Ventilatory decrements in former asbestos cement workers: a four year follow up

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ABSTRACT A four year follow up of the ventilatory function in former asbestos cement workers has been performed to determine whether any further decrease occurred after cessation of exposure. Seventy five of 125 subjects were eligible for re-examination and were compared with local referents. None showed signs of asbestosis but 32% had pleural plaques at the renewed examination. Cumulative asbestos exposure calculated as fibre x years had been estimated individually in the original examination. After adjustment for age, height, tracheal area, and smoking category the FVC and FEV₁ for all exposed subjects were on average 7% v 6% less than predicted from the referents and twice as much for the subjects with the highest exposure. The four year declines in FVC and FEV₁ were larger than in the referents, significantly so for FEV₁. There were no significant correlations between pleural plaque and ventilatory function after adjustment for exposure. Thus the age adjusted reduction in ventilatory function had progressed during the follow up period despite the cessation of exposure and the lack of radiological signs of asbestosis.

Many cross sectional studies of lung function among workers exposed to asbestos have been published but few longitudinal ones. The age adjusted results from cross sectional studies may not necessarily correspond with those of longitudinal studies and might not be valid for the determination of the prognosis.¹

Decreased ventilatory function was observed in a cross sectional study of Swedish asbestos cement workers.² The aims of this four year follow up of the workers examined in 1976 were to compare the decline in ventilatory function with referents selected in 1976 from the same geographical area, to assess the exposure effect relations, to study the association between pleural plaques and loss of ventilatory function, and to examine the comparability of cross sectionally predicted versus longitudinally determined decrements after four years.

STUDY GROUPS

A health examination, including chest radiography and lung function testing, was offered to all workers at an asbestos cement plant in the middle of Sweden

when production ceased in 1976. Only male actively employed smokers and never smokers with at least ten years of employment were included in the calculations, ex-smokers and pensioners being excluded to obtain homogeneity. In 1976 the final study group comprised 77 smokers and 48 never smokers, a total of 125 subjects.

Referents were chosen from three plants without exposure to asbestos and associated with the same industrial health centre that served the asbestos cement plant. These plants produced fertilisers, cement products, and wood products. Seventy six referents were selected to provide valid regression equations for comparison.

The degree of follow up is displayed in table 1. Forty three exposed smokers of the 77 originally examined and 32 exposed never smokers of the 48 originally examined took part in the 1980 follow up. The corresponding numbers for the referents were 28 of the 40 smokers and 28 of the 36 never smokers. Four exposed subjects and three referents had moved from the county and eight exposed subjects and five referents chose not to take part. Surgical operation was the reason in four of these cases and one subject could not attend owing to his bed-ridden wife.

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Table 1 Study groups 1976 and 1980 by smoking habits. Reasons for non-participation and exclusions

	Exposed	Referents
Examined in 1976	125 77 smokers 48 never smokers	76 40 smokers 36 never smokers
Reasons for non-participation 1980:		
Moved from county	4	3
Non-respondents	8	5
Dead	6	3
Reasons for exclusion:		
Stopped smoking since 1976	31	9
Started smoking since 1976	1	—
Examined in 1980	75 43 smokers 32 never smokers	56 28 smokers 28 never smokers

Six exposed subjects and three referents had died. In five of the six exposed cases the cause of death was known and had no obvious relation to the exposure to asbestos (two cases of cancer of the rectum, two of myocardial infarction, and one of lung embolus).

Thirty one exposed subjects and nine referents had stopped smoking since 1976 and one subject had started. As ex-smokers are heterogenous with reference to airway disorders and were excluded from the calculations in the 1976 investigation they were also excluded from the follow up calculations.

Descriptive information on the exposed and the referent group is displayed in table 2. The exposed subjects are divided according to the occurrence of

pleural plaques. Subjects with pleural plaques were five years older and had been smoking seven years more on average than the exposed subjects without pleural plaques, a difference which is to be expected with regard to the latency time for the occurrence of pleural plaques. The exposure in fibre-years did not differ between exposed subjects with or without pleural plaques.

