TruCut^R needle biopsy in asbestosis and silicosis: correlation of histological changes with radiographic changes and pulmonary function in 41 patients

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ABSTRACT A percutaneous needle biopsy was performed with a TruCut^R needle on 41 patients with suspected pneumoconiosis. Patients selected for biopsy tended to have brief or unusual dust exposure, as well as questionable radiographic opacities. Sixteen had been exposed to asbestos, 13 to silica and 12 to mixed dust containing quartz, coal, iron, asbestos and talc. All patients in the asbestos group and most in the other two groups had a reduced transfer factor. Most patients in the asbestos group and about 25% of the other patients had restrictive ventilatory impairment. Chest radiographs were assessed according to standard films of the ILO U/C International Classification (International Labour Office, 1972). In 25 patients radiographic opacities were absent or scanty (categories 0-1/1). The dominant radiographic feature of many patients exposed to asbestos was a ground-glass appearance or a bilateral elevation of the diaphragm, or both, features difficult to assess according to the ILO U/C scheme. Most histological changes were those usually seen in pneumoconiosis. However, in only two patients with silicosis were silicotic nodules detected. The specimens of seven patients showed a granulomatous inflammation. The severity of alveolar wall involvement correlated well with the transfer factor value but poorly with radiographic changes. The profusion of radiographic opacities also correlated poorly with functional impairment. As a diagnostic tool the needle biopsy was valuable in asbestosis and slightly less so in mixed-dust fibrosis. The biopsy specimens showed changes compatible with asbestosis in 75% of the suspected cases and in 86% of those in which asbestosis was the final diagnosis. In the mixed-dust group pneumoconiosis was confirmed in 67% and 80%, respectively. In the diagnosis of silicosis an open biopsy is probably more reliable than a percutaneous one, particularly if radiographic changes are minimal. Histological changes in the needle biopsy specimen were compatible with silicosis in only 36% of the suspected cases and in 63% of those in which the final diagnosis was silicosis.

The diagnosis of pneumoconiosis depends to a great extent on a suitable history, usually occupational, of exposure to dust. For judging the severity of disease and its progression, great reliance has traditionally been placed on the chest radiograph. In many types of pneumoconiosis, however, the radiographic changes have not been found to reflect fully the severity of the histological lesions, or the loss of function. In early cases of asbestosis, for instance, the chest radiograph may either be normal or may show only pleural thickening, bilateral elevation of the diaphragm or a ground-glass appearance (Gaensler *et al.*, 1972; Soutar *et al.*, 1974). When opacities are rounded, as in silicosis, assessment of

the radiograph often leads to an overestimation of functional impairment. Linear opacities are recognisable only in advanced interstitial disease, as in asbestosis, and in their assessment functional impairment tends to be underestimated (Gaensler *et al.*, 1972).

Pulmonary function studies, particularly spirometry and the measurement of diffusing capacity, are important in the screening of the pneumoconioses. Reduced transfer factor and restrictive ventilatory impairment are a common functional profile. Other types of profile are, however, reported (Bjure *et al.*, 1964; Muldoon and Turner-Warwick, 1972; Fournier-Massey and Becklake, 1975). Chronic bronchitis may modify the results of functional studies.

When the dust exposure is unusual or otherwise

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uncertain, open lung biopsy has been documented as a generally valuable diagnostic aid (Van Ordstrand *et al.*, 1955; Theodos *et al.*, 1955; Gaensler *et al.*, 1972; Fitzgerald *et al.*, 1973) and the needle biopsy (Jack needle) has been reported to be valuable in diagnosing asbestosis (Mann and Sinha, 1966; Walton and Skeoch, 1968). Scott and Hunt (1975) did not, however, find the Jack-needle biopsy useful in the diagnosis of asbestosis.

Over the past five years, in our study of diffuse lung diseases, we have evaluated a number of patients suspected of having pneumoconiosis. In addition to clinical and radiographic assessment and physiological measurements, we also obtained, with a TruCut^R needle, a biopsy specimen for histological examination. We report here (1) our experience with this biopsy technique as a diagnostic tool in suspected asbestosis and silicosis, and (2) how morphological changes correlated with respiratory function and radiographic changes.

