Plaques, etc. No Opacities	Small Opacities 0/1 No Large Opacities	Small Opacities ≥1/0 No Large Opacities
n	421	62	82	77
Age	47	48	51	53
Cigarette Smoking				
Current	48%	45%	52%	47%
Ex	27%	24%	32%	36%
Never	25%	31%	16%	17%
Years Smoked	27	28	29	33
Pack-Years	23.0	26.0	26.3	33.5
Average Packs/Day	.92	.87	.94	1.00
Years Employed	21.6	22.0	22.5	22.6
<18	20%	10%	9%	4%
18–29	76%	85%	82%	91%
≥30	3%	5%	10%	5%
Estimated Average Exposure Concentration (mppcf)	5.0	4.7	5.2	5.8
Estimated Cumulative Exposure (mppcf-yrs)	105	113	123	135
Years of Follow-Up Since Hire	35.6	35.7	36.3	36.0

*medians and percentages

It is unlikely that the small differences in smoking and exposure distributions of these X-ray groups could account for their marked differences in lung cancer mortality. However, in order to explicitly account for these factors, two other methods of analyses were used to analyze the mortality experience of these 642 workers: survival and case-control.

SURVIVAL ANALYSIS

Cox's Proportional Hazards model was used to determine if death due to lung cancer differed between two X-ray groups: those with small opacities ≥1/0 and all other groups combined. The logarithm of pack-years and age were the most significant factors ($p < .01$); after accounting for these factors, only X-ray category was significant (one-tailed $p = .026$). Plant and the various exposure indices were not significant.

To see if the inclusion of never-smokers, none of whom had lung cancer, influenced these results, the analysis was repeated on smokers only; the results were essentially identical.

In these analyses, after accounting for pack-years and age, the estimated relative risk for lung cancer for those with small opacities ≥1/0 compared to the other groups combined was 2.4.

CASE-CONTROL ANALYSIS

Each of the 25 lung cancers occurring 20 or more years after hire (and excluding the case with large opacities) was matched to four controls. For each case, the four controls were selected randomly from the set of all workers who: 1) were approximately the same age as the case (most within one year), 2) were of the same race, 3) were alive when the case died, and 4) were either a current or ex-smoker (since all cases had been smokers).

A description of the cases and controls appears in Table IV. Compared with the controls, the cases had a higher percentage of current smokers (68% versus 58%), had started smoking at an earlier age, on average, and had a higher mean pack-years. Mean durations of employment were similar, but the cases had higher median concentration and cumulative exposure. Concerning X-ray category, the cases had a higher percentage with small opacities ≥1/0 (36% versus 16%), although a slightly lower percentage with 0/1 (16% versus 22%).

Ignoring other factors, the odds ratio for lung cancer from having small opacities ≥1/0 compared with all others combined is 2.95 (84[9]/16[16]).

Table III

Observed and Expected Deaths 20 or More Years After Hire,
During 6/1970–12/1983, by X-ray Category in 1969

	No Abnormalities	Pleural Thickening and/or Plaques No Opacities	Small Opacities 0/1	Small Opacities ≧1/0
All Malignancies	22/24.8 88.9	5/3.9 126.8	12/5.7 210.2*	12/5.4 221.5†
Respiratory Cancer	10/ 9.8 102.2	2/1.5 129.7	4/2.3 176.7	9/2.1 424.3†
Other Cancer	** 2/ 2.7 73.1	** 1/0.4 232.0	†† 4/0.6 653.6†	0/0.6 0
Mesothelioma	5	1	2	0

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*p < .02 based on Poisson distribution
†p < .01 based on Poisson distribution
**Includes one liver cancer.
††Three with site unspecified; one "generalized abdominal carcinoma".
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Multiple logistic regression analysis for a matched design (using the PHLGM procedure in SAS) was used to compare the cases with the controls. The most important factor was pack-years of smoking (p = .01). After pack-years, average concentration of exposure was marginally significant (one-tailed p = .051), as was cumulative exposure (one-tailed p = .062). After accounting for pack-years, concentration, cumulative exposure and cigarette smoking status, X-ray category (small opacities ≥1/0 versus all others combined) was statistically significant (one-tailed p = .024).

In the full model, the estimated odds ratio for lung cancer risk for those with small opacities ≥1/0 was 3.0. If the odds ratio is considered to be an approximate estimate of relative risk, then this estimate is somewhat higher than the estimate of 2.4 obtained in the survival analysis.

DISCUSSION

As would be expected, this population of asbestos cement workers, most of whom had substantial, long-term asbestos exposure, has experienced the major health risks known to be related to asbestos exposure: asbestosis, excess lung cancer and mesothelioma.

The excess lung cancer risk, however, was found to be restricted to those workers with X-ray evidence of asbestosis, as determined by a panel of three independent readers. No excess lung cancer risk was observed among those with no evidence of asbestosis, not even among the sub-group employed at least 22 years, for whom exposure indices were comparable to those with small opacities ≥1/0 on X-ray.

We conclude that the mortality experience of this population supports the view that asbestos is a lung carcinogen because of its fibrogenicity; lung cancers occurring among those without X-ray evidence of asbestosis can be attributed to smoking rather than asbestos exposure. If these findings are confirmed in studies of other asbestos-exposed populations, then workplace exposure levels which are effective in preventing asbestosis would be expected to also prevent detectable increases in lung cancer risk in the future.

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Table IV

Description of the 25 Lung Cancer Cases* Occurring ≥20 Years After Hire and the 100 Matched Controls

	Controls	Cases
Mean Age	53.6	53.7
Cigarette Smoking		
Current	58 (58%)	17 (68%)
Ex	42 (42%)	8 (32%)
Mean Age Started	18.7	16.6
Mean Pack-Years	29.6	40.0
Mean Years Employed	23.1	22.5
Estimated Asbestos Exposure (medians)		
Concentration (mppcf)	4.8	5.8
Cumulative (mppcf-yrs)	115	145
1969 X-Ray Category		
No Abnormalities	55 (55%)	10 (40%)
Pleural Thickening, +/- Plaques	7 (7%)	2 (8%)
Small Opacities 0/1	22 (22%)	4 (16%)
Small Opacities ≥1/0	16 (16%)	9 (36%)

*excluding the case with large opacities on 1969 x-ray

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SMALL AIRWAY IMPAIRMENT FINDINGS AT THE SCREENING OF 639 ASBESTOS WORKERS WITH EXPOSURE HISTORY OF 20 YEARS

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Small airway impairment was observed and first reported by Leuallen and Fowler[3] in 1955 as a sensitive parameter in early detection of expiratory airflow obstruction.

Early pathophysiological findings by Wright and Colleagues[8] stated that inflammation in both respiratory and membranous bronchioles, goblet cells metaplasia of the epithelium in membranous bronchioles are the pathologic features resulting in impairment of FEF_{25-75} volumes.

Not many in literature but few authors investigations postulate that the Small Airway Disease (SAD) represents significant airway obstruction in peripheral bronchioles and such may represent an early manifestations of chronic lung disease when it may be amenable to treatment.

Peripheral airway are the quiet zone and the early insult to this area by offending factors such as mixed solvents, chemical dust, gases, fumes, vapors, moldy hay, moldy air particles, polycyclic aromatic hydrocarbon, man-made fibers were documented.

This concept supported by Petty[7] and coworkers' investigations in small airway impairment and also Myint and Myint[4] postulated the early findings of FEF_{25-75} impairment with mixed chemical exposures.

MATERIALS AND METHODS

This paper intends to discuss the findings of small airway impairment in asbestos workers with different trades. This paper also discusses a crucial point that these workers are exposed to NOT ONLY ASBESTOS but ASBESTOS contaminated with ENVIRONMENT CHEMICALS, COMBUSTIBLE PRODUCTS and many other offending factors as STONE DUST, CEMENT DUST, SO_2 GAS, FIBREGLASS DUST, CIGARETTE SMOKE, GASES AND FUMES.

