Clinical, Radiological, and Physiological Findings in Asbestosis

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ASBESTOS is the name given to a group of minerals composed of fibrous silicates of magnesium and iron. The inhalation of significant amounts of asbestos dust over an extended period of time can produce a symptomatic form of pneumoconiosis. The principal symptoms are dyspnea and cough, the former being usually more prominent than the latter. Both symptoms increase in severity as the disease progresses. The major clinical signs are diminished breath sounds, basilar crepitations, limited chest expansion, clubbing, and cyanosis. Clubbing and cyanosis are usually seen in the more advanced stages of this disorder. Chronic bronchitis and emphysema are associated with this disease, the emphysema being more of a localized than a diffuse obstructive type. Cor pulmonale is the major complication and the usual cause of death from asbestosis. There is also an increased incidence of carcinoma of the lung in asbestosis. The most characteristic finding on the chest roentgenogram is a reticulonodular shadowing of both lung fields especially in the lower parts together with pleural thickening and/or pleural calcification and a shaggy border to the heart (Fig 1).[1] Cardiac enlargement, predominantly right ventricular, is seen late in the course of this disease. The most consistent pathological change is a dense fibrosis containing macrophages with absorbed dust particles, which in many areas obliterate the pulmonary architecture. A pattern of endarteritis with intimal hyperplasia consistent with pulmonary hypertension and bronchiolectasia are associated major findings. Rather striking is the presence of elongated, terminally-clubbed bodies, both segmented and unsegmented, in the respiratory bronchioles or embedded in the fibrous tissue or both. The pleura often shows a dense fibrotic thickening (Fig 2).[2] The clinical and pathological features are indicative of a pronounced dysfunction of the respiratory mechanism. This has been confirmed by studies of pulmonary function which show both a disturbance in ventilatory function and diffusion capacity.[3] The main functional defect is asbestosis is a reduced diffusion capacity of the lungs. The purpose of the present study was twofold: (1) to make clinical, electrocardiographic, and physiological observations on 21 workers who were exposed to asbestos dust for an extended period of time and who had radiological findings consistent with asbestosis, and (2) to relate the changes in lung function in asbestosis to the clinical and radiological signs of the disease.

Fig 1.—A 61-year-old asbestos insulator with a 36-year exposure to asbestos dust. Reticulonodular shadowing predominantly in the lower lung fields. There is also obscuration of the left cardiac border.

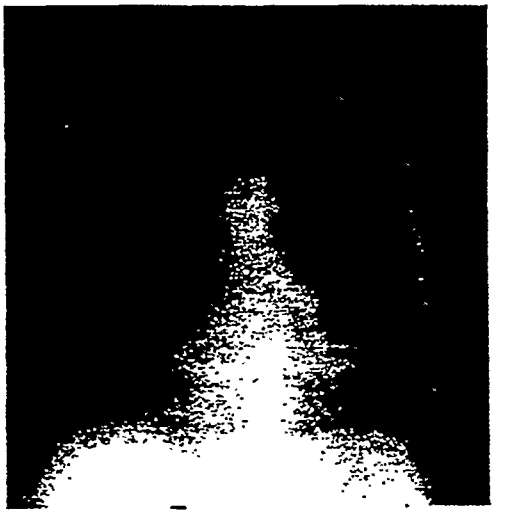

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TABLE 1.—*Clinical, Electrocardiographic, and Roentgenologic*

Case	Age, Yr	Exposure, Yr	Cough (Yr)	Dyspnea	Abnormal Lung Findings	Clubbing	Electrocardiogram
1	45	23	Pr (10)	0	None	0	Normal
2	77	55	0	E	Distant breath sounds; basal rales	+	Normal
3	64	40	0	0	None	0	Normal
4	72	54	NPr (5)	0	None	0	Normal
5	54	20	Pr (2)	0	None	+	Normal
6	39	18	0	0	None	0	Normal
7	41	16	Pr (5)	0	None	0	Normal
8	57	14	0	E	None	+	Normal
9	40	15	0	0	None	0	Low T waves in left precordial leads
10	57	35	0	0	Distant breath sounds; basal rales	0	Sinus arrythmia
11	47	22	NPr (6)	E	Basal rales	0	Normal
12	45	18	0	0	None	0	Normal
13	63	35	Pr (10)	E	Rhonchi, distant breath sounds	0	Rt bundle branch block
14	52	25	0	0	None	0	T-waves inverted in left precordial leads
15	52	15	NPr (2)	0	None	0	Normal
16	40	18	Pr (20)	0	None	+	Normal
17	68	46	Pr (10)	E	Basal rales	0	Normal
18	63	38	0	E	Basal rales	0	Normal
19	54	32	0	0	Basal rales	0	Normal
20	53	37	NPr (30)	0	Basal rales	+	Low T waves in left precordial leads
21	61	36	0	E	Basal rales	+	Coving of leads I, AVL and left precordial leads consistent with digitalis effect
Mean	54.5	29.2					