Patients

SELECTION OF PATIENTS

From a needle biopsy series (TruCut^R) of over 350 patients with diffuse lung diseases, we selected 41 subjects, comprising three women and 38 men, aged 34–71 years (mean 51 yr). The indication for a needle biopsy was an undiagnosed diffuse lung disease suspected of being a pneumoconiosis.

All patients fulfilled the following criteria:

1. their chest radiograph or pulmonary function measurements, or both, suggested the presence of a diffuse lung disease;
2. their occupational history allowed for the possibility of pneumoconiosis;
3. their suspected pneumoconiosis was believed to be produced by inorganic dust;
4. as far as could be determined, their suspected diffuse lung disease had no aetiology except pneumoconiosis.

EXPOSURE HISTORY

Sixteen patients had been exposed mainly to asbestos (asbestos group), 13 mainly to quartz

(silica group) and 12 to mixed dust that contained quartz, coal, iron, asbestos and talc (mixed-dust group).

Table 1 shows, for all patients, the duration of dust exposure and the interval between the first exposure and the time of the needle biopsy.

For 20 patients there was some doubt about whether their dust exposure was adequate. Five patients had been exposed to inorganic dust for less than five years. For five patients the intensity of dust exposure was open to doubt: two had dismantled old lagging, two had periods of insulation work using asbestos-cement products, and one had packed rubber balls (talc exposure). For another 10 patients the quality of dust exposure seemed questionable: five had been exposed to mixed dust while welding with an electric arc, grinding with emery or doing similar work; two had quarried limestone (possibly contaminated by silica); one had worked in a glass factory; one had transported raw apatite; and one had cut pavement flags.

The remaining 21 patients gave histories of exposure to dust which were considered to be sufficient to cause pneumoconiosis.

SYMPTOMS AND SIGNS

Four patients had no symptoms; they were included in the series when routine chest radiography showed opacities. In 30 patients the prominent symptom was shortness of breath on exertion, with or without a dry or productive cough. A dry cough was the only symptom of four patients, and pain in the chest was the only symptom of three others.

Crepitant rales were heard on auscultation in 12 patients in the asbestos group and in two patients in the mixed-dust group. Five patients in the asbestos group had digital clubbing.

Methods

PULMONARY FUNCTION STUDIES

Vital capacity (VC) and forced expiratory volume in 1 second (FEV_{1.0}) were recorded with a spirometer (Bernstein, Kifa). The observed values were expressed as a percentage of the reference values given by Berglund *et al.* (1963). Diffusing capacity

Table 1 Dust exposure in 41 subjects with suspected pneumoconiosis

Type of exposure	No. of patients	Age range (yr)	Dust exposure	
			Duration (yr)	Interval between onset and lung biopsy (yr)
Asbestos	16	34–59 (48)	0–6–30 (13)	8–34 (22)
Mixed dust	12	37–63 (54)	10–30 (20)	10–43 (37)
Silica	13	38–71 (54)	5–42 (20)	14–49 (26)

Means in parentheses.

(DLCO) was measured by using the single-breath method for carbon monoxide (Ogilvie *et al.*, 1957) and the reference values of Cotes (1965).

ASSESSMENT OF CHEST RADIOGRAPHS

All chest radiographs were assessed and coded by two radiologists (OK and MV) in conformity with the standard films of the ILO U/C International Classification, 1971 (International Labour Office, 1972).

NEEDLE BIOPSY TECHNIQUE

All biopsies were performed with a TruCut[®] needle (Travenol Laboratories Inc., Deerfield, Illinois, USA), the inside diameter of which was 1.4 mm. The method used has been described in detail elsewhere (Tukiainen, 1975). Briefly, after local anaesthesia and under fluoroscopic guidance, the needle was inserted into the right lower lobe. Regardless of where radiographic opacities were most profuse, specimens were always taken from a peripheral area of the lung, about 1–3 cm from the visceral pleura in the posterior region of the lobe.

HISTOLOGICAL PROCESSING AND EVALUATION

The biopsy specimens were fixed in 10% formaldehyde, embedded in paraffin, cut in serial sections and stained with Prussian blue, Van Gieson, periodic acid–Schiff (PAS), diastase–PAS, haematoxylin and eosin (H and E) and methyl-pyronin green. For this study all specimens were re-examined by a pathologist (ET).