During the period of 1986–87 asbestos workers with exposure history to asbestos more than 20 years were included in this study. The total of 639 asbestos workers with different trade unions were 200 sheet metal workers, 110 pipefitters, 70 insulators, 120 boiler makers, 60 bricklayers, 70 iron workers, and 20 others were electricians, plasterers, and millwright exposed to asbestos fibers. Among them were

cigarette smokers, cigarette non-smokers, and ex-cigarette smokers.

Asbestos screening physicals included vital signs, chest X-ray PA view using International Labour Organization (ILO) Standard criteria technique and interpretation, Pulmonary Function Test (PFT) performed on Jones Pulmonar II in standing position with good effort and cooperation. The Standard Criteria of American Thoracic Society 1979 was used. Results obtained were FVC, FEV_1, FEF_{25-75} and FEV_1-FVC ratios. Predicted values of Knudson were preferred. Due considerations were given to ethnic factor calculation. Seventy-five percent of the predicted value readings was taken as the normal range. The values were corrected to BTPS. The best of at least three spirograms was chosen. Testing was performed by trained and qualified technicians. And the last test included Hemocult Stool Test. The results of these findings were dictated and reported to their attending physician. Many of their union officials distributed education materials on asbestosis and addresses of cigarette smoking cessation clinics were given.

RESULTS

Table I shows number of asbestos workers in different trades and number of cigarette smokers, non-smokers and ex-smokers in each trade. The total numbers of 148 non-cigarette smokers, 336 cigarette smokers and 155 of ex-cigarette smokers were analyzed.

Table II indicates the prevalence of Small Airway Disease (SAD) among asbestos workers who participated in this study. It is interesting to note that those who do not smoke cigarettes; of 154 workers of which 37.01% had Small Airway Disease (SAD). The reading of FVC, FEV_1 and FEV_1-FVC ratios were within normal range in this group of non-smokers. Again cigarette smokers 314 had 50.63% of SAD, whereas ex-smokers of cigarettes 151 shows 40.39% SAD.

Table III information about the incident of asbestosis in chest X-ray profusion between 1/1-3/3 according to ILO Classification of Film 1980. Cigarette smokers have higher incidence of parenchymal scarring as had been previously documented by many researchers on synergistic action of cigarette smoking and asbestos exposure.

Table I

Screening of Asbestos Workers Belonging to Different Unions

UNION	NON SMOKERS CIGARETTES	SMOKERS CIGARETTES	EXSMOKERS CIGARETTES
200 SHEET METAL	40	130	30
50 INSULATORS	16	24	10
110 PIPE FITTERS	23	51	36
120 BOILER MAKERS	27	67	26
60 BRICK LAYERS	19	21	25
70 IRON WORKERS	19	31	24
20 OTHERS ELECTRICIAN, PLASTERER, MILLWRIGHT	4	12	4
TOTAL	148	336	155

Table II

Prevalence of Small Airway Diseases (SAD) Among Asbestos Workers Exposure History Over 20 Years

NON SMOKERS OF CIGARETTES 154	37.01%
CIGARETTE SMOKERS 314	50.63%
EXSMOKERS OF CIGARETTES 151	40.39%

INSULATORS, SHEET METAL WORKERS, PIPE FITTERS, BOILER MAKERS, BRICK LAYERS, IRON WORKERS

Table III

Incident of Asbestosis Classified as 1/1 to 3/3 Reference to ILO Classification Film 1980

CIGARETTE SMOKERS	34.71%
NON SMOKERS OF CIGARETTES	20%
EXSMOKERS OF CIGARETTES	23%

Figure 1 illustrates clearly that due to synergistic action, the less smoking history of cigarettes, the higher the percentage of normal chest X-ray findings among 200 sheet metal workers union members.

Slides I, II, and III show with asbestos suit how they are contaminated with combustion products, grease, and chemicals in removal jobs. One can imagine the beginning of their trade before the stringent regulations the inhalation of various toxic offending factors as mentioned above in addition to notorious asbestos victim.

DISCUSSIONS

Many questions raised in this study were: (1) is this abnormal small airway performance related to asbestos exposure alone or mixed inhalation of offending agents contaminated to asbestos fibers, and in addition to environment where they work exist many factors which can also insult small airway volumes.

The small airway has been shown to be a more reproducible and sensitive measure and it relates closely to the closing volume at which the small bronchioles at the bases of the lungs closed during forced expiration.

Another question raised: (2) is small airway impairment in asbestos exposed populations possibly early sign to observe and prevent chronic lung diseases?

The results of these findings clearly demonstrates that non-cigarette smokers have considerable prevalence of abnormal FEF_{25-75} performance.

Therefore, the insult done to small airways is coming from either asbestos or asbestos fiber coated with other by-product chemicals. One cannot completely rule out that boiler makers were heavily exposed to other irritants such as SO_2, gases, stone dusts, cement dusts. Similarly sheet metal workers are exposed to welding fumes, fibreglass dust in addition to asbestos.

As this study indicates a signal parameter involved. It requires further confirmation before it is assumed that SAD is an early indicator of PFT impairment in asbestos workers, therefore, future epidemiologic studies should be taken with a larger population.

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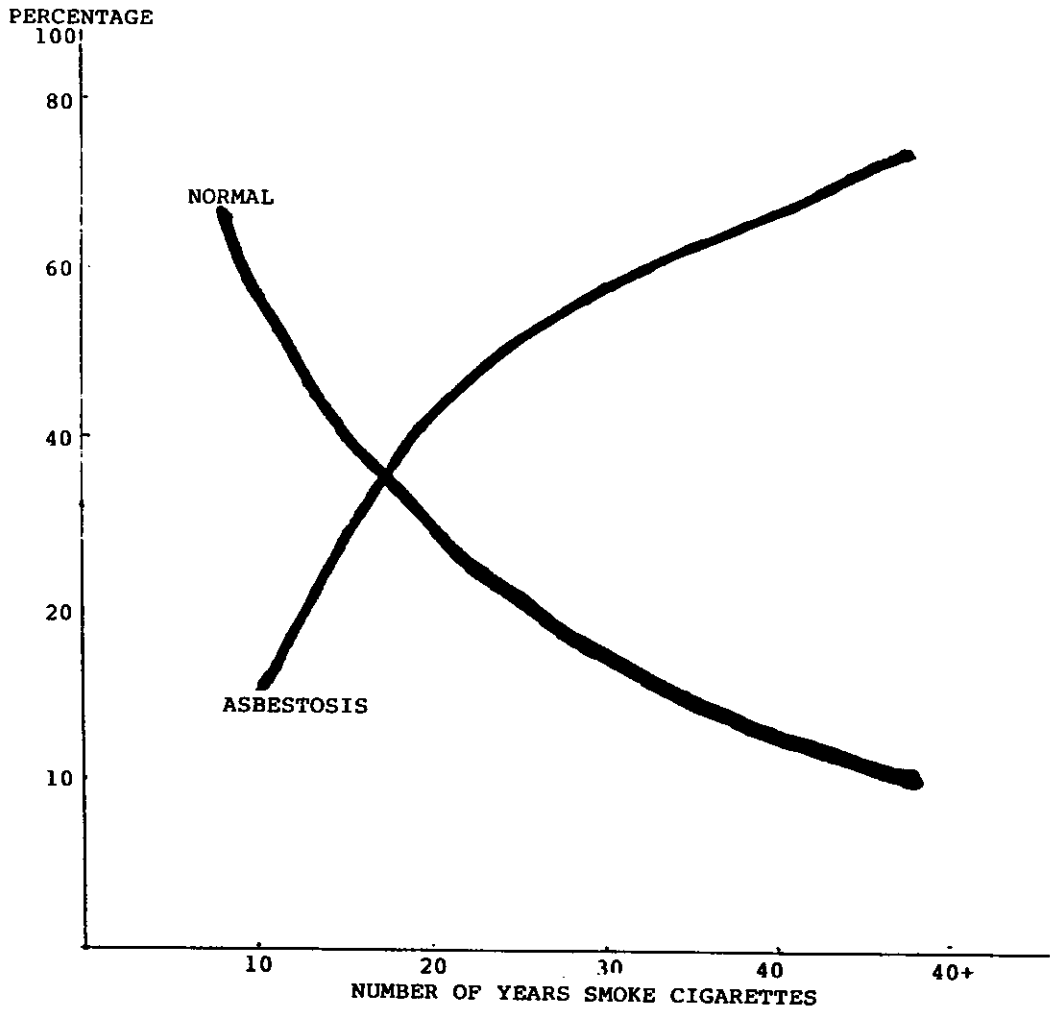
Figure 1. Sheet Metal Workers Union Central Florida, asbestos screening February/March 1987.