0 = none; + = minimal; ++ = moderate; +++ = severe; E = on exertion; P = present; Pr = productive; NPr = nonproductive; PI = pulmonary infiltration; OCB = obliteration cardiac border; OCPS = obliteration costophrenic sinus; PL = plaques (pleural and diaphragmatic); Emph = emphysema; and CE = cardiac enlargement.

Material and Methods

Twenty-one persons employed as asbestos insulators comprised the study group. Each had more than a ten-year history of exposure to asbestos dust and roentgenographic findings compatible with asbestosis. Each subject underwent a detailed medical, social, and occupational history, a clinical examination, a 12-lead electrocardiogram, a chest roentgenogram, and a battery of pulmonary function tests. The pulmonary function tests included vital capacity (VC), one-second vital capacity (VC_1), residual volume (RV), total lung capacity (TLC), and diffusion capacity for carbon monoxide ($D_{L_{CO}}$). The vital capacity and one-second vital capacity were measured by a Krogh spirometer and the volume changes of the spirometer were electrically recorded on a Texas Rectiriter recorder. The residual volume was determined by the nitrogen dilution method using the closed circuit technique as recommended by Wright and Gilford.[4] All lung measurements were determined at ambient temperature and pressure, saturated (ATPS). The values for residual volumes were corrected for the dead space of the breathing tube and the phase of expiration in which the subject was connected to the spirometer. The $D_{L_{CO}}$ was determined at rest by the single breath technique described by Ogilvie et al.[5] Normal values for vital capacity, residual volume, total lung capacity, and the ratio of residual volume to total lung capacity were calculated using the best regression equations of Needham et al.[6] For $D_{L_{CO}}$ the observed readings were used. The control group was comprised of 50 men whose occupations varied and who had no occupational dust exposures. The 95% confidence intervals used in the study for all the lung parameters were based on the data obtained from the control group.

Findings

The predominant clinical, electrocardiographic, and roentgenographic findings of the 21 asbestos workers are given in Table 1. The lung function data are shown in Table 2. The comparative clinical and physiological findings in control and asbestos worker groups are shown in Table 3.

Clinical.—The asbestos workers ranged in age from 39 to 77 years, with a mean of 54.5 years. The mean age of the control groups was 49.2 years with a range of 35 to 63 years. The mean ages of the two groups were not statistically different. Ten of the asbestos workers had a chronic cough of between 2 and 30 years' duration. In six, the cough was productive and the remaining

Findings in 21 Cases of Asbestosis

	Roentgenologic Findings			
PI	OCB	OCPS	PL	Emph
+	P	P	0	0
+++	P	P	0	0
+	0	P	P	0
++	P	P	P	0
++	P	P	0	0
+	P	0	0	0
++	0	P	0	0
++	0	P	P	0
+	P	P	0	0
+++	P	P	P	0
+++	P	P	0	P
++	0	P	0	0
++	0	P	0	0
+	0	0	P	0
+	0	P	0	0
++	0	0	0	0
++	0	P	0	P
+	P	P	0	0
+	0	P	0	0
++	0	0	0	0
+++	P	0	0	0

four had a dry cough. Seven of the 21 had exertional dyspnea. Basilar crepitations were found in eight of 21 workers. Six individuals had clubbing. These clinical findings as shown in Table 3 were appreciably greater than those in the control group. A positive smoking history was obtained in 16 of the 21 asbestos workers (76.2%) whereas 21 out of 50 (42.0%) in the control group gave a positive smoking history. This difference in proportion was statistically significant. The criterion for positive smoking history was 20 cigarettes per day for a minimum of five years.