Methods

The chest radiographs were of standard size and obtained from frontal, lateral, and oblique projections, thus increasing the sensitivity for detecting pleural plaques.³ All films were classified according

Table 2 Characteristics of the exposed group and 56 referents in 1980. Exposed subjects with and without pleural plaques (pp) are presented separately

Parameter	With pp (n = 24)	Without pp (n = 51)	All (n = 75)
<i>Exposed subjects</i>			
Age	Mean 59.1 Median 60.5 Range 37-68	Mean 53.8 Median 53.4 Range 33-69	Mean 55.5 Median 57 Range 33-69
Height (cm)	Mean 173.1 Median 173.8 Range 156-187	Mean 176.1 Median 174.3 Range 162-193	Mean 175.1 Median 174.2 Range 156-193
Tracheal area (mm ²)	Mean 332 Median 329 Range 252-414	Mean 355 Median 347 Range 201-640	Mean 347 Median 331 Range 201-640
Fibre-years	Mean 20.9 Median 19.5 Range 0-48	Mean 19.1 Median 17.0 Range 0-60	Mean 19.7 Median 17.8 Range 0-60
Smoking years (n = 43)	Mean 40.6 Median 40.0 Range 20-52	Mean 33.4 Median 32.0 Range 14-53	Mean 36.0 Median 37.2 Range 14-53
<i>Referents (n = 56)</i>			
Age	Mean 49.4 Median 50.2 Range 33-66		
Height (cm)	Mean 175.5 Median 176.1 Range 165-194		
Tracheal area (mm ²)	Mean 351.0 Median 347.0 Range 201-548		
Smoking years (n = 28)	Mean 31.2 Median 31.5 Range 17-50		

to the ILO requirements⁴ by a qualified reader, a member of the National Pneumoconiosis Panel. The exposed workers had another chest radiograph in 1980 but the referents underwent radiography only in 1976. Pleural abnormalities were classified as plaques only when other causes such as postinfectious changes, surgery, or trauma could be excluded.

The tracheal area was obtained from the frontal and lateral diameters, assuming an elliptical figuration. All the films were read and evaluated by the same reader without knowledge of exposure status.

The ventilatory function was measured with the subjects in a sitting position using a calibrated rubber sealed spirometer (Vitalograph). The tests were performed by the same trained nurse for both the exposed and referent groups on both occasions but a different Vitalograph was used in 1980. The best result of at least three tests of each variable was used for statistical analysis. The two best recordings did not differ more than 5% in any single individual. The parameters recorded were the forced vital capacity (FVC) and the forced expiratory volume in one second (FEV₁).

STATISTICAL ANALYSIS

The predicted results for the exposed subjects were calculated from the regression equations of the referents using the 1980 data. The independent variables used were quantitative (age, height, and tracheal area) and dichotomous (smoking). Differences in lung volumes between the study groups in 1980 and four year decrements were analysed using analysis of covariance. The exposed subjects were divided into three exposure categories based on individually determined cumulative exposure (fibre-years). The limits for the fibre-years tertials used in the 1976 study yielded three groups of approximately equal magnitude and have been applied in the follow up analyses.

EXPOSURE DATA

Exposure data from the studied industry were reported in the previous paper.² In summary, the average fibre concentrations were estimated to have been about 2 fibres/ml in the 1950s and the 1960s and 1 fibre/ml during the 1970s. A few dust measurements before 1970 indicated a general dust level of 10 mg/m³. The vast majority of asbestos used was chrysotile but a few hundred tons of crocidolite and amosite had been used earlier. Despite the relatively low exposure levels at this plant the median cumulative exposure for the exposed group was 17.5 fibre-years due to the requirement of at least 10 years employment.

The mortality experience of the entire cohort of men employed at least three months at this plant

(*n* = 1216) has been reported.⁵ No statistically significant increase in respiratory diseases or lung cancer associated with exposure to asbestos could be observed. The main reasons for this non-positive outcome were assumed to be the relatively low average fibre levels, the predominant use of chrysotile, and the limited period of follow up for long term employed men.