The specimen was considered suitable for study if it contained at least 20 alveoli and alveolar ducts. The specimens were classified by size: those less than 2.5 mm in length were small, those between 2.5 and 5.0 mm were medium, and those more than 5.0 mm in length were large.

Thickening of the alveolar wall was estimated to be mild, moderate or marked by a method described

P. Tukiainen, E. Taskinen, O. Korhola, and M. Valle

in detail elsewhere (Tukiainen, 1975). The alveolar wall was judged to be mildly thickened if its thickness was less than one-half the diameter of the alveolar lumen; it was considered to be moderately or markedly thickened depending on by how much its thickness exceeded one-half of this diameter. The thickness of a normal alveolar wall did not exceed that of three parallel tissue cells.

The criteria for a histological diagnosis of pneumoconiosis were:

1. dust particles or ferruginous bodies in lung tissue (identified by conventional light microscopy and histological staining);
2. a tissue reaction against dust particles (intra-alveolar, alveolar wall or perivascular inflammatory reaction);
3. interstitial or marked perivascular fibrosis;
4. disturbed general alveolar structure (excluding emphysema) or pathognomic alterations (i.e. silicotic nodule), or both.

If all criteria were met, the diagnosis of pneumoconiosis was confirmed. If the first three were met, the diagnosis was probable pneumoconiosis. If only the first two were fulfilled the case was interpreted as a tissue reaction caused by dust particles.

Results

PULMONARY FUNCTION STUDIES

Transfer factor was lowered in all patients in the asbestos group (DLCO mean = 55%, range = 22–75% of predicted value) and in all patients except two in the mixed-dust group (DLCO mean = 56%, range = 37–94%) (Table 2). In the silica group DLCO values varied between 40% and 94% (mean = 69% of the predicted value).

Of the 41 patients, seven had obstructive ventilatory impairment (that is, an FEV_{1.0} less than 63% of FVC).

Table 2 Pulmonary function determined spirometrically and by the measurement of gas transfer factor in 41 subjects with suspected pneumoconiosis

Pulmonary function	Asbestos group	Mixed-dust group	Silica group	Total no. of patients
Normal transfer factor	—	2	5	7
Spirometry:				
normal	—	1	4	5
obstruction	—	—	1	1
restriction	—	1	—	1
Lowered transfer factor	16	10	8	34
Spirometry:				
normal	4	5	5	14
obstruction	—	2	—	2
obstruction and restriction	1	2	1	4
restriction	11	1	2	14
Total no. of patients	16	12	13	41

ASSESSMENT OF CHEST RADIOGRAPHS

Table 3 shows the results of the radiographic assessments. In 25 subjects, including 11 of the 16 patients in the asbestos group, radiographic opacities were mild or lacking (categories 0–1/1). Eight of the patients exposed to asbestos had bilateral elevation of the diaphragm and four had opacities with a ground-glass appearance, both features difficult to categorise with the ILO U/C 1971 scheme. One patient in the asbestos group, who was later shown to have histological asbestosis, had no radiographic opacities (Figure 1a). The other 15 all had small irregular opacities (s-t) that were always most profuse at the base of the lung. All except one patient exposed to asbestos had pleural thickening. In two patients exposed to asbestos, local infiltrates were later found to be attributable to bronchial carcinoma (Figure 1a).

Of the 25 patients in the silica and mixed-dust groups, three patients had no radiographic opacities, nine had rounded opacities (p-r) (Figures 2a, b) and 13 had small irregular opacities (s-t). In only one patient among the last-mentioned were large opacities observed (A id). In eight patients exposed to silica and in two exposed to mixed dust, opacities were most profuse in the upper and middle regions of the lung.

In the silica and mixed-dust groups 13 patients had pleural thickening and seven had radiographic emphysema. Three patients in the silica group had enlarged hilar lymph nodes.

HISTOPATHOLOGY

The biopsy specimen obtained from 13 patients was large, from 14 medium, from 11 small and from one it was inadequate; two biopsies yielded no lung tissue. Among the patients in the silica and mixed-dust groups the size of the specimen correlated significantly ($p < 0.01$) with diagnostic outcome: pneumoconiosis was probable or confirmed in 13 of the 18 patients whose specimen was medium or large, and in none of the six patients whose specimen was small. In the asbestos group there was no such correlation.