Table IV
Prevalent of Small Airway Diseases in Different Asbestos Trades

UNION	NON SMOKERS CIGARETTES SAD	SMOKERS CIGARETTES SAD	EXSMOKERS CIGARETTES SAD
200 SHEET METAL			
50 INSULATORS	16 – 8 – 50%	24 – 9 = 37.50%	10 – 4 = 40%
110 PIPE FITTERS	23 – 9 = 39%	51 – 22 = 43.13%	36 – 17 = 47.22%
120 BOILER MAKERS	27 – 11 = 40.7%	67 – 34 = 50.74%	26 – 8 = 30.76%
60 BRICK LAYERS	19 – 5 = 26.3%	21 – 9 = 42.85%	25 – 12 = 48%
70 IRON WORKERS	19 – = 26.3%	31 – 13 = 41.93%	24 – 7 = 29%
20 OTHERS, ELECTRICIAN, PLASTERER, MILLWRIGHT			
TOTAL	148	336	155

LUNG FUNCTION AND LUNG SYMPTOMS IN RAILROAD EMPLOYEES WITH ASBESTOS EXPOSURE—A 5 YEAR FOLLOW-UP STUDY

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ABSTRACT

175 male employees of railroad service and repair shops were examined in 1981 and 1986 by questionnaire/interview (occup. history, smoking, lung symptoms) and measurement of lung function by Vitalograph. (See other abstract for result of X-ray study).

Asbestos exposure of low to moderate intensity has occurred mainly between 1940 and 1960. On the basis of occupational history a cumulative index of asbestos exposure has been established for each study person. The whole group was divided into 4 exposure groups.

Results: Mean age was 65.1 years. FVC and FEV_1 fell significantly and were negatively related to asbestos exposure. The annual fall for FVC AND FEV_1 was 90 and 86 ml respectively. Smokers had lower lung function values than non-smokers, but the 5-year decrease was not different between the subgroups. Prevalence of dyspnoea (grade 2 and more) was 64% in the highly exposed group against 35% and below in the other exposure groups. Neither cough nor cough and sputum were related to asbestos exposure.

Conclusion: The results support the hypothesis, that asbestos related lung disease might progress even many years after mild to moderate exposure has taken place. The result should however be taken with caution because of the short observation period and the relatively advanced age of the examined men.

No Paper provided.

CHEST RADIOGRAPHS IN RAILROAD EMPLOYEES WITH ASBESTOS EXPOSURE —A 5 YEAR FOLLOW-UP USING ILO 1980 CLASSIFICATION

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INTRODUCTION

Radiological signs of pleural asbestosis indicate previous asbestos exposure. The presence of only pleural changes without fibrosis is generally considered to occur many years after low level asbestos exposure has taken place. A dose-effect relationship for purely pleural asbestosis has not yet been established.

While it is known that pleural changes progress over the years[3] the risk for a higher incidence of parenchymal changes in cases with pleural asbestos is still disputed.

Some authors have suggested that lung fibrosis might develop in patients with pleural asbestosis.[2,6,7] In order to study more closely the above mentioned questions a cohort of railway employees with a previously established history of exposure to asbestos has been examined with a 5 year interval (1981 and 1986).

MATERIAL AND METHODS

In 1978 263 men were selected out of 1192 employees at the repair and maintenance workshops of the Danish Railroads. Among the selected were 87 men who previously had been reported for pleural asbestosis and 176 controls. 209 accepted to participate in the study of 1981, in 1986 there were 175 (84%). Thirteen had died and 21 did not wish to participate again. This report will concentrate on the results of the examination of 175 men in 1981 and 1986.

Exposure to asbestos dust has mostly occurred between 1945 and 1965. An individual index of asbestos exposure had been established in 1981 on the basis of work history concerning 28 different working procedures at the workshops. The exposure index was updated for the 5 year period.

Chest radiographs were made posteroanterior and lateral view) by the same technique in 1981 and 1986. The quality of the films was controlled immediately. If necessary, the radiographic examination was repeated.

Two experienced readers read pairs of the blinded radiographs for each participant. The films were presented on the viewcase at random order. The ILO 1980 Classification of radiographs of the pneumoconioses was used for recording following standard instructions and using standard radiographs for comparison.[5] For each person two columns on the classification sheet were used. Data from the classification sheet were first analyzed for each reader separately. Then the two readers results were compared with each other for each feature on the classification. Only when both readers agreed on bilateral changes for a particular feature it was considered to be a positive finding; otherwise it was considered negative. Small opacities were pathological (fibrosis) with profusion 1/1 or greater in at least both lower zones. For pleural calcifications extent was registered for each site separately.

The combined results were analyzed for prevalence in 1981 and 1986, for 5-year incidence and finally for a possible relation to asbestos exposure index.

RESULTS

Table I shows asbestos exposure index and the distribution into 4 exposure groups in 1981 and 1986. Index 200 corresponds roughly to one year (200 days) of daily asbestos exposure. Only a few participants had been exposed to asbestos after 1981. Groups I and II have had low level, group III and IV high level exposure.

The time period since first exposure was more than 40 years for 32% and more than 30 years for 47% of all men in the cohort. Mean age was 65.1; 72% of the men were between 60 and 70 years old.

Quality

All radiographs were readable. Most were of good, a few of acceptable quality. The pleura was not clearly visible in 2 cases in 1981 and in 1986.

Small Opacities

Table II shows profusion divided into 3 categories for 1981 and 1986, profusion 1/1 to 2/1 belonging to the same category. Profusion of grade 1/1 and higher was found in 7 cases in 1981. Two of these were in 1986 found in category below 1/1 and one of these in a higher category. Sixteen new cases of category 2 were diagnosed in 1986 which means a total of 21 cases of fibrosis in 1986 against 7 in 1981. Table III shows the prevalence of profusion category 2 and 3 in relation to exposure groups. A correlation between profusion of small opacities and increasing dose can be seen. Table IV shows the prevalence of tick (v) for small opacities in the 3 lung zones in 1981 and 1986 distributed among the exposure groups. An increase for middle and lower zones is

Table I
Asbestos Exposure in Railroad Employees. Index and Distribution into 4 Exposure Groups in 1981 and 1986

Exposure group	Asbestos Index	1986 Number of persons	%	1981 Number of persons	%
I	0 – 15	19	10.9	23	11.0
II	16 – 559	62	35.4	81	38.8
III	560 – 3150	68	38.9	74	35.4
IV	3151 – 22000	26	14.8	31	14.8
		175	100.0	209	100.0

Table II
Profusion of Small Opacities in Chest Radiographs of Railroad Employees in 1981 and 1986

		1986 0/– – 1/0	1/1 – 2/1	2/2 – 3/+	N
1981	0/– – 1/0	152	16	0	168
	1/1 – 2/1	2	4	1	7
	2/2 – 3/+	0	0	0	0
	N	154	20	1	175

shown in all exposure groups. Both readers recorded almost exclusively small opacities of irregular type and small size (type s,t). The most frequent letter combination was "s-t" which was registered by both readers 11 times in 1981 and 21 times in 1986.

No large opacities were registered.

Pleural Thickening

The number of positive findings of pleural thickening is presented for 1981 and 1986 in Table V. Bilateral pleural thickening of the diaphragm and of the costophrenic angle was recorded in 18 and 11 cases in 1981 and in 22 and 14 cases in 1986. Special attention was placed on diffuse pleural thickening and pleural plaque, as shown on Table VI. An increase of prevalence for both pleural changes over the 5 year period and a positive relation to exposure, except for exposure group IV was observed. The dose-effect correlation was significant. The recordings of width and extent for diffuse pleural thickening showed an increase between 1981 and 1986 for all symbols a,b,c and 1,2 and 3 respectively. These results were not analyzed more closely.

