Serial pulmonary function tests in patients with asbestosis

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Britton, M. G., Hughes, D. T. D., and Wever, A. M. J. (1977). Thorax, 32, 45–52. Serial pulmonary function tests in patients with asbestosis. Serial lung function tests were performed on 17 patients with asbestosis. A marked fall in the transfer factor often preceded any significant decline in the vital capacity. Changes in vital capacity and transfer factor did not appear to give any indication of the prognosis in these patients. Death was more commonly due to carcinoma of the lung than to the effects of the lung fibrosis.

The abnormalities of pulmonary function in patients with asbestosis have been well described (Williams and Hugh-Jones, 1960; Regan et al., 1971). In 1965 Bader et al. reported follow-up measurements on 13 asbestos workers using vital capacity, maximum breathing capacity, and blood gas measurements. They concluded that vital capacity was the most sensitive index of progression of the disease and correlated well with radiological changes and progression of dyspnoea in half the cases. However, reports of serial studies in patients with asbestosis are rare and we have been unable to find a study with serial measurements of transfer factor.

A retrospective study of 120 patients who had lung function tests at The London Hospital for possible asbestosis between 1960 and 1975 showed that, by 1975, 50 had proven asbestosis and nine had mesothelioma (Britton and Hughes, 1976). The 50 patients have produced a group of 17 in whom serial lung function tests were carried out over a 4- to 12-year period. The data from these patients have been studied to determine whether pulmonary function tests, especially the vital capacity and transfer factor, might be helpful in predicting the prognosis in cases of asbestosis.

Patients and methods

The 17 patients were in- or out-patients at The London Hospital and were referred to the Lung Function Laboratory for an assessment of pulmonary function. Each patient performed tests of peak flow rate, forced expiratory volume in one second (FEV₁), forced vital capacity (FVC), and Pco₂. The transfer factor was estimated twice by the single breath carbon monoxide method using a Resparameter and the mean result was recorded. The methods used in the laboratory for these tests have already been described (Hughes and Empey, 1972), and the predicted values were those of Cotes (1968).

All patients fulfilled the mandatory criteria for the diagnosis of asbestosis (Parkes, 1973) by the time of their most recent assessment. These are:

1. definite asbestos exposure;
2. bilateral basal crepitations;
3. radiological changes of diffuse interstitial fibrosis in the lower halves of the lung fields;
4. impairment of lung function.

Clubbing, pleural plaques, dyspnoea on effort, and the demonstration of asbestos bodies in the sputum provide corroborative evidence. In a few cases crepitations may be absent in the presence of early radiographic evidence of asbestosis.

The patients had tests on more than one occasion, and all of them had no further asbestos exposure after their first tests. Hence the changes shown in the serial tests represent the natural history of asbestosis rather than any changes from further exposure.

Results

The results for FEV₁, peak flow, and Pco₂ are not reported since the most significant changes were in FVC and transfer factor. In fact in no case

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was the Pco₂ elevated while the FEV₁/FVC ratio was less than 70% in only two cases. Some relevant data concerning the 17 patients, including their smoking habits are shown for convenience in Table 1. All the patients had abnormal radiographs by the end of the study, and all except patients 8, 10, and 15 are known to have received a pneumoconiosis board pension.

INITIAL RESULTS
The results of the initial tests of the 17 patients expressed as a percentage of predicted values are shown in Table 2.

Assuming a normal value to be greater than 75% of predicted, the patients may be divided into the following groups:

<table>
<thead>
<tr>
<th>Patient</th>
<th>Born</th>
<th>Age</th>
<th>Exposure</th>
<th>Diagnosis</th>
<th>Died</th>
<th>Smoking</th>
<th>Cause of death</th>
<th>No. of tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1903</td>
<td>70</td>
<td>1943-53</td>
<td>1960</td>
<td>1972</td>
<td>Smoker</td>
<td>Carcinoma</td>
<td>2</td>
</tr>
<tr>
<td>2</td>
<td>1906</td>
<td>62</td>
<td>1922-26</td>
<td>1939</td>
<td>1969</td>
<td>Non-smoker</td>
<td>Carcinoma</td>
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<tr>
<td>3</td>
<td>1908</td>
<td>67</td>
<td>1940</td>
<td>1975</td>
<td>1975</td>
<td>Non-smoker</td>
<td>Carcinoma</td>
<td>3</td>
</tr>
<tr>
<td>4</td>
<td>1908</td>
<td>66</td>
<td>1928-32</td>
<td>1965</td>
<td>1974</td>
<td>Smoker</td>
<td>Carcinoma</td>
<td>5</td>
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<tr>
<td>5</td>
<td>1911</td>
<td>61</td>
<td>1942-43</td>
<td>1966</td>
<td>1972</td>
<td>Non-smoker</td>
<td>Carcinoma</td>
<td>4</td>
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<tr>
<td>6</td>
<td>1912</td>
<td>57</td>
<td>1927-64</td>
<td>1964</td>
<td>1969</td>
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<tr>
<td>7</td>
<td>1918</td>
<td>57</td>
<td>1934-64</td>
<td>1963</td>
<td>1974</td>
<td>Ex-smoker</td>
<td>Bronchopneumonia</td>
<td>2</td>
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SERIAL STUDIES
All the patients had lung function tests performed on a variable number of occasions (Table 1). The serial changes in each individual's vital capacity and transfer factor in absolute values are plotted either against the number of years before death in the seven patients who had died (Figs. 1 and 2) or against the date in years for those still living (Figs. 3 and 4).