Biopsy specimens were usually small when opacities were sparse. Small specimens were obtained from eight of the 15 patients with category 0/0–1/0 opacities and from only four of the 25 patients in higher categories ($p < 0.01$).

Most histological alterations in confirmed or probable pneumoconiosis resembled those seen in many other interstitial lung diseases (Table 4). The interstitial changes in most instances were mild. When viewed by itself, the granulomatous reaction

Table 3 Assessment of chest radiographs of 41 subjects with suspected pneumoconiosis (ILO U/C International Classification, 1971 (International Labour Office, 1972))

Category	No. of patients			Total	Rounded opacities				Irregular opacities				Large opacities	
	In each radiological subcategory				Type		Number of zones affected		Type		Number of zones affected		Aid	
					q	r	Mean	Range	s	t	Mean	Range		
0	0/– 0	0/0 5	0/1 0	5										
1	1/0 10	1/1 10	1/2 3	23	2	2	2.6	2–4	11	8	3.4	2–6		
2	2/1 4	2/2 6	2/3 2	12	2	2	4.0	2–6	3	5	4.0	2–6	1	
3	3/2 0	3/3 1	3/4 0	1		1	6							
Grand total				41	4	5			14	13			1	

Table 4 Histological findings in 25 subjects who fulfilled the criteria of confirmed or probable pneumoconiosis

Histological finding	Silicosis (5 patients)	Mixed-dust fibrosis (8 patients)	Asbestosis (12 patients)	Total no. of patients
Alveolar macrophages	3	8	9	20
Alveolar epithelial hyperplasia	1	5	7	13
Interstitial inflammation	1	3	7	11
Interstitial fibrosis	5	7	12	24
Perivascular inflammation	5	5	6	16
Granulomata	1	2	4	7
Silicotic nodules	2	—	—	2

(a)

Fig. 1 (a) In a 53-year-old man, who had been dismantling old lagging for 9 yr, the chest radiograph showed a small infiltrate in the right upper lobe, but no diffuse opacities (ILO U/C 1971: 0/0). D_{LCO} was 39% of predicted value. Needle biopsy showed alveolar macrophages and epithelialisation, alveolar and interstitial ferruginous bodies, and perivascular round-cell infiltration, with coal, pigment, and silica particles. Alveolar walls were moderately thickened by fibrosis and showed mild chronic inflammation. Histological diagnosis: confirmed asbestosis. An operation performed because of the upper lobe infiltrate showed an epidermoid carcinoma as well as asbestosis. (b) Detail of the biopsy specimen with numerous alveolar macrophages and ferruginous bodies. Alveolar epithelialisation and mild interstitial inflammation are also present.

(b)

(a)

Fig. 2 (a) In a 40-year-old man, who had been working with modelling clay for 10 yr, the chest radiograph showed rounded opacities mainly in the upper and middle fields (ILO U/C 1971: 2/3 r). DLCO was normal. (b) Needle biopsy showed mild interstitial fibrosis, perivascular round-cell infiltration with coal pigment and silica particles, and a silicotic nodule that contained silica particles. Histologically confirmed silicosis. (Low power.)

(b)

Fig. 3 (a) In a 50-year-old woman, who was exposed for 10 yr to talc contaminated with asbestos while packing rubber balls, the chest radiograph showed rounded and irregular opacities mainly in the lower fields (ILO U/C 1971: 2/2 q-s). DL_{CO} was 58% of predicted value. (b) Needle biopsy showed alveolar macrophages and ferruginous bodies in alveoli and interstitium; mildly thickened alveolar walls infiltrated by round cells; and perivascular granulomata that contained numerous large birefringent particles (talc?). Histological diagnosis: probable talcosis. (Low power, polarised light.)

(a)

(b)

Fig. 4 (a) In a 52-year-old man, who had been employed as an arc welder in a foundry for 16 yr, the chest radiograph showed irregular opacities mainly in the lower fields (ILO U/C 1971: 2/1 t) and mild bilateral pleural thickening. DL_{CO} was 44% of predicted value. (b) Needle biopsy showed alveolar macrophages and many iron particles, alveolar and interstitial ferruginous bodies, as well as alveolar walls moderately thickened by fibrosis. Perivascular spaces were infiltrated with lymphocytes and macrophages and contained numerous silica, coal and iron particles. Histologically confirmed mixed-dust pneumoconiosis. (Low power.)