Table III
Profusion of Small Opacities 1/1 and Higher on Chest Radiographs of Railroad Employees;
Prevalence in 1981 and 1986 in 4 Exposure Groups (%);
Actual Numbers of Participants in Each Exposure Group

EXPOSURE GROUPS

	I	II	III	IV
1981	0	3	3	12
1986	0	10	12	27
N	19	62	68	26

Table IV
Profusion of Small Opacities in Three Zones on Chest Radiographs of Railroad Employees;
Prevalence (%) in 1981 and 1986 Among Exposure Groups

EXPOSURE GROUPS

	I		II		III		IV	
	81	86	81	86	81	86	81	86
UPPER	0	0	2	2	0	7	8	8
MIDDLE	0	16	5	16	4	20	24	28
LOWER	0	21	8	23	7	28	20	36

Table V
Pleural Thickening on Chest Radiographs of Railroad Employees in 1981 and 1986;
Number of Cases

	1981	1986
Pleural thickening diffuse (A)	34	38
Pleural thickening plaque (B)	7	8
Pleural thickening (A) + (B)	14	19
Total pleural thickening	55	65

Table VI
Pleural Thickening on Chest Radiographs of Railroad Employees;
Prevalence (%) in 1981 and 1986 Among 4 Exposure Groups

EXPOSURE GROUPS

		N	I %	II %	III %	IV %
Pleural thickening	1981	84	11	36	54	89 ***
	1986	102	16	47	65	85 ***
Pleural th.diffuse	1981	48	0	16	35	54 ***
	1986	57	0	24	43	50 ***
Pleural plaque	1981	21	5	10	9	31 *
	1986	27	5	11	13	39 **
N Total		175	19	62	68	26

$$\text{Chi}^2 \text{ for trend:} \quad \begin{array}{l} *** \ p = 0.001 \\ ** \ p = 0.003 \\ * \ p = 0.020 \end{array}$$

As a rule when pleural thickening was recorded on the lateral chest wall it was always situated in the middle and lower zones.

Pleural Calcifications

The total number of pleural calcifications on the diaphragm and the chest wall recorded in 1981 and 1986 and distributed among exposure groups is shown on Table VII. An increase over the 5-year period as well as a positive relation to exposure can be seen.

Symbols

Only few symbols were recorded, and have not yet been analyzed.

DISCUSSION

For this radiological study severe diagnostic criteria for positive radiological findings were applied. These were in total agreement between readers on individual bilateral changes and a profusion of small opacities of at least 1/1 for the

Table VII

Pleural Calcification on Chest Radiographs of Railroad Employees;
Prevalence (%) in 1981 and 1986;
Distribution Among Exposure Groups

EXPOSURE GROUPS

	N	I	II	III	IV
1981	22	0	8	15	27
1986	28	5	8	21	31

diagnosis of fibrosis. Pleural changes and fibrosis were recorded in 58 and 12% respectively of the cohort. Pleural calcifications were found in 16%.

These figures partly confirm the results on radiological changes recorded in railroad employees[6,7] and in other trades with comparable exposure to asbestos.[4,9] In several studies though a higher prevalence of fibrosis was recorded in high exposure groups. The rather high prevalence for pleural changes can be due to the initial selection of cases when the cohort was established.

In this cohort with mainly pleural changes, more than 30 to 40 years after first exposure, a 5-year increase of fibrosis from 7 to 21 cases is surprising. The prevalence and 5 year incidence of fibrosis is clearly dose related (see Table III). This indicates a long latency for the appearance of asbestos related lung fibrosis. Others have suggested the presence of a mild form of lung fibrosis in older patients with pleural asbestosis,[1,8] while it seems to occur extremely seldom as a form of premature aging process according to others.[3]

Lung fibrosis was mostly combined with pleural thickening. But in a few cases it occurred isolated (one case in 1981 and 3 in 1986).

In agreement with other reports some progression of the pleural changes was observed over the 5-year period as well for the number as for the extent and width of pleural thickening and of pleural calcification.[3]

The radiological changes on the lateral chest wall seem to be more suitable for recording and follow-up than the changes on the diaphragm and costophrenic angles.

The dose effect correlation for pleural thickening is noteworthy. The results indicate that progression of pleural changes is most pronounced in the groups with high exposure. There is no explanation for this unusual result which is in contradiction to the generally accepted view that radiological changes in pleural asbestosis are dose independent but related to age and time since first exposure. Age difference between the exposure groups was minimal. Furthermore there was no association between age and exposure index.

The results of this study are only applicable for this selected cohort which—besides an overrepresentation of cases with pleural changes—is characterized by heterogeneity in degree and duration of exposure and by heterogeneity in attrition.[10] Taking these bias into consideration one can expect that the results probably overestimate the true prevalence/incidence of the recorded radiological changes.

CONCLUSION

In a heterogenous cohort of elder railway employees with more than 30 years after first exposure to asbestos dust pleural asbestosis developed in a way similar to what is described by others. Surprisingly the progression of these pleural changes is dose related.

The incidence of fibrosis has increased in this cohort with mainly pleural asbestosis.

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RADIOGRAPHIC PROGRESSION OF ASBESTOSIS WITH AND WITHOUT CONTINUED EXPOSURE

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Early in this century asbestosis in the textile industry was recognized as a rapidly progressive disease, with death often in less than 7 years. By 1933, Merewether,[13] a most astute observer, concluded ". . . since unaltered asbestos fibers also can be found in the lungs years after last exposure, it is evident that asbestos dust trapped in the lungs remains and continues to exert its fibrosis-producing power for at least many years." He was also the first to recognize a latent period: ". . . a certain minimum fibrosis-producing amount, as it were, of asbestos dust must be trapped in the lungs . . . and also a certain "maturation" period must elapse before that amount of fibrosis is developed." Finally, he predicted that ". . . preventive measures which have applied for 17 years . . . have lengthened the period before fibrosis becomes fully developed." Over the next 30 years his observations were confirmed such that by 1964 asbestos-related manifestations generally were not seen less than 20 years after initial exposure.

Asbestosis has been referred to as a relentlessly progressive disease, even after exposure has ceased, a dictum often restated in textbooks, by medical section reports, by commissions and in reviews. Indeed, Gilson,[7] summarizing the 1964 New York Academy Meeting, proposed research to determine whether there is a detectable stage of asbestosis at which progression ceases after removal from dust. Later still, in 1977, Wagner[23] concluded that ". . . at present there is no published evidence that removal from exposure will prevent progression of asbestosis." Recently some studies have suggested that progression is not inevitable.[2,8,16,17,19,22]

During the past 12 to 22 years we have studied prospectively at yearly intervals groups of employees in six plants, to observe the earliest manifestations of pulmonary fibrosis, to study the physiologic effects of pleural disease, and to address the question of progression. When we presented preliminary results two years ago it was noted that the group no longer exposed was older, and had first exposure earlier than the group with continued exposure.[6] Also, questions were raised concerning smoking histories, the prognostic implications of initially low profusion and the incidence of "attacks" as opposed to true profusion. We now present updated

results, groups matched for age, years since first exposure, and for smoking habits, and details concerning low profusion and "attacks."

METHOD

Survey Studies

Annual examination included a medical and detailed occupational history, a physician-administered questionnaire, chest physical examination, forced vital capacity and flow derivatives, single breath diffusing capacity and anteroposterior and lateral chest roentgenograms sometimes supplemented by oblique views.

Radiographic Interpretation

Films were interpreted by two "B" readers only one of whom was aware of the timing and nature of the exposure. Generally, interobserver agreement was good.[11] Recordings since 1980 were made according to the most recent ILO scheme[9] and earlier readings were translated by comparison of standard films.[14,21] Two interpretations were available as described for coalworkers pneumoconiosis.[1,10,15] Prospectively, films were categorized at each visit without recourse to other films, to be referred to as "apart reading." For this project, the entire series of films was displayed in order of date, and profusion recorded once more, this to be called the "side-by-side" reading.