Results

1980 INVESTIGATION

The decline in ventilatory function among the asbestos cement workers in 1976 had progressed during the follow up period. Table 3 shows the FVC and FEV₁ for the exposed subjects expressed as a percentage of the predicted from the regression equations of the referents' 1980 data. A clear exposure effect relation is obtained after division into three fibre-years categories. FVC and FEV₁ for the lowest exposure category was 98.3% and 99.8% of predicted and for the highest exposure category 88.1% and 85.8% (test for linear trend *p* = 0.04 and 0.007 respectively). The exposure dependent decline was noted in exposed subjects without pleural plaques but not in those with pleural plaques, where the highest lung function is found in the middle exposure category (table 4).

Table 3 Mean FVC and FEV₁ for the exposed subjects in 1980 as a percentage of predicted from the regression equations of the referents. Three exposure categories based on fibre-years (approximate tertials)

Parameter	Fibre-years			All exposed
	<14	15-22	≥23	
FVC %	98.3	94.2	88.1*	93.8
FEV ₁ %	99.8	92.6	85.8**	93.1
No	28	23	24	75

Test for linear trend: **p* = 0.04 ***p* = 0.007.

Table 4 Mean FVC and FEV₁ for the exposed subjects in 1980 as a percentage of predicted from the regression equations of the referents and categorised for pleural plaques (pp). Three exposure categories based on fibre-years (approximate tertials)

Parameter	pp	Fibre-years		
		≤14	15-22	≥23
FVC %	Yes	97.3	105.2	91.2
	No	98.9	91.9	85.9
FEV ₁ %	Yes	98.3	99.8	92.5
	No	100.8	91.0	81.0
No		28	23	24

A regression analysis of the lung function in the exposed subjects in 1980 yielded statistically significant coefficients for age and height in FVC and FEV₁ and smoking in FEV₁. The coefficients for fibre-years and tracheal area did not reach statistical significance.

FOUR YEAR DECREMENTS AMONG THE EXPOSED
The four year decrements were larger for the exposed than for the referents (table 5). The decrements increased by fibre-years categories and the trend is statistically significant for FEV₁.

An analysis of variance within the exposed group with height, age, and tracheal area as covariates and fibre-years, pleural plaques, and smoking habits as independent categorical variables showed that the cumulative exposure had affected both lung function parameters, although the results were statistically significant only for FEV₁ ($p = 0.02$) (table 6). An even stronger influence was observed for smoking ($p < 0.01$). There were no differences between those with and without pleural plaques after the adjustments.

LONGITUDINAL VERSUS CROSS SECTIONAL RESULTS

The observed values of the referents in 1980 were compared with the age adjusted values predicted from the regression equations derived from the 1976 data of the same individuals. The observed and predicted average values were similar, FVC 4.92 versus 4.97 litres and FEV₁ 3.91 versus 3.92 litres. Pearson's correlation coefficients for individual observed and predicted lung volumes in the referents were 0.75 for FVC and 0.69 for FEV₁.

Discussion

The main result of this follow up study was a progressive decrease in FEV₁ for former asbestos cement workers when compared with referents. The ventilatory decrements correlated significantly with the exposure both as linear trend over exposure strata and in the analysis of variance. The group with high-

est exposure lost 9% of their FVC and 8% of their FEV₁ compared with four years earlier, whereas the group with lowest exposure lost no more than the referents—that is, about 5% in both parameters (table 5).

VALIDITY

The most critical aspect of a follow up study is the estimation of possible biases from non-participants in the later investigation. In this study the main reason for non-inclusion in the follow up calculation was stopping smoking, and more exposed individuals than referents became ex-smokers during the follow up period.

The ventilatory function of the 31 exposed ex-smokers in 1976 was therefore compared with the standard Swedish reference material.⁶ FEV₁ in 1976 was on average 99.6% of expected and for exposed smokers who continued their habit 98.7%. Thus there does not seem to be any overestimation or underestimation of the ventilatory reduction in 1980 as the result of the exclusion of those who had stopped smoking.

