

## THE FOLLOW-UP STUDY OF LUNG FUNCTION IN ANTINUCLEAR POSITIVE AND NEGATIVE ASBESTOS WORKERS

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### ABSTRACT

In two surveys with a two-year interval 142 asbestos workers were examined in respect to X-ray changes due to asbestosis and lung function. The presence of antinuclear antibodies (ANA) in the sera of these persons was determined.

It was found that the worsening of lung function and increase in the frequency of asbestosis was higher in the asbestos workers with ANA than in those lacking the autoantibodies. However, the worsening of lung function results appeared in all investigated groups to be independent of the presence or absence of ANA. This suggests that in some cases of the asbestos induced lung disease some factors which are not linked with ANA play an important role in its pathogenesis.

The occurrence of antinuclear antibodies (ANA) and rheumatoid factor (RF) in asbestosis is well documented<sup>7,9,11</sup>. The presence of ANA is correlated with the symptoms of lung fibrosis<sup>10</sup>. However, these autoantibodies were also found in some cases with long occupational exposure to asbestos but lacking an X-ray diagnosis of asbestosis<sup>7</sup>. It is suggested that ANA may contribute to lung fibrosis by accelerating the process<sup>8</sup>, but the hypothesis has not been fully documented.

The aim of this work was to evaluate the role of ANA in the pathomechanism of asbestosis. The present follow-up study was undertaken to correlate the presence of ANA and progress in lung abnormalities. The present results were collected during three years of observation.

### SUBJECTS AND METHODS

#### Asbestos workers

All investigated persons were employees of an asbestos textile factory. The study consisted of two surveys. The first was made in 1973–1974 and included 386 persons. Two years later 142 asbestos workers, mainly those with long

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lasting exposure and lung function abnormalities, were reexamined. The present results concern 142 asbestos workers who were examined in both surveys. Some details about the workers are given in Table 1.

TABLE 1  
Summary of data concerning asbestos workers.

Antinuclear antibodies	Number of cases	F/M ratio	Age (years)		Duration of exposure		Smokers*	
			Mean	Range	Mean	Range	Women	Men
Absent in both surveys	95	52/43	45	24-63	15	4-29	28 (41)	76 (278)
Present only in one survey	20	17/3	46	28-56	14	3-24	29 (69)	33 (180)
Present in both surveys	27	21/6	47	26-60	18	4-28	19 (58)	66 (267)

\*Percentage of smokers and mean index of smoking in brackets.

#### Medical examination

All asbestos workers underwent a detailed medical examination according to a standard questionnaire. The diagnosis of asbestosis was based on the X-ray examination of the lung and was assessed according to the ILO/UC 1971 Classification of Radiographs of Pneumoconioses<sup>4</sup>. Chronic bronchitis was diagnosed when a productive cough lasted at least three months in two consecutive years. The smoking of cigarettes was estimated by an index of smoking which was computed by means of the following formula: years of smoking  $\times$  average number of cigarettes smoked per day.

#### Lung tests

Vital capacity (VC) and forced expiratory volume in one second (FEV<sub>1</sub>) were recorded in all subjects on a Pulmotest Spirometer (Godart). A definite impairment of ventilatory function was diagnosed if the results were lower than 60% of the predicted values taken from the list of the CECA Committee on Standardization of Respiratory Functional Tests<sup>1</sup>.

The single breath carbon monoxide diffusing capacity (D<sub>CO</sub>) was measured by means of a carbon monoxide analyser (Godart). The results were expressed as a percentage of the predicted values. The results below 70% of the predicted values were taken as abnormal.

Blood gases were analysed in arterialised capillary blood. The partial pressures of blood oxygen and carbon dioxide as well as blood pH were measured with Micro-Astrup instrument (Radiometer) at rest and, with a few exceptions, at 60W for women and 90W for men during exercise on bicycle ergometer (Zimmermann). The oxygen partial pressure P<sub>O<sub>2</sub></sub> below 70 mm Hg

(9.33 kPa) at rest, and still below this value at exercise, or below the value of 70 mm Hg (9.33 kPa) at exercise, with a depression during exercise of at least 5 mm Hg (0.67 kPa), was taken as abnormal.