(b)

present in seven patients was difficult to distinguish from that seen in sarcoidosis and other granulomatous inflammatory diseases. Granuloma was defined according to Warren (1976) as a focal chronic inflammatory reaction characterised by accumulation and proliferation of leucocytes, principally of the mononuclear type. One such case is illustrated in Figure 3. The results of clinical examinations made in order to confirm or exclude sarcoidosis in the seven patients with granulomata in their biopsy specimen are shown in Table 5.

In the asbestos group, histological changes were predominantly interstitial, and resembled the mural type of fibrosing alveolitis. One such case, in which the chest radiograph was normal and the gas transfer defect was marked, is illustrated in Figure 1b.

In patients with 'pure' silica exposure, most lesions tended to be perivascular. Histological changes were usually mild. In only one patient was end-stage fibrosis and markedly disturbed tissue configuration a prominent feature. Typical hyaline silicotic nodules were detected in only two patients (Figure 2b).

In the mixed-dust group, the histological changes were either mainly alveolar or mainly perivascular. In a patient exposed to talc contaminated by asbestos (Figure 3), changes were predominantly perivascular. Figure 4 shows the interstitial tissue reaction in a foundry worker. The specimens of two patients showed widespread interstitial fibrosis but no dust particles, and the diagnosis of silicosis could not be confirmed.

HISTOLOGICAL CHANGES AND FINAL CLINICAL DIAGNOSIS

Six patients fulfilled the criteria for a clinical diag-

nosis of pneumoconiosis in that they had an adequate history of dust exposure and a profusion of radiographic opacities of more than 1/1 on the standard films of the ILO U/C International Classification (Tables 6 and 7). In five of these, histological alterations were compatible with confirmed or probable pneumoconiosis. In 15 of the 17 patients with 'adequate' radiographic opacities (categories 1/2-3/3; Tables 6 and 7), the biopsy specimen showed alterations compatible with confirmed or probable pneumoconiosis. One of the two exceptions was in the silica group and one was in the mixed-dust group.

In the asbestos group the needle biopsy yielded new diagnostic information in nine of the 13 clinically suspected and in all three of the clinically probable cases (Table 6). Hence, of the 14 patients in whom the final diagnosis was asbestosis, the needle biopsy provided valuable information in 12 (86%). In two patients this diagnosis was made solely on clinical grounds (cases labelled by ‡ in Table 6): this comprised an adequate history of dust exposure, crepitant rales on auscultation, category 1/0 or 1/1 opacities with pleural thickening and calcification, a lowered gas transfer factor and restrictive ventilatory impairment. The patient with minimal opacities (1/0) also had clubbing and his biopsy showed ferruginous bodies and perivascular inflammatory changes; the biopsy of the other patient did not show any lung tissue. Two patients with histologically verified asbestosis subsequently underwent thoracotomy for bronchial carcinoma, and asbestosis was again diagnosed.

In the mixed-dust group, the needle biopsy yielded diagnostic information in seven of the 11 clinically suspected cases and in the one that was

Table 5 *Clinical findings in seven subjects with granulomata in the needle lung biopsy*

Subject	Mantoux tuberculin test	Urinary calcium excretion	Serum γ -globulins	Kveim test	Pleural changes in radiograph	Other examinations	Final diagnosis
1	1 TU positive	Normal	Normal	Negative	None	Mediastinoscopy normal. Needle biopsy 4 yr later: silicotic nodules	Silicosis
2	1 TU positive	Normal	Normal	Negative	None	Autopsy: mixed dust pneumoconiosis	Mixed dust pneumoconiosis
3	1 TU positive	Normal	Normal	Negative	None	—	Mixed dust pneumoconiosis (talcosis)
4	1 TU positive	Normal	Normal	Not examined	Pleural thickening and calcification	—	Asbestosis
5	1 TU positive	Normal	Not examined	Not examined	Pleural thickening and calcification	—	Asbestosis
6	1 TU positive	Normal	Not examined	Not examined	Pleural thickening and calcification	—	Asbestosis
7	1 TU positive	Normal	Normal	Not examined	Pleural thickening	—	Asbestosis

Table 6 Correlation between needle biopsy findings and the clinical likelihood of pneumoconiosis based on suitable dust exposure history and radiographic opacities* in 41 subjects with suspected pneumoconiosis

