Mortality in cases of asbestosis diagnosed by a pneumoconiosis medical panel

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ABSTRACT One hundred and fifty five male cases of asbestosis certified by the London Pneumoconiosis Medical Panel during 1968–74 were followed up during 1978–9, 4–11 (mean 7·5) years after certification. Fifty nine patients had died, 23 (39%) from lung cancer, 6 (10%) from mesothelioma, and 11 (19%) from other respiratory causes. The number of observed deaths was 2·25 times greater than expected and 7·4 times greater than expected for lung cancer. Adenocarcinoma was the commonest histological type but other cell types were also increased. Finger clubbing (p < 0·01) and percentage of predicted FEV_1 (p < 0·01) were of value in predicting death, but increasing profusion of small opacities greater than 1/0 (ILO/U-C international classification of radiographs of pneumoconiosis, 1971), duration of exposure to asbestos, time from first exposure to asbestos, and percentage of predicted vital capacity and transfer factor did not predict death.

Patients certified as having asbestosis frequently ask about the implications of such certification for them in terms of survival, the development of cancer, and progression of the asbestosis. This paper attempts to provide such information for survival and for lung cancer. McVittie[1] followed up 247 workers certified during 1955–63 and recorded 59 deaths. Twenty one (36%) were due to lung cancer, 17 (29%) were due to asbestosis and three (5%) were due to mesothelioma. Berry[2] carried out a mortality study of workers certified by the London, Swansea, and Cardiff Panels from 1952 to 1976 and some of these cases are included in this study. Of 283 male deaths, 102 (36%) were due to lung cancer, 57 (20%) to asbestosis, and 25 (9%) to mesothelioma. He found the main factor influencing mortality was the clinical state of the men at the time of certification as reflected in the percentage disability awarded, but he did not relate mortality to clinical, radiographic, or physiological variables. In this study we have attempted to examine in greater detail the factors that predict mortality.

Patients and methods

From 1968 onwards claimants coming before the London Pneumoconiosis Medical Panel seeking pen-

sions for asbestosis have had respiratory function tests carried out at the Brompton Hospital. At this visit a clinical questionnaire including a history of asbestos exposure was completed, physical examination was performed, and a serum sample was collected. Most of these claimants were seen by MTW. From 1968 to the end of 1974 155 men were seen in whom the panel independently made the diagnosis of asbestosis. The guidelines used for the diagnosis of asbestosis[3] at this time state that, given exposure to asbestos, two of the features breathlessness, finger clubbing, basal rales, radiological changes, and reduced gas transfer would be strongly suggestive of asbestosis.

Fifty nine deaths had occurred by the end of August 1979. The mortality data have been examined and an attempt has been made to identify the clinical features which on initial examination predict death.

FEV_1, forced vital capacity (FVC), and vital capacity (VC) were recorded with a low inertia spirometer and single breath transfer factor (T_{LCO}) was measured with a Resparameter Mark 3. The tests were carried out with the subjects seated and wearing a nose clip and the results have been expressed as percentages of the predicted normal values on the basis of the data of Cotes.[4]

Chest radiographs were available for all cases and were independently categorised according to the 1971 ILO/U-C classification of radiographs of pneumoconiosis[5] by three experienced readers. Inter-

Table 1 *Observed and expected mortality in the first five years after certification of asbestosis according to radiographic category*

		All deaths		
Radiographic category	Years of observation	Observed (O)	Expected (E)	O/E
0	173	3	2·91	1·0
1	373	28	6·87	4·1
2 + 3	151	9	3·98	2·3
All	697	40	13·76	2·9*

*Four mesothelioma deaths occurred in 697 man years of observation, three in category 1, and one in category 2

Table 2 *Observed and expected mortality in the first 10 years after certification of asbestosis according to radiographic category*

		All deaths		
Radiographic category	Years of observation	Observed (O)	Expected (E)	O/E
0	297	6	5·97	1·0
1	579	38	12·28	3·1
2 + 3	231	14	7·40	1·9
All	1107	58	25·65	2·2*

*Six mesothelioma deaths occurred in 1107 man years of observation, five in category 1, and one in category 2.