The comparability between the asbestos cement workers and the referents for factors other than exposure was discussed in the earlier publication,² and several of the possible confounding factors are included in the statistical analyses.

LONGITUDINAL VERSUS CROSS SECTIONAL RESULTS

The referents had lung volumes close to the numbers predicted from their own 1976 regression equations. This is not in agreement with some other studies where cross sectionally predicted decrements were larger than the longitudinal ones actually measured.^{1,7} A biased estimate of the decline in lung volumes would be the case if the first examination (but not the second one) includes smokers who later stop smoking as a consequence of symptoms of impaired lung function. This bias was avoided by the exclusion of the ex-smokers from both examinations.

Table 5 Mean four year decrements in FVC and FEV₁ (Δ FVC, Δ FEV₁) in exposed subjects and referents as percentage of the lung volumes in 1976. The exposed subjects are displayed in three exposure categories based on fibre-years (approximative tertials)

Parameter	Exposed subjects (fibre-years)				Referents
	≤ 14	15-22	≥ 23	All	
Δ FVC FVC ₁₉₇₆ %	-4.5	-7.3	-8.2*	-6.6	-4.5
Δ FEV ₁ FEV ₁ 1976 %	-4.6	-8.2	-8.7**	-7.0	-5.6
No	28	23	24	75	56

Test for linear trend: * $p = 0.06$ ** $p = 0.03$.

Table 6 Analysis of variance. The influence of the independent variables fibre-years, pleural plaques, and smoking habits by the covariates height, age, and tracheal area on the decrements in FVC and FEV₁ 1976–80. The effects of the independent variables are expressed as percentage of the lung volumes in 1976 adjusted for the covariates and the other independent variables

Variable	No*		Adjusted decrements	
			ΔFVC	ΔFEV ₁
Fibre-years	≤14	28	4.32	4.20
	15–22	23	7.42	8.49
	≥23	23	8.58	9.17
Pleural plaques	Yes	24	6.34	6.43
	No	50	6.74	7.39
Smoker	Yes	44	8.53	9.41
	No	30	3.79	3.66

*Data missing for one person.

The annual average decrease for the referents was around 55 ml in FVC and 50 ml in FEV₁, which is more than expected from standard Swedish reference material.⁶ These decrements are also slightly greater than those reported in a longitudinal study of asbestos cement workers from Italy, 48 ml/year in subjects with more than 15 years since first asbestos exposure.⁷ Noxious effect from the referents' exposure to industrial pollutants might be the explanation and would agree with the similar decrements in the asbestos cement group with slight exposure. If so the impact of exposure to asbestos cement has been underestimated.

A bias in the ventilatory function tests could also explain the greater than expected decrements in the referents. The procedure was the same at the two investigations but the pieces of apparatus differed and as only the last one was properly calibrated, the possibility exists that the first one gave too large volumes. This would not invalidate the follow up results and the comparison between exposed and referents but possibly would invalidate the degree of the differences.

EVALUATION OF THE RESULTS

The mainly obstructive pattern could be explained by the aerodynamic properties of the dust generated from the handling and trimming of the asbestos cement products.⁸ A considerable portion of the particles are too large to reach the alveoli and will be deposited in the airways, causing an obstructive impairment. The effects reported are therefore considered to be the results of exposure to asbestos in combination with rather high dust levels.

There was a weak indication of synergistic—that is, more than additive—effect between smoking and fibre-years. The indications were present only for

FVC and not considered strong enough to justify a separate analysis.

Age, smoking, and fibre-years had a statistically significant influence on the decrease in lung function whereas pleural plaques did not have any further effect on the lung volumes after adjusting for the other factors.

The decrements during the four year follow up were greater than expected despite the fact that the exposure had ceased. So far, the progressing loss in ventilatory function is probably of clinical significance only for the highest exposed subjects, but former asbestos cement workers seem to be a health risk group, even in the absence of asbestosis. Even moderate decrements in FEV₁ have been associated with increased mortality.⁹ (I Annesi and F Kauffmann, paper presented at XXI International Congress on Occupational Health, Dublin, September 1984).

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