Biopsy finding	No. of patients	Clinically probable pneumoconiosis	Clinically suspected pneumoconiosis		
		Radiographic opacities and dust exposure adequate	Radiographic opacities adequate: dust exposure doubtful	Radiographic opacities questionable: dust exposure adequate	Radiographic opacities questionable: dust exposure doubtful
Asbestos exposure					
Confirmed pneumoconiosis	4	1	1	1	1
Probable pneumoconiosis	8	2	2	4	—
Tissue reaction	1	—	—	1‡	—
Normal lung tissue	2	—	—	—	2
No lung tissue	1	—	—	1‡	—
Total	16	3	3	7	3
Mixed dust exposure					
Confirmed pneumoconiosis	4	1	3	—	—
Probable pneumoconiosis	4	—	—	1	3
Tissue reaction	3	—	1‡	2‡	—
Normal lung tissue	1	—	—	—	1
Total	12	1	4	3	4
Silica exposure					
Confirmed pneumoconiosis	3	—	3	—	—
Probable pneumoconiosis	2	1	1	—	—
Tissue reaction	6	1‡	—	5†	—
Normal lung tissue	1	—	—	—	1
No lung tissue	1	—	—	—	1
Total	13	2	4	5	2

*Radiographic changes: profusion 1/2 or more in ILO U/C International Classification, 1971.

†Includes 2 patients with interstitial fibrosis but no detectable dust particles and 2 others whose final clinical diagnosis was pneumoconiosis: 1 of these had inadequate biopsy specimen.

‡Includes 1 patient whose final clinical diagnosis was pneumoconiosis.

Table 7 Correlation between biopsy findings and the profusion of radiographic opacities in 41 subjects with suspected pneumoconiosis

Biopsy finding	Profusion of radiographic opacities			
	0/0-1/0	1/1	1/2-3/3	Total
Asbestos exposure				
Confirmed pneumoconiosis	1	1	2	4
Probable pneumoconiosis	2	2	4	8
Tissue reaction	—	1*	—	1
Normal lung tissue	2	—	—	2
No lung tissue	1*	—	—	1
Total	6	4	6	16
Silica and mixed-dust exposure				
Confirmed pneumoconiosis	—	—	7	7
Probable pneumoconiosis	2	2	2	6
Tissue reaction	4	3*	2*	9
Normal lung tissue	2	—	—	2
No lung tissue	1	—	—	1
Total	9	5	11	25

*In all patients the final clinical diagnosis was pneumoconiosis.

clinically probable. Hence, of the 10 patients in the mixed-dust group whose final diagnosis was pneumoconiosis, the biopsy confirmed the diagnosis

in eight (80%). Two patients were diagnosed on clinical grounds (cases labelled by ‡ in Table 6). One, a foundry worker, had an adequate history of dust exposure, category 1/1 rounded opacities and a mild gas transfer factor defect; his lung biopsy showed perivascular fibrosis with dust particles. In the other patient, who had been exposed to quartz, asbestos, coal and iron while working in a glass factory, there was some doubt about the degree of dust exposure. However, he had category 2/2 irregular opacities, pleural thickening and a marked gas transfer defect; his biopsy specimen showed a perivascular fibrotic reaction with dust particles.

The pneumoconiosis verified histologically in one patient was later confirmed at autopsy.

Of the eight patients in the silica group in whom the final diagnosis was silicosis (five diagnosed histologically, three clinically) the needle biopsy provided diagnostic information in five (63%). One of these had clinically probable disease and the remaining four, all of whom had at least category 1/2 opacities, were among the 11 in whom silicosis was suspected. The three patients diagnosed on clinical grounds (cases labelled by ‡ and † in Table 6) all had a lowered gas transfer factor and a history of

adequate exposure to quartz; their biopsies showed only a tissue reaction. One had category 1/2 and two had category 1/1 opacities.

An open biopsy was later performed on two patients with suspected silicosis because the needle biopsy had shown a normal lung in one and no lung tissue in the other. Both had normal lungs except for the presence of a single small silicotic nodule in the former. Both patients had pleural thickening, category 0/0–1/0 opacities and a questionable history of dust exposure. Recently, in one patient a further needle biopsy was performed because of the unusually rapid progression of the pulmonary opacities and suspected silicotuberculosis (case 1, Table 5). The first biopsy had shown histological changes categorised as probable silicosis. In the second, well-formed silicotic nodules were found.