#### Determination of autoantibodies

ANA in sera were detected with the immunofluorescence method and RF by means of the sheep cell agglutination test (SCAT) and latex human gamma-globulin test. A test serum screening dilution of 1 in 10 was used for ANA and of 1 in 8 for SCAT. RF reaction was considered positive if serum was positive in SCAT or latex gamma-globulin test.

Statistical analysis was performed by means of the  $\chi^2$  test with Yates modification.

### RESULTS

In two surveys 142 asbestos workers were examined. They were divided into three groups according to the presence or absence of ANA. A total of 67% workers did not have ANA in both surveys. The rest of the group had ANA in both surveys (19%) or only in one (14%). In the group of asbestos workers with ANA there was a prevalence of women (81%) over men. The percentage for the group of workers lacking ANA was 55%.

Asbestos workers with ANA at least in one survey had more frequently asbestosis and lung function impairment than those lacking ANA (Table 2). There was a marked clustering of workers with lung abnormalities in the group of ANA positive workers during the first and the second survey. Asbestos

TABLE 2  
Asbestos workers with impairment of lung function and asbestosis in two surveys.

Parameter	Survey	Antinuclear antibodies					
		Absent in both surveys		Present only in one survey		Present in both surveys	
		N	%	N	%	N	%
VC less than 60% of predicted value*	First	13	14	6	30	6	22
	Second	25	26	7	35	12	44
P <sub>O</sub> <sub>2</sub> less than 9.33 kPa*	First	4	5	2	11	4	17
	Second	14	16	5	26	8	33
D <sub>CO</sub> less than 70% of predicted value*	First	6	9	4	29	2	10
	Second	8	12	3	21	6	30
Asbestosis**	First	2	2	2	12	7	26
	Second	4	4	4	24	8	30

\*Not all workers underwent all lung function tests in both surveys; those who did not were excluded from the calculation.

\*\*Diagnosis of asbestosis was based on X-ray picture, cases with doubtful X-ray and non-constant X-ray asbestosis changes were excluded from the calculation.



workers with persistent and long lasting (at least two years) presence of ANA did not differ significantly from those having ANA only in one survey in respect to the incidence of asbestosis and lung function abnormalities (Table 2).

In two years of observation the worsening of lung function and increased frequency of asbestosis were observed in all investigated groups (Fig. 1 and Table 2). However, in the group of workers lacking ANA only two out of 95 workers (2%) showed X-ray asbestotic changes which were absent during the first survey. At the same time in 3 out of 47 workers from the group of workers having ANA at least in one survey (6%) asbestosis became radiologically evident. The difference in the incidence of newly diagnosed cases of asbestosis between the groups with and without ANA is not statistically significant. During the two-year interval 20% of asbestos workers with the persistent presence of ANA and only 6% of the workers lacking ANA in both surveys became abnormal in respect to the results of the single breath carbon monoxide diffusing capacity test. The percentage of asbestos workers with the worsening of  $P_{O_2}$  results were 17% and 10% in the groups having and lacking ANA in both surveys, respectively. However, these differences were not statistically significant. In the group of asbestos workers having ANA only in one survey the tendency to a more serious determination of lung function was confined only to the  $P_{O_2}$  results. An increase in the number of workers with the VC results below 60% of the predicted values was similar in the groups of workers with and without ANA (Fig. 1). In some cases an improvement in lung function was also observed.