Employment and Exposure

These are summarized in Table I. The shipyards had large employment, occupations generally did not change, and we followed only selected groups such as pipecoverers, shipfitters, welders, guards and painter-sweepers. At the paper plants and asbestos products plant we followed all employees most of whom eventually participated in nearly all of the available tasks. Paper A manufactured mostly filter paper for gas masks, and automotive products; and from 1952 to 1956 they made a non-paper web on a carding machine for cigarette filters.[5] Paper B made mostly gaskets, and Paper C manufactured electrical insulation paper. The asbestos plant specialized in insulation board.

Extent and Type of Exposure

Detailed exposure data were available only for Ship A where

Table I

Survey Plants and Type and Duration of Exposure

Plant		Known Asbestos Exposure Type	Years & Amount		Survey Years First	Total
Ship A:	New Naval Ship	Mixed[X]	45-72	< 5 mppft;[#]	1966	19[*]
Ship B:	Submarine	Mixed[X]	To 72	Decreasing;[#]	1976	10[*]
Paper A:	Filter, Gaskets	Chrocid.	To 72	Severe, None Since	1971	16
Paper B:	Filter, Gaskets	Chrys.	61 to	Present: Slight;[#]	1973	16
Paper C:	Insul. Paper	Chrys.	To 72	Moderate;[#]	1976	12
Plant:	Insul. Board	Mixed[X]	To 72	5 mppft,[#]	1970	18

[#] Since 1972 <2 f/cc   [*] Selected Groups Not Seen Annually   [X] With Amosite

pipecovering exposures had been kept below 5 mppft since 1945.[14] At other plants data available since 1972 indicated exposures below 2 f/cc. Fiber mix at the shipyards and asbestos plant included a good deal of amosite because of U.S. Navy specifications.[4] At Paper A, only crocidolite imported from South Africa and Bolivia was used, and asbestos use was discontinued in 1972.[5] At Paper B and C only Canadian chrysotile was used. Because retired persons and those now employed elsewhere were encouraged to return for examination we were able to follow some persons who were no longer exposed.

Case Selection and Definition

For this study analysis was limited to parenchymal disease. We reviewed "apart readings" of all 1764 persons, and for study of progression we selected only those 522 who had been followed for six or more years (Table II). The others were lost to follow-up, had died, or had been hired more recently. Roentgenograms for this smaller group were then displayed for "side-by-side" readings. "Progression" or "regression" was recorded when there was a 2-step or greater change of the 11-step ILO scale. (We did not use the lowest reading of 0/−.)

RESULTS

Prevalence of Asbestosis

This study confirmed our impression that asbestosis is a disappearing disease. Figure 1 shows that among persons first exposed before 1950, 47.6% had developed fibrosis. This decreased to 18.0% for 1950-1959, and among those first exposed after 1959 only 2.0% had developed asbestosis. Furthermore, among those first exposed during the past 38 years only 1 developed advanced disease. However, even in the group with the shortest follow-up, the earliest exposure was 28 years ago. Asbestosis varied also for different employments. At one extreme, among those first employed at Ship A before 1950, the prevalence to date has been 65%. At the other end of the spectrum, at Paper B and C, with

work largely with encapsulated chrysotile, only 6% and 8% respectively had asbestosis and this was always of minimal degree.

Progression and Regression

The 522 persons followed for 6 or more years had a mean age of 52 ± 11 years and were followed for 11 ± 3 years (Table II). Concerning progression, once more the type of employment was important: Worsening of 2 or more steps varied from 3.9% for Paper C to 39.0% for Ship A. Interestingly, among those with no further exposure progression was much more frequent (36%) than among those with continued exposure (9%).

It was suggested that progression was more common among those no longer exposed was because they were 9 years older, had been exposed for 9 more years and were followed 4 years longer (Table II). Therefore we displayed the mean years since first exposure against the percent of cases progressing for each of the 8 groups (Figure 2). There was a striking correlation (r=0.76). To exclude this variable, we selected two subgroups matched for age and years since first exposure, with and without further exposure. This matching of 74 pairs greatly reduced the difference with respect to progression, now 30% and 23% respectively (Table III). The remaining difference could be explained from data shown in Table II: The 3 groups that were no longer exposed historically all had had occupations with known heavy exposure, largely as pipecoverers and with crocidolite carding. By contrast, most of those with continued exposure had worked largely with encapsulated chrysotile.

Because smoking may affect progression we matched 60 pairs of smokers and nonsmokers for age and years since first exposure. They also matched exactly for years exposed and for years followed up (Table III). Among the smokers there was a significantly higher proportion who progressed.

A distinction has been made between a situation referred to as "onset," "first appearance of an abnormality," or "at-

Table II

Age, Exposure and X-ray Changes of Group Followed for >6 Years

Plant	Expos.	Total #	6 Plus Yrs.	Last Mean Age	Years First Expos.	Years Follow Up	Radiographic* No Change	Pro-gress	Re-gress
Ship A:	Discont	41	41	58±12	28±10	14±6	24	16 (39%)	1
	Low	148	107	53± 9	24± 8	11±5	80	21 (20%)	6
Ship B:	Low	665	65	51±11	22± 9	7±1	56	1 (2%)	8
Paper A:	Discont	260	66	56± 9	30± 7	14±3	39	24 (36%)	3
Paper B:	Low	306	116	51±13	21±13	11±3	103	5 (4%)	8
Paper C:	Low	163	51	49±12	20± 9	8±1	49	2 (4%)	0
Plant:	Discont	28	22	68± 7	39± 9	11±3	15	7 (32%)	0
	Low	153	54	45±11	16± 8	11±3	47	5 (9%)	2
Mean	Discont	329	129	59± 9	31± 9	14±4	78 (61%)	47 (36%)	4 (3%)
Mean	Low	1,435	393	50±11	22±10	10±3	335 (85%)	34 (9%)	24 (6%)
Total		1,764	522	52±11	24±10	11±3	413 (79%)	81 (16%)	28 (5%)

* "Separate Reading"