In order to appreciate the interrelationship between vital capacity and transfer factor at various stages of the disease the serial tests of three patients, each a representative example of one of the three main groups, are illustrated:

Group 1 Patient 9 Fig. 5
Group 2 Patient 10 Fig. 6
Group 4 Patient 17 Fig. 7

The percentages in parentheses on these graphs represent the percentage of predicted values at the time of the initial test.

Some comparisons have also been made between those patients who have died (1-7) and those patients who are still living (8-17). The changes in absolute values and percentage of predicted values for both vital capacity and transfer

Table 1 Characteristics of the patients with serial lung function tests

<table>
<thead>
<tr>
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<th>Died</th>
<th>Smoking</th>
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<td>Bronchopneumonia</td>
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Table 2 Initial results of all patients with relationships to first exposure

<table>
<thead>
<tr>
<th>Patient</th>
<th>Time from first exposure to initial test (years)</th>
<th>Vital capacity as % of predicted</th>
<th>Transfer factor as % of predicted</th>
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<td>61</td>
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<td>50</td>
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<td>32</td>
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Fig. 3 Serial studies of vital capacity in living patients 8–17.

Fig. 4 Serial studies of transfer factor in living patients 8–17.
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Fig. 5 Serial changes in transfer factor and vital capacity of patient 9 (the percentages in parentheses represent the percentage of predicted values at the time of the first test).

Fig. 6 Serial changes in transfer factor and vital capacity of patient 10.
Fig. 7 Serial changes in transfer factor and vital capacity of patient 17.

Fig. 8 Serial changes in transfer factor and vital capacity of patient 5.
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Table 3  Some comparisons between the living and dead patients

| Patient | Average age on 1 Dec. '75 or at death (years) | Average no. of years since first exposure | Average yearly fall in Transfer factor (mmol min⁻¹ kPa⁻¹) | % of predicted TF | Vital capacity (ml) | % of predicted VC | Average values within a year of death or end of study of
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</thead>
<tbody>
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<td>1-7</td>
<td>63</td>
<td>39</td>
<td>0.41</td>
<td>4.25</td>
<td>140</td>
<td>3.79</td>
<td>3.55</td>
</tr>
<tr>
<td>8-17</td>
<td>62</td>
<td>38-3</td>
<td>0.15</td>
<td>1.78</td>
<td>58</td>
<td>0.65</td>
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</tr>
</tbody>
</table>

Conversion: SI to traditional units—Transfer factor: 1 mmol min⁻¹ kPa⁻¹ = 2.9 ml min⁻¹ mmHg⁻¹.

probably lasting over an 8–12 year period. Patient 10 (Fig. 6) is shown as an example of these changes which were seen in the patients of group 2. The vital capacities rarely fell below 50% of predicted, and 40% of predicted for the transfer factor.

Finally, the patients in group 4 showed constant but impaired values throughout their period of study, varying from six to nine years, the only exception being a gentle decline in the transfer factor of patient 13. Figure 7 shows the results of patient 17 with a vital capacity of 1.45 litres and a transfer factor of 4 mmol min⁻¹ kPa⁻¹ (11.9 ml min⁻¹ mmHg⁻¹), both measurements remaining constant over a nine-year period, as an example of this group.

The chest radiograph of patient 12, taken at the time of presentation, showed extensive pleural fibrosis in the left hemithorax with calcified plaques over both diaphragms. This possibly explains why the vital capacity was impaired before there was any change in the transfer factor.

Discussion

Although the changes seen varied with the different groups, it appeared that after a variable interval of time following exposure to asbestos there is an initial marked fall in the transfer factor which precedes any significant decline in the vital capacity. This was followed by a steady decline in the vital capacity of most of the patients, greater than one would expect due to aging alone, thus supporting the findings of Bader et al. (1965).

Perhaps the changes seen in the three main groups of patients may represent the disease process at different stages of its development, and it might be postulated that in the patients of group 4 the disease has burnt itself out. However, there was no correlation between the functional changes seen initially and the date and duration of exposure.

Death may occur at any time along this progression and, of the seven deaths in this study, six were from carcinoma, and three of these were non-smokers (2, 3, and 5). The emergence of a carcinoma of the lung in these patients did not appear to make any significant differences to the lung function tests, although in the terminal stages of the illness there may be a more rapid decline in the vital capacity and/or transfer factor (Fig. 8).

In our experience with this small number of patients, serial lung function tests, although useful in diagnosis, appear to be of little help in assessing the prognosis of individual cases of asbestosis. There is a need for further longitudinal studies to include more frequent measurements and correlation with radiological changes in the lung and pleura.

We are indebted to the Wellcome Foundation for financial support.

References


Regan, G. M., Tagg, B., Walford, J., and Thomson,


Requests for reprints to: Dr. D. T. D. Hughes, The London Hospital, London E1.