Table 3 *Observed and expected mortality of men certified as having asbestosis by age*

	5 year observation				10 year observation			
Age (y)	Years of observation	Observed deaths (O)	Expected deaths (E)	O/E	Years of observation	Observed deaths (O)	Expected deaths (E)	O/E
30–39	24	—	0·03	—	33	—	0·51	—
40–49	128	2	0·60	3·3	173	3	0·81	3·7
50–59	259	17	3·09	5·5	400	22	4·84	4·5
60–69	255	18	7·84	2·3	405	24	13·26	1·8
70–79	31	3	1·92	1·6	96	9	6·43	1·4
All	697	40	13·48	2·97	1107	58	25·85	2·24

observer and intraobserver variation of profusion score was measured and found to be small, and so the median reading for each film has been used in analysis.

The cause of death was obtained from the death certificate and compared, where possible, with the cause of death recorded by the panel, which normally examines the lungs post mortem in certified cases of asbestosis. The histology of bronchial carcinomas was obtained from panel records and hospital notes. The expected mortality of the study group was calculated by the subject years at risk method.[6] The probability of death at a given age was obtained from life tables—the Registrar General's *Decennial Supplement for England and Wales 1970–72.* Observed and expected mortality was compared by the χ^2 test, and where appropriate the data were treated as a Poisson variable. A discriminant analysis was used to investigate the value for predicting death, of age at presentation, finger clubbing, duration of exposure, and time from first exposure to asbestos, lung function (percentage of predicted $TLCO$, VC, and FEV_1), and the radiographic score for small intrapulmonary opacities (12 point scale of the 1971 ILO/U-C classification).
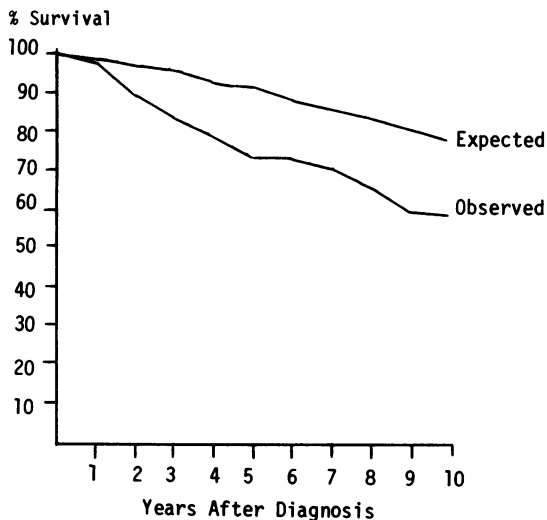
Results

In 23 cases the death certificate gave lung cancer as the cause of death (table 3). Twenty of these cases were examined by the panel and in all cases the death certificate diagnosis was confirmed. The panel found lung cancer in a further three cases where lung cancer did not appear on the death certificate. Eleven men died from respiratory causes other than lung cancer or mesothelioma. No death occurred from laryngeal cancer and there was no excess mortality from gastrointestinal cancer.

Lung cancer deaths			*Respiratory deaths*			*Other deaths (excluding mesothelioma*)*		
Observed (O)	*Expected (E)*	*O/E*	*Observed (O)*	*Expected (E)*	*O/E*	*Observed (O)*	*Expected (E)*	*O/E*
2	0·37	5·4	1	0·36	2·8	0	2·18	—
13	0·87	14·9	3	0·87	3·4	9	5·12	1·8
3	0·50	6·0	2	0·62	3·2	3	2·85	1·1
18	1·74	10·34	6	1·85	3·24	12	10·15	1·18

Lung cancer deaths			*Respiratory deaths*			*Other deaths (excluding mesothelioma*)*		
Observed (O)	*Expected (E)*	*O/E*	*Observed (O)*	*Expected (E)*	*O/E*	*Observed (O)*	*Expected (E)*	*O/E*
3	0·74	4·1	2	0·78	2·6	1	4·45	0·2
16	1·50	10·7	5	1·66	3·0	12	9·11	1·3
4	0·87	4·6	4	1·12	3·6	5	5·42	0·9
23	3·11	7·39	11	3·56	3·08	18	18·98	0·95

Tables 1 and 2 and the figure summarise the mortality data after five and 10 years of observation, by which times there had been 40 and 58 deaths respectively. There is an excess mortality at five and 10 years ($p < 0.001$), due to an excess of deaths from lung cancer ($p < 0.001$), respiratory disease ($p < 0.001$), and mesothelioma. There is no basis for predicting deaths due to mesothelioma, but six deaths in 1107 man years of observation is clearly excessive for what is a rare disease.

These tables show no rise in mortality with increasing severity of asbestosis as assessed by radiographic profusion of small opacities, except in the case of death due to respiratory disease. Thirty six cases were certified with a category 0 radiograph and no overall excess mortality was found in this group, but mortality from lung cancer (observed 3, expected 0·74) was significantly increased ($p < 0.03$).