In the two patients whose needle biopsy contained a silicotic nodule, a mediastinal lymph node biopsy showed changes suggestive of silicosis.

HISTOLOGICAL, RADIOGRAPHIC AND FUNCTIONAL CORRELATIONS

For all patients, the mean gas transfer factor was significantly lower ($P < 0.01$) when the alveolar wall was moderately or markedly thickened than when it was normal or slightly thickened (Table 8). In no patient group did vital capacity correlate with the degree of alveolar thickening. The profusion of radiographic opacities also correlated poorly with the degree of wall thickening. Vital capacity tended to be more reduced in patients with than without interstitial fibrosis ($P < 0.05$) (Table 8). This correlation was more striking ($P < 0.01$) if only those patients were taken into account who had no spirometrically demonstrable obstructive ventilatory impairment. In addition, functional disturbances correlated poorly with the profusion of opacities. Radiographic appearance correlated with gas transfer factor values in the asbestos group ($P < 0.05$) but not in the silicosis group; there were, however, striking individual exceptions. Vital capacity was significantly lower in patients with pleural thickening of any kind than in those free

from pleural thickening ($P < 0.001$). No similar relationship existed between D_{LCO} and the presence of pleural thickening.

Discussion

In these patients the indication for biopsy tended to be present in subjects with relatively early disease. Compared with the histological changes in an autopsy series (Heard and Williams, 1961), those that we observed were more cellular and showed less end-stage fibrosis. In asbestosis and in some cases of mixed-dust fibrosis the histological picture resembled the mural type of fibrosing alveolitis with large mononuclear cells in the alveolar spaces, alveolar epithelial-cell hyperplasia, mixed leucocytic infiltration of the alveolar walls and various degrees of alveolar fibrosis (Scadding, 1974). In these cases the differential diagnosis was based largely on the identification of dust particles or ferruginous bodies in the alveolar walls or perivascular area. In the majority of cases of mixed-dust fibrosis and in silicosis the lesions tended to be concentrated perivascularly. It must be borne in mind that the presence of dust particles (even asbestos bodies) does not prove that this dust is the cause of the disease. Dust particles accumulate in scarred lung irrespective of the aetiology, and small amounts of dust, especially particles of coal and quartz, are often seen in the lungs of industrial workers. In this study, significance was attached to the accumulation of dust and the detection of ferruginous bodies only when they were found in excess.

Seven of the 25 patients in whom the final diagnosis was pneumoconiosis (confirmed or suspected) had granulomata in their biopsy specimen. Gaensler *et al.* (1972) also detected granulomata in many of the open biopsy specimens obtained from patients in the early stages of pneumoconiosis. Clinical follow-up and sputum examinations (negative) provided a basis for the exclusion of tuberculosis in our seven cases with granulomata. The patients had not been exposed to beryllium, or to any organic dust which might have induced

Table 8 Correlation between the mean values for vital capacity and carbon monoxide-diffusing capacity expressed as a percentage of the predicted values and the alveolar wall involvement in 39 subjects with suspected pneumoconiosis

Pulmonary function	Degree of alveolar wall involvement			
	Normal–mild thickening	Moderate–marked thickening	No interstitial fibrosis	Interstitial fibrosis
No. of patients	32	7	13	26
VC % of predicted (mean $\pm$ SD)	83.5 $\pm$ 17.8	82.7 $\pm$ 14.9 ^{NS}	89.3 $\pm$ 17.4	79.5 $\pm$ 14.3*
D_{LCO} % of predicted (mean $\pm$ SD)	63.3 $\pm$ 16.8	40.4 $\pm$ 11.1**	64.6 $\pm$ 17.8	56.3 $\pm$ 18.0 ^{NS}

NS = not significant: * = $P < 0.05$; ** = $P < 0.01$.

allergic alveolitis. Sarcoidosis could not be confirmed in any of the cases. Even though no Kveim tests or extrapulmonary biopsies had been made in the four cases with asbestosis, the clinical examinations, and in particular the follow-up from two to six years, did not show any signs of sarcoidosis.

It has been reported that granulomata occur occasionally in asbestosis (Gaensler *et al.*, 1972; Warren, 1976). Although asbestos itself may be responsible for granulomata, a number of other known causes of this process must be considered.