Table III

Subgroups Matched for Exposure, Age and Smoking

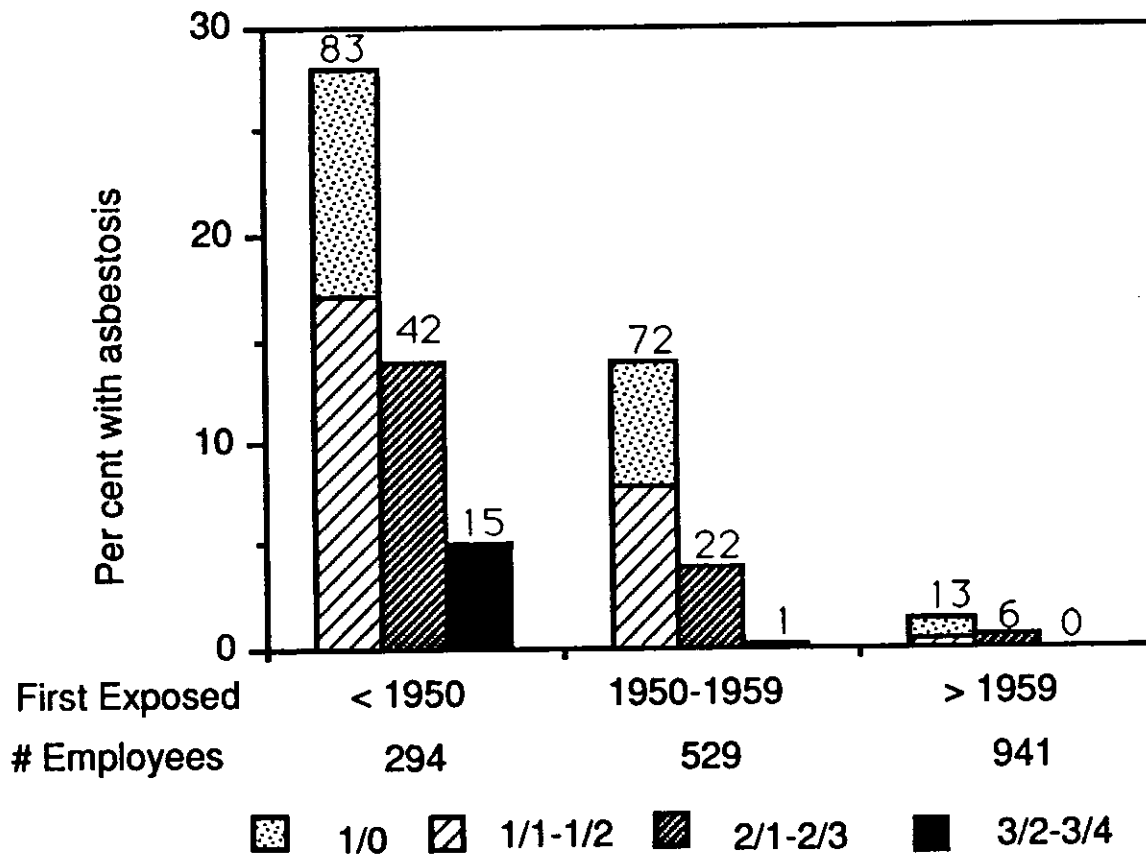| Exposure	#	Last Mean Age	Yrs. First Expos	Mean Yrs. Expos	Yrs. Follow Up	Radiographic Unchang #	%	Progres #	%
Matched for age and years since initial exposure									
Discont.	74	57±10	29± 9	19±10	12± 5	52(70)		22(30)	
Low Level	74	57± 9	29± 9	29± 9	11± 5	57(77)		17(23)	
Matched for smoking , age and years since initial exposure									
Smokers	60	53±12	25±11	22±11	9± 4	49(82)		11(18)	
Nonsmok.	60	52±12	25±11	23±11	9± 3	53(88)		7(12)	

Figure 1. Prevalence and profusion of irregular small opacities at last visit of 1,764 employees seen during industrial surveys. There were 254 (14.4%) with presumed asbestosis. The prevalence decreased from 47.6% for those first exposed before 1950 to 18.0% for 1950–1959, and was only 2.0% for those first exposed during the past 28 years. Exclusion of 1/0 readings would have reduced these three figures to 36.4%, 10.2% and 0.6% respectively.

tack" where the previous film was normal, as opposed to "true progression," that is, a worsening compared to a previous less-than-normal film.[10,15] This is analyzed in Table IV. *Numerically*, "attack" was more frequent (25 vs. 12 for continued exposure, and 31 vs. 17 for discontinued exposure), largely because initially asbestosis was uncommon. However for *percentages* the reverse was true: About one-half of the patients with initially moderate disease progressed.

We defined progression as a 2-step or greater change in the 11-step ILO scale in accord with others.[2] In Table IV, we also compared the frequency of 2-step progression to 3 or more step changes: The two were about equally common, 19 vs. 18 cases for low exposure, and 22 vs. 26 cases for discontinued exposure.

The prognostic significance of different low level readings has been questioned. Table V shows no impressive difference: Among those with continued exposure progression was 15% for 0/1 and 16% for 1/0; and for discontinued exposure these figures were 44% for 0/1 and 30% for 1/0. However, an initial reading of definite minimal asbestosis,

that is 1/1, had a somewhat worse prognosis in relation to progression particularly among persons still working.

The possibility of "regression" has been discussed in relation to coalworkers pneumoconiosis.[1,10,15] In other studies of asbestos-exposed persons "regression" was seen sometimes when only 2 films were available for comparison[2] but was not seen when there were serial films.[3] In our series "regression" was recorded in Table II for 28 persons (5%), but our Table II was derived from "apart readings." Subsequently we displayed all annual films for "side-by-side" reading and then there usually was an obvious explanation for an earlier higher reading (Table VI). As a result, for all subsequent analyses we incorporated this group into the "no change" category.

DISCUSSION

The effect of continued low exposure in a shipyard was detailed by Rossiter et al.[16] Their results were comparable to our shipyard experience: During 9 years 25% of laggers and 16% of asbestos sprayers progressed but there was little change among other employees. Other reports of progression all concerned retired miners: Among often briefly ex-

Table IV
"Attack" versus True Progression
(522 Cases Observed ≥ 6 Years)

Continued Low Level Exposure (393)

Initial ILO	Total Number		Progression 2 Step # (%)	≥ 3 Step # (%)	Total # (%)
0/0-0/1	328	"Attack"	13 (4.0)	12 (3.6)	25 (7.6)
1/0-1/2	56	Progress.	4 (7.1)	5 (8.9)	9 (16.0)
2/1-2/3	9	Progress.	2 (22.2)	1 (1.1)	3 (33.3)
3/2-3/4	0	Progress.	0	-	0
Total	393		19 (4.8)	18 (4.6)	37 (9.4)

Discontinued Exposure (129)

Initial ILO	Total Number		Progression 2 Step # (%)	≥ 3 Step # (%)	Total # (%)
0/0-0/1	86	"Attack"	15 (17.4)	16 (18.6)	31 (36.0)
1/0-1/2	30	Progress.	2 (6.6)	8 (26.7)	10 (33.3)
2/1-2/3	12	Progress.	5 (41.7)	2 (16.7)	7 (58.4)
3/2-3/4	1	Progress.	0	-	0
Total	129		22 (17.1)	26 (20.2)	48 (37.3)

Table V
"Regression" from Apart Reading

Explanation from "Side-by-Side" Reading	
"Regression" among 522 Cases	28
Technical	
Underexposed, Poor contrast	10
Inadequate Inspiration	3
Pleural Disease	
Regressing Effusion	2
Confusion with Face-on Plaques	4
Decreasing Congestive Failure	3
Progressing Emphysema	3
Decreasing Obesity	2
Comparison Film Lost	1