The overall mortality ratio in the second five years of observation was 1·51, suggesting that the excess risk of death diminishes with time. Two factors may contribute to this. Firstly, the cases with a category 0 radiograph at presentation do not have an increased overall mortality ratio and so form an increasing proportion of the at risk population as time elapses. Secondly, table 3 shows a falling mortality ratio in the higher age groups, suggesting that those who survive are at less risk.

Discriminant analysis showed that finger clubbing ($p < 0.05$), age ($p < 0.025$), and percentage of predicted FEV_1 ($p < 0.01$) were of value in discriminating between survivors and non-survivors. Finger clubbing predicted both death and radiographic progression of asbestosis and is the subject of a separate paper.[7] The mean percentage of predicted FEV_1 at presentation was almost 8% higher in the survivors (72·3% (SD 17·3) v 64·5 (18·3)). The separation achieved by the discriminant function resulted in an estimated misclassification in 28% of cases.

It was not possible to study the effect of cigarette smoking. Of the 155 men, only five had never smoked. Only one of these men died, from pleural mesothelioma.

Survival after certification in men with asbestosis.

Table 4 *Histology of bronchial carcinoma according to radiographic category*

Histological type	Radiographic category				
	0	*1*	*2*	*3*	*Total*
Adenocarcinoma	1	6	3	1	11
Squamous cell	1	7	1		9
Oat cell		4			4
Undifferentiated	1				1
Unknown		2			2
Total	3	19	4	1	27

The histology of the tumour in the 26 men known to have lung cancer is shown in table 4. One had two primary tumours (an adenocarcinoma and a squamous carcinoma). Adenocarcinoma (41%) was the most common histological type and accounted for four of the five tumours arising in lungs with the most severe fibrosis as assessed radiographically (category 2 and 3).

Discussion

The overall mortality in the 10 years after certification was 2·26 times greater than expected. The excess was due entirely to deaths from lung cancer, mesothelioma, and other respiratory causes.

Lung cancer was present in 26 (44%) of the deaths but appeared on the death certificate in only 23 (39%) of cases. These proportions are similar to those reported by McVittie[1] and Berry[2] in their mortality studies of certified asbestosis. Berry,[2] using the cause of death as determined by the panels rather than the death certificate, found a ratio of observed to expected deaths from lung cancer of 8·7 among cases certified after 1965 where death was within 10 years. The ratio in our cases certified during 1968–74 was 7·4 on the basis of death certificate data (table 3) and 8·4 on the basis of information from the panel.

Adenocarcinoma (41%) was the most common histological type. Whitwell *et al*[8] in a larger study of the cell type in cases of asbestosis certified by panels made the same observation and other workers have commented on the frequency of adenocarcinoma in asbestosis. Kannerstein and Churg[9] found no excess of adenocarcinoma in a case-control study of lung cancer associated with asbestos exposure but many of their subjects did not have asbestosis. It is difficult to be certain whether the incidence of adenocarcinoma is increased in asbestosis because of the lack of any comparable series of cases of lung cancer without exposure to asbestos. The frequency of adenocarcinoma in different series depends on whether the histological specimen was obtained at bronchial biopsy, operation, or necropsy. Even postmortem

series are not strictly comparable because of the higher necropsy rate in asbestosis than in the general population. In men without asbestosis Whitwell *et al*[8] found that the proportion of adenocarcinoma rose from 2% in bronchial biopsies to 27% at necropsy. He thought that the true incidence lay between 15% and 20%.

The evidence from this study and others suggests that adenocarcinoma complicates asbestosis more frequently than other cell types. This being so, it might be expected that those with more severe asbestosis might be more likely to develop adenocarcinomas, and there is some evidence (table 4) that this cell type is proportionately more frequent in those with higher profusion scores for small opacities on the chest radiograph. Whitwell *et al* found adenocarcinoma to be more common in cases with histologically more severe fibrosis. Although adenocarcinoma appears to be proportionately more frequent in asbestosis, table 2 shows that the 11 cases of adenocarcinoma do not account for the 23 (including cases proved by the panel) excess cases of lung cancer. Probably therefore other cell types are increased, but to a lesser extent, in asbestosis.

An excess mortality from gastrointestinal cancer has been detected in some[10-12] but not all populations exposed to asbestos. In this study of heavily exposed workers no excess of gastrointestinal cancer was found, despite the fact that many of them had worked in the factory studied by Newhouse[10] and many were laggers and presumably exposed to an environment similar to those reported by Elmes.[11] Both these authors detected an excess of alimentary cancer. It is not clear why certified cases of asbestosis should not show an excess of gastrointestinal cancer.