In the six patients in whom a diagnosis of pneumoconiosis was made on clinical grounds, histological confirmation might appear to be unnecessary. In four of these patients justification for the biopsy was the long interval, from 11 to 20 years, between their last dust exposure and the onset of symptoms; a fifth patient had rheumatoid arthritis which caused some diagnostic difficulties; in the sixth patient the biopsy confirmation was hardly necessary. In addition to these six cases, the biopsy served no useful purpose in seven further cases diagnosed despite the absence of histological confirmation. In one of these, no lung tissue was obtained. In the other six cases the biopsy specimen showed an excess of dust particles or ferruginous bodies, and perivascular fibrosis. These changes indicated the possibility of pneumoconiosis, although the extent of the changes did not satisfy the histological criteria of pneumoconiosis.

Our results suggest that, even though the specimen obtained is small, the needle biopsy is a valuable diagnostic tool in troublesome cases of asbestosis in which radiographic changes are mild or lacking. This observation contrasts with that of Scott and Hunt (1975) who used a Jack needle in their biopsy series. The regions of the lungs usually first affected by asbestos exposure are the lower lobes. The most marked alterations occur in the subpleural zone of the posterior parts of the lower lobes (Caplan *et al.*, 1965), that is, the exact site from which the needle biopsy was taken. Moreover, in asbestosis the histological changes are uniformly distributed (Spencer, 1977).

The diagnosis of asbestosis was made from biopsy findings in three patients who, from 12 to 30 years before the biopsy, had been exposed to dust for periods ranging from seven months to three years. Clearly, asbestosis can appear for the first time after a long period of latency following brief but intensive exposure (Soutar *et al.*, 1974).

In silicosis the needle biopsy was far less helpful for diagnosis than in asbestosis, especially in patients with mild radiographic changes. Silicotic nodules usually measure more than 2–3 mm in diameter and

are unevenly distributed, with lesions more prominent in the upper lobes (Spencer, 1977). In many of our silicotic patients radiographic changes were concentrated in the upper lobes, whereas all biopsies were taken from the right lower lobe. It is obviously difficult, moreover, to get all or even part of a silicotic nodule into a needle, the internal diameter of which is 1.4 mm. Furthermore, in an early stage of pure silicosis with few nodules the surrounding air spaces are usually not affected, or else the changes are emphysematous. Because a needle biopsy, for these reasons, is often unrepresentative, open biopsy is preferred when silicosis is suspected, especially if the radiographic changes are slight.

In patients with mixed-dust exposure, irregular fibrotic lesions develop and typical silicotic nodules rarely, if ever, appear. Initial perivascular collagen formation spreads fairly rapidly into the interstitium, resulting in pneumoconiotic changes called mixed-dust fibrosis (Parkes, 1974). As a diagnostic tool the needle biopsy was somewhat less useful in mixed-dust fibrosis than in asbestosis but, because patients exposed to mixed dust had rather uniformly distributed opacities at the base of their lungs, more useful than in silicosis.

In general, lung biopsy is indicated only if the differential diagnosis includes a disease which can be treated. An additional indication for lung biopsy in cases of suspected pneumoconiosis may be the possibility of an award of compensation (Gaensler *et al.*, 1972). Some authors (Parkes, 1974) are reluctant to recommend lung biopsy because of the occasional undesirable, even fatal, outcome with both open biopsy (Gaensler *et al.*, 1972), and needle biopsy (Youmans *et al.*, 1970; Boylen *et al.*, 1973). We have performed needle lung biopsies in more than 350 cases of diffuse lung disease without serious complications. Our biopsies are always performed under fluoroscopic guidance, and in the peripheral part of the lower lobe, although the lower lobes are not always the part of the lungs most affected. We believe that serious complications have been avoided by the application of this method of biopsy.

Despite the small size of specimen obtained by a needle biopsy, the histological, radiographic and functional correlations we observed were similar to those reported by Gaensler *et al.* (1972) for their series of open lung biopsies. Their results suggested that, in evaluating functional impairment from histological features, the number, size and character of the obvious and large foci of tissue lesions are of little importance. The histological determinant for adequate function appeared to be the integrity and appearance of the intervening lung tissue. Our results are consistent with this view.

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