posed Canadian chrysotile miners, 9.3% showed definite 2-step progression after 17 years,[2] while chrysotile miners in Italy[17] and Corsica,[22] with longer and heavier exposure, showed progression in 32.1% to 46%, respectively. Findings concerning Australian crocidolite miners are obscured by a statistical treatment dealing with "relative rates of progression."[3] Also, their results are not like any others: Median exposure was only 4 months, and asbestosis was sometimes seen only one year after initial exposure. Progression among those who developed asbestosis in 0-9 years was 8 times more common than when fibrosis first appeared after 20 years. Clearly, crocidolite is a bad actor also with respect to asbestosis. Next to fiber type and occupation, years since first exposure was the most relevant variable, and others have found the same.[2,3,8] Most likely this is due to obviously heavier exposure many years ago, and not because of relentless progression of any degree of asbestosis. Most observers[19,22] but not all[8] have found more progression with initially more severe grades of asbestosis. Our finding of more progression among smokers was shared by Rossiter et al.[16] who found progression among 9% of smokers and ex-smokers while there was no progression among 33 nonsmokers. In other smaller series ex-smokers tended to
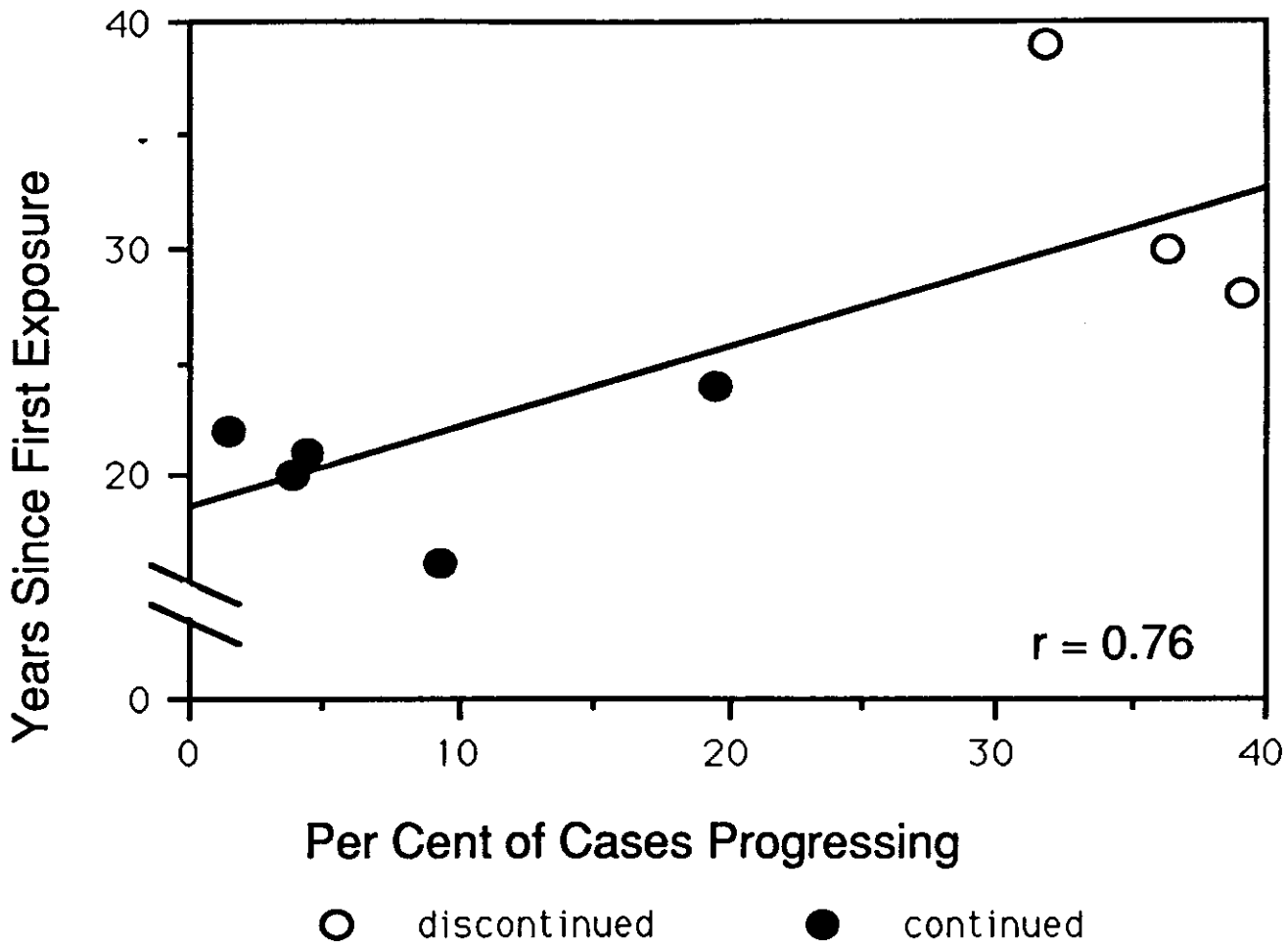
Figure 2. The percent of cases who progressed by 2 or more steps on the 12-step ILO scale during an observation period of 11 ± 3 years are compared to mean years since first exposure for 8 groups of employees. There was much less progression among the 5 groups who continued to have low level (<2 f/cc) exposure during the period, but their first exposure was also more recent than for the 3 groups who had no further exposure.

fare worst.[19,22] A profusion of 1/1 is helpful for diagnosis in the clinical context.[20] Here we have elected a profusion of 1/0 to denote possible minimal fibrosis because this reading may have some significance for epidemiologic studies. However, referring to Figure 1, a profusion of 1/0 accounted for 29% of all of our cases of asbestosis, and a choice of 1/1 to denote minimal disease would have changed our results considerably.

SUMMARY

Asbestosis appears to be a disappearing disease in that the prevalence has decreased from 47.6% with exposure prior to 1950 to 2.0% among those first exposed since 1960. Follow-up averaging 11 ± 3 years of 522 persons indicated progression among 9% of those with continued exposure and among 36% of those with no further exposure. More frequent progression in the latter group was related to both earlier and more severe exposure, and to a slightly longer period of follow-up. "Attack," as opposed to worsening of

previous disease, accounted for two-thirds of all cases. Progression rates did not differ with initially low profusion readings of 0/0, 0/1 or 1/0, but a 1/1 reading carried a somewhat worse prognosis. Among 60 pairs matched for age and years since first employment, there was significantly more progression among 60 smokers than 60 nonsmokers.

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Table VI
Prognosis with Initial Low Profusions

Continued Low Level Exposure

Initial ILO	Total #	Progression					
		2 Step		≥ 3 Step		Total	
		#	(%)	#	(%)	#	(%)
0/0	280	9	(3)	8	(3)	17	(6)
0/1	48	3	(6)	4	(8)	7	(15)
1/0	25	1	(4)	3	(12)	4	(16)
1/1	22	3	(14)	3	(14)	6	(27)

Discontinued Exposure

Initial ILO	Total #	2 Step #	(%)	≥ 3 Step #	(%)	Total #	(%)
0/0	68	11	(16)	13	(19)	24	(35)
0/1	18	5	(28)	3	(17)	8	(44)
1/0	10	0		3	(30)	3	(30)
1/1	15	2	(13)	5	(33)	7	(47)

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THE RELATIONSHIP BETWEEN PULMONARY FUNCTION AND MORTALITY IN MEN SEEKING COMPENSATION FOR ASBESTOSIS

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INTRODUCTION

Exposure to asbestos dust may carry a risk of shortened life expectancy associated with increased mortality rates from respiratory diseases and cancer. A variety of epidemiologic studies have demonstrated dose-response relationships between estimates of personal exposure to asbestos dust, expressed either as cumulative exposures or as time-weighted exposures, and mortality risk.

It may sometimes be desirable to be able to assess the asbestos-associated risk for individuals or groups. Dose-response relationships in the literature may be used to make predictions when it is feasible to calculate estimates of personal or group exposures. For most individuals exposed to asbestos, however, personal exposure records or records of airborne asbestos levels will not exist, and such a calculation will not be possible. In these circumstances, it would be useful if one could find a surrogate for the exposure record for the purpose of prognosis.

It has been demonstrated that the results from two commonly used clinical tests, namely the chest radiograph and pulmonary function tests, are associated with measures of exposure to asbestos dust, with the test result worsening in response to increasing exposure.[1,2] It would thus be expected that these clinical test results might serve as surrogates for missing exposure histories in a mortality dose-response relationship. It has indeed been shown that mortality risk is associated with radiographic scores.[1] It is the purpose of this paper to demonstrate that the results of pulmonary function testing are also predictive of the risk of death from asbestos-associated diseases.

MATERIALS AND METHODS

Subjects in this study were 161 men who had been examined by the physicians of an Advisory Panel to the Ontario Workers' Compensation Board in the years 1962 through 1978, in connection with claims for compensation for asbestosis. Workers were examined in the Laboratory of the Occupational Chest Disease Service of the Ontario Ministry of Labour and underwent medical, radiographic, and pulmonary function examinations. Occupational, medical, and smoking histories were obtained by the examining physician. Any man known to have a malignancy at the time of the index examination was excluded from the present analysis.

Eighty-eight (55%) of the applicants were awarded a disability pension for asbestosis at the time of the index examination, 33 (20%) were awarded a pension at subsequent examinations, and 40 (25%) have not been awarded a disability pension to this date. The results of lung function testing at the time of the initial disability examination provide the data for this analysis.

The claimants were given a standard spirometric examination and the Morris reference equations were used to standardize the results of FVC and FEV_1 for age and height.[3] Workers were followed-up for mortality through the end of 1986. For examination of the association between test results and mortality rates, subjects were divided into 4 groups according to the quartile of the study population in which the test result fell.

Person-years at risk, from the time of the entry examination until death or the end of follow-up, were calculated with the Person-Years computer program.[4] An examination of the age distribution of the person-years at risk indicated that they were similar across pulmonary function quartiles, indicating that a direct comparison of Standardized Mortality Ratios (SMR) was valid. The Person-Years program was thus used to compute SMRs using the general male population of Ontario as the reference population. Poisson regression analysis was used to model the relationships between pulmonary function percentiles and SMRs.[5]

RESULTS

Ninety-nine (61%) of the 161 claimants had worked in the asbestos-cement industry, 38 (24%) had worked as insulators, and the remainder (15%) had worked in a variety of other asbestos-exposed occupations.