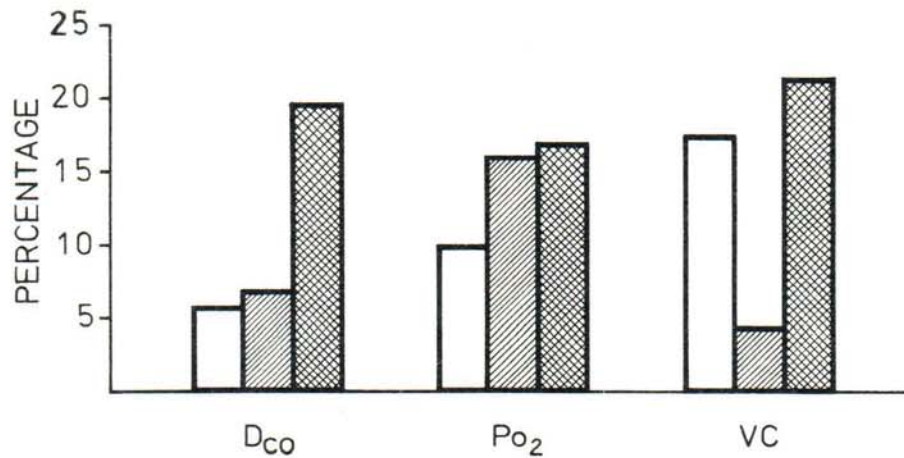


FIG. 1 - Percentages of cases which became abnormal in respect to lung function in the two-year interval.  - ANA absent in both surveys;  - ANA present in one survey;  - ANA present in both surveys.

There was no significant difference in the incidence of the symptoms of chronic bronchitis between the workers having and lacking ANA.

RF was present in 4% of asbestos workers, independently of the presence or absence of ANA.

#### DISCUSSION

In this pilot study we showed a definite worsening of lung function in asbestos workers, in the two-year interval. The percentage of workers with impaired lung function almost doubled in two years. The most prominent progression was found in the results of VC,  $P_{O_2}$  and  $D_{CO}$  tests. These parameters reflect ventilatory insufficiency with impairment of gas exchange. No progression was found in respect to  $FEV_1$  values. This pattern of lung function impairment is typical of asbestosis<sup>12</sup>. The changes in the lung physiology of asbestos workers are concordant with the radiographic observation which revealed 5 new cases of asbestosis during the second survey in comparison to the first one. Therefore, we can assume that in the investigated group the progression in the lung fibrosing process appeared during the two-year period of observation. It was of interest to investigate the correlation between asbestos related immunological abnormalities and the fate of asbestos workers. Now, it is well documented that impairment in cellular immunity, autoantibodies formation and hyperimmunoglobulinaemia are significantly correlated with asbestosis<sup>3,5,6,7,11</sup>. In our work we evaluated the correlation between ANA and an increase in the percentage of cases newly diagnosed as those with asbestos related lung disease. The worsening of lung function appeared in all investigated groups which were made on the ground of presence or absence of ANA (Table 2). However, Figure 1 and Table 2 show that the number of new cases with abnormal  $P_{O_2}$  results and asbestosis was highest in the group consisting of asbestos workers having ANA. Considering carbon monoxide diffusing capacity the number of new abnormal cases was increased mainly in the group of asbestos workers with long lasting ANA existence. The  $D_{CO}$  test abnormal results are common in asbestosis, and it is suggested that the impairment of carbon monoxide diffusing capacity may be found earlier than the radiographic appearance of asbestosis<sup>12</sup>. Therefore, our longitudinal observation of asbestos workers suggests the precipitating role of ANA in the process of lung fibrosis. Our observation is supported by the experimental data suggesting that the injection of serum containing ANA aggravated turpentine induced pleurisy in rats (quoted by Pepys and Turner-Warwick<sup>8</sup>). However, the differences in the number of new cases with asbestos related lung diseases between groups having and lacking ANA are not statistically significant. This is partly due to a relatively small number of investigated workers and a short period of observation. Also it is possible that like ANA RF can play a role in the progression of lung disease in asbestos workers. The experiment of DeHoratius and Williams<sup>2</sup> is in favour of this possibility. In our study RF was found evenly distributed in all groups. However, when a more accurate and sensitive technique was employed (the double antibody solid phase radioimmunoassay) for antiglobulin measurement it

was found that IgM antiglobulin values were slightly higher in some ANA negative cases of asbestosis than in those with ANA and in the control group (Nineham and co-workers, in preparation). Therefore, apart from ANA in some cases of the asbestos induced lung disease some factors which are not linked with ANA play an important role in the pathogenesis of the disease.

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