An association has been shown between asbestos exposure and laryngeal cancer by some[12 13] but not all[14] workers. No cases were found in this series but it is a relatively rare disease, accounting for only one death in 50 000 a year, and a small study could easily fail to reflect an excess mortality rise.

A discriminant analysis was used to examine factors that might be of value in predicting death. Three indices of lung function were studied—percentage of predicted FEV_1, VC, and TLCO. Only percentage of predicted FEV_1 proved useful. At first sight this is a surprising observation. FEV_1 is reduced in diseases with a restrictive ventilatory defect but to a similar or lesser extent than vital capacity. In this study there was no significant difference in VC between the survivors (72·4% (SD 16·9%)) and the non-survivors (68·2% (16·8%)). So percentage of predicted FEV_1 is unlikely to be simply reflecting the severity of the restrictive defect. There are at least two other possible explanations. Firstly, most (97%) of the men studied were or had been cigarette smokers. This habit is

associated with both lung cancer[15] and airflow limitation[16] and the predictive value of FEV_1 may be reflecting these associations. Secondly, many workers have found evidence of airway disease in asbestos workers[17][18] and there is evidence that this is related to asbestos exposure as well as cigarette smoking. The relative importance of these associations cannot be further elucidated in this study.

Certified cases of asbestosis with a category 0 profusion score for small opacities did not have any overall increase in mortality, although mortality for lung cancer and other respiratory causes was increased. This lack of mortality is in strong contrast to cases with category 1 and 2 profusion scores, where the overall mortality rate was considerably increased. The category 0 cases did have an increased mortality from lung cancer and other respiratory causes and this could be a consequence of asbestos exposure, but other explanations are possible, Claimants coming before a pneumoconiosis medical panel are a highly selected group and the presence of any respiratory symptoms in association with asbestos exposure is likely to be an important selective factor and may account, at least in part, for the pattern of mortality seen. The normal overall mortality and the lower rates of progressing fibrosis (paper in preparation) seen in category 0 cases raises doubt about the reliability of the diagnosis of asbestosis in the absence of definite radiographic evidence of pulmonary fibrosis.

Given radiographic evidence of pulmonary fibrosis (profusion score > 1/0), the severity of asbestosis assessed by the score for profusion of small opacities did not predict outcome. This finding was to some extent unexpected given the known correlations between asbestos exposure and the profusion of small opacities[19] on the chest radiograph in exposed work forces and between exposure and mortality.[14][20][21] Liddell *et al*[22] in epidemiological studies of Canadian asbestos miners and millers have found the chest radiograph to be a good predictor of mortality. Small opacities of profusion > 0/1 were associated with increased mortality, but no attempt was made to examine the effects of increasing profusion on mortality. Our results, obtained in a highly selected group of patients, are in keeping with those of Liddell *et al* in so far as both studies point to a difference in mortality in those with and without small opacities on the chest film.

A lack of correlation between radiographic appearance and mortality in cryptogenic fibrosing alveolitis has been found in both treated[23][24] and untreated[24] cases, and the risk of death from lung cancer in these patients has been shown to be independent of radiographic severity.[25] These findings in another fibrosing lung disorder lend credence to our findings that the severity of fibrosis assessed radiographically does not predict mortality.

Neither of the indices of asbestos exposure, duration of exposure and time from first exposure, predicted death. Once again, given the known relationships between exposure and mortality, the result appears surprising. The exposure data used were crude and could have obscured a real relationship but no correlations were found between mortality and profusion of small opacities on the chest film despite the high quality of the radiographic data. It therefore seems possible that, given sufficient asbestos exposure to develop certifiable asbestosis, life expectancy may be relatively independent of the dose of inhaled asbestos and the radiographically assessed severity of the fibrosis. What then determines life expectancy? The effects of cigarette smoking could not be assessed directly because only five of the 155 men were lifelong non-smokers, but the value of FEV_1 in predicting death suggests that the known synergistic effects of cigarette smoking and asbestos exposure is important.

Finger clubbing at presentation was associated with an increased mortality. The significance of finger clubbing[7] is the subject of a separate paper, but its effect in predicting mortality was not accounted for by either age or asbestos exposure. It appears to be a marker that identifies a subgroup of patients with certified asbestosis who suffer more severely from the effects of inhaled asbestos, but the determinants of this enhanced susceptibility remain unknown.

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