The mean age at examination was 54.2 years, with a range from 35 to 75 years. Fifty-eight of the claimants had died by the end of 1986, while 27.9 deaths would have been expected in the general population (SMR = 194).

Table I gives the SMRs for various causes for the 4 quartiles of FVC (Percent Predicted) in the study population. The age distributions are similar in the 4 groups so that the SMRs may be legitimately compared. Most of the subjects were smokers, with only 7% claiming never to have smoked, and the distribution of smokers was similar across the quartiles. There is a monotonic increase in the All Causes SMR across

Table I

The Relationship Between FVC (Percent Predicted) and Mortality Ratios

	GROUP 1 (N=41)			GROUP 2 (N=40)			GROUP 3 (N=40)			GROUP 4 (N=40)		
Mean Age (Standard Deviation)	52.4 (8.6)			54.7 (9.1)			55.8 (8.2)			53.9 (9.5)		
Range of FVC Percent Predicted	84.3 – 125			74.6 – 83.9			64.1 – 74.5			28.5 – 63.9		
Mean FVC% (Standard Deviation)	94.1 (8.9)			78.9 (3.1)			69.5 (3.5)			53.0 (9.4)		
	OBS	EXP	SMR	OBS	EXP	SMR	OBS	EXP	SMR	OBS	EXP	SMR
ALL CAUSES OF DEATH	4	6.45	62	10	9.44	106	19	6.38	298	25	5.68	440
ALL MALIGNANCIES	1	1.84	54	6	2.46	244	9	1.75	514	8	1.49	537
CHEST MALIGNANCIES+	0	0.68	0	3	0.85	353	5	0.64	781	4	0.53	755
ABDOMINAL MALIGNANCIES+	0	0.55	0	3	0.76	396	3	0.54	559	2	0.47	429
RESPIRATORY DISEASES	0	0.35	0	1	0.69	145	4	0.39	1030	10	0.43	2350
CIRCULATORY DISEASES	3	3.13	96	0	4.84	0	4	3.21	125	3	3.27	92

NOTES: +Chest Malignancies includes Lung Cancer and Pleural Mesothelioma

+Abdominal Malignancies includes ICD 150.0 to ICD 159.9

quartiles, with the most spectacular changes occurring in the SMRs for Respiratory diseases. No respiratory deaths were observed in the group with the best FVC while there was a 23-fold excess of respiratory deaths in the group with FVC averaging 53% of predicted.

The relationship between the All Cause SMRs and Mean FVC (Percent Predicted) was modelled with Poisson Regression analysis. There was a strongly significant linear association (Chi-Squared = 24.2; df = 1; P <0.001) and the best fitting equation was:

$$SMR = 834 - 8.36 * FVC\%.$$

There were also strong associations between the Mean FVCs and the SMRs for malignant diseases and respiratory diseases.

The test results for FVC and FEV_1 were highly correlated (r = 0.86), so it is not surprising that the findings for the relationships between quartiles of FEV_1 and SMRs had a similar structure (Table II). There was again a highly significant linear association between Mean FEV_1 (Percent Predicted) and All Cause SMRs (Chi-Squared = 25.2; df = 1; P <0.001) and the best fitting equation was:

$$SMR = 787 - 7.27 * FEV_1\%.$$

Various authors have proposed criteria, which combine information from several tests, for grading impairment of pulmonary function. One such proposal appears in the text by Morgan and Seaton.[6] Table III compares the SMRs

of those without impairment (Group 1: FVC and FEV_1 both at least 80% of predicted) with the SMRs of those with varying degrees of impairment. Group 2 consists of all those not in Group 1. Group 3 consists of those with FVC and FEV_1 both 70% or less of predicted and group 4 of those with FVC and FEV_1 both no more than 60% of predicted. Groups 2, 3, and 4 are not mutually exclusive and contain overlap in membership. Those without impairment had a favorable mortality experience in comparison with the general population (possibly an example of the "healthy worker effect") while the most severely impaired had a marked increase in mortality rates.

DISCUSSION

This analysis has demonstrated that the results of pulmonary function testing were predictive of mortality risk in a group of 161 men examined because of workers' compensation claims for asbestosis. About half of the claimants were awarded compensation at the time of the index examination while a quarter have not yet been classified as having a disability due to asbestosis. Mortality risk was found to be strongly associated with reductions in FVC and FEV_1 and regression equations were fitted to the data. The risk coefficients are derived from relatively small numbers of men and need to be replicated in other groups of asbestos-exposed workers before the quantitative result can be generalized.

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Table II

The Relationships Between FEV_1 (Percent Predicted) and Mortality Ratios

	GROUP 1 (N=42)			GROUP 2 (N=39)			GROUP 3 (N=40)			GROUP 4 (N=40)		
Mean Age (Standard Deviation)	53.9 (9.3)			54.2 (9.0)			54.2 (8.7)			54.5 (8.8)		
Range of FEV1 Percent Predicted	93.7 - 130			79.8 - 93.5			65.0 - 79.2			26.6 - 64.0		
Mean FEV1 (Standard Deviation)	101.3 (7.5)			86.1 (4.2)			71.1 (4.2)			50.4 (9.2)		
	OBS	EXP	SMR	OBS	EXP	SMR	OBS	EXP	SMR	OBS	EXP	SMR
ALL CAUSES OF DEATH	4	8.90	45	14	6.06	231	15	7.35	204	25	5.64	444
ALL MALIGNANCIES	2	2.42	83	8	1.67	479	7	1.95	359	7	1.50	467
CHEST MALIGNANCIES[+]	1	0.86	116	5	0.61	820	3	0.69	437	2	0.54	373
ABDOMINAL MALIGNANCIES[+]	1	0.74	135	1	0.51	196	4	0.60	666	2	0.47	429
RESPIRATORY DISEASES	0	0.58	0	1	0.37	270	4	0.49	816	10	0.35	2864
CIRCULATORY DISEASES	1	4.46	22	2	3.01	67	3	3.73	80	4	2.88	139

NOTES: [+]Chest Malignancies includes Lung Cancer and Pleural Mesothelioma

[+]Abdominal Malignancies includes ICD 150.0 to ICD 159.9

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Table III

The Relationships Between Various Impairment Criteria and Mortality Ratios

IMPAIRMENT CATEGORIES NOTE THAT CATEGORIES 2, 3, AND 4 ARE NOT MUTUALLY EXCLUSIVE	GROUP 1 (N=51) FVC PERCENT >= 80 AND FEV1 PERCENT >= 80			GROUP 2 (N=110) NOT GROUP 1 FVC PERCENT AND FEV1 PERCENT BOTH NOT >= 80			GROUP 3 (N=48) FVC PERCENT <= 70 AND FEV1 PERCENT <= 70			GROUP 4 (N=23) FVC PERCENT <60 AND FEV PERCENT <60		
	OBS	EXP	SMR	OBS	EXP	SMR	OBS	EXP	SMR	OBS	EXP	SMR
ALL CAUSES OF DEATH	6	10.43	58	52	17.51	297	26	7.68	339	17	2.94	577
ALL MALIGNANCIES	3	2.84	106	19	4.70	404	9	2.06	437	4	0.75	533
CHEST MALIGNANCIES+	2	1.01	197	7	1.68	417	4	0.74	541	2	0.26	769
ABDOMINAL MALIGNANCIES+	0	0.87	0	8	1.45	552	2	0.64	313	1	0.24	420
RESPIRATORY DISEASES	0	0.68	0	15	1.12	1339	9	0.49	1837	6	0.20	3000
CIRCULATORY DISEASES	2	5.22	38	8	8.86	90	3	3.92	77	2	1.54	129

NOTES: +Chest Malignancies include Lung Cancer and Pleural Mesothelioma

+Abdominal Malignancies include ICD 150.0 to ICD 159.9