Electrocardiographic. — Electrocardiographic findings were normal in 15 asbestos workers. Of the remaining six, one had sinus arrhythmia, one had a right-bundle-branch block, one showed abnormalities consistent with digitalis effect, and three showed low or inverted T waves in left precordial leads. No individual demonstrated electrocardiographic findings consistent with the major criteria of cor pulmonale, including a deviation of the electrical axis of the QRS complex of more than 90°, prominent R wave in AVR, rSR^1 pattern in V_1, and prominent P waves in leads II and III.

Roentgenographic.—In eight individuals, the pulmonary infiltration was classified as grade 1, in nine as grade 2, and in four as grade 3. The criteria for classification are as follows: grade 1, a reticulated appearance in the lower lung fields; grade 2, a reticulonodular infiltration involving approximately 50% of the total lung area; and grade 3, a

TABLE 2.—*Lung Function Data in 21 Exposed Asbestos Workers*

	VC			VC_1		RV			TLC			RV·TLC			
Case	Obs	Pred	% Pred	Obs	% VC	Obs	Pred	% Pred	Obs	Pred	% Pred	Obs	Pred	% Pred	D_{CO} Obs
1	2900	4229	68.6	2045	70.5	1485	2083	71.3	4385	6561	66.8	33.9	33.0	102.7	27.3
2	1690	2573	65.7	1100	65.1	2170	2563	84.7	3860	5460	70.7	56.2	46.9	119.8	8.3
3	2385	2588	92.2	2025	84.9	1995	2221	89.8	4380	4950	88.5	45.6	43.0	106.7	19.3
4	1665	2528	65.9	1280	76.9	1240	2683	46.2	2905	5190	56.0	42.7	48.7	87.7	20.7
5	2025	3254	62.2	1890	93.3	2030	2189	92.7	4055	5511	73.6	50.1	39.3	127.5	16.9
6	3195	4480	71.3	2700	84.5	2245	1736	129.3	5440	6680	81.4	41.3	27.6	149.6	41.7
7	3060	4245	72.1	2520	82.4	1715	1684	101.8	4775	6420	74.4	35.9	28.2	127.3	21.7
8	2225	3809	58.4	1980	89.0	2150	2411	89.2	4375	6441	67.9	49.1	38.9	126.2	19.9
9	3105	4377	70.9	2025	65.2	2430	2268	107.1	5535	6571	84.2	43.9	34.4	127.6	19.6
10	2855	3740	76.3	1755	61.5	2150	2098	102.5	5005	6340	78.9	42.9	35.5	120.8	17.6
11	2025	3760	53.9	1755	86.7	1225	1818	67.4	3250	5960	54.5	37.7	32.3	116.7	13.3
12	3915	4215	92.9	3105	79.3	1865	1900	98.2	5780	6540	88.4	32.3	30.8	104.9	20.4
13	1395	3255	42.9	955	68.5	2820	2022	139.5	4215	5880	71.7	66.8	37.0	180.5	30.5
14	3215	3420	94.0	2790	86.8	1820	1598	113.9	5035	5670	88.8	36.1	31.3	115.3	24.4
15	4230	4190	101.0	2720	64.3	3035	2578	117.7	7265	6790	107.0	42.0	38.9	108.0	13.1
16	3710	4280	86.7	3060	82.5	1475	1960	75.3	5185	6430	80.6	28.5	31.3	91.1	24.2
17	1485	3438	43.2	1215	81.8	2260	2937	76.9	3745	6350	59.0	60.3	46.9	128.6	9.2
18	2385	3640	65.5	1620	67.9	2165	2652	81.6	4555	6440	70.7	47.7	42.5	112.2	13.0
19	1620	3323	48.8	1225	75.6	1200	1901	63.1	2820	5610	50.3	42.6	35.5	120.0	18.3
20	2700	3578	75.5	2115	78.3	1395	1607	87.4	4095	5940	68.9	34.1	30.6	111.4	19.9
21	1530	3394	45.1	885	57.8	2075	2417	85.9	3605	6000	60.1	57.7	41.1	140.4	11.6
Mean			69.2		76.3			91.5			73.4			120.2	19.6

Obs = observed; Pred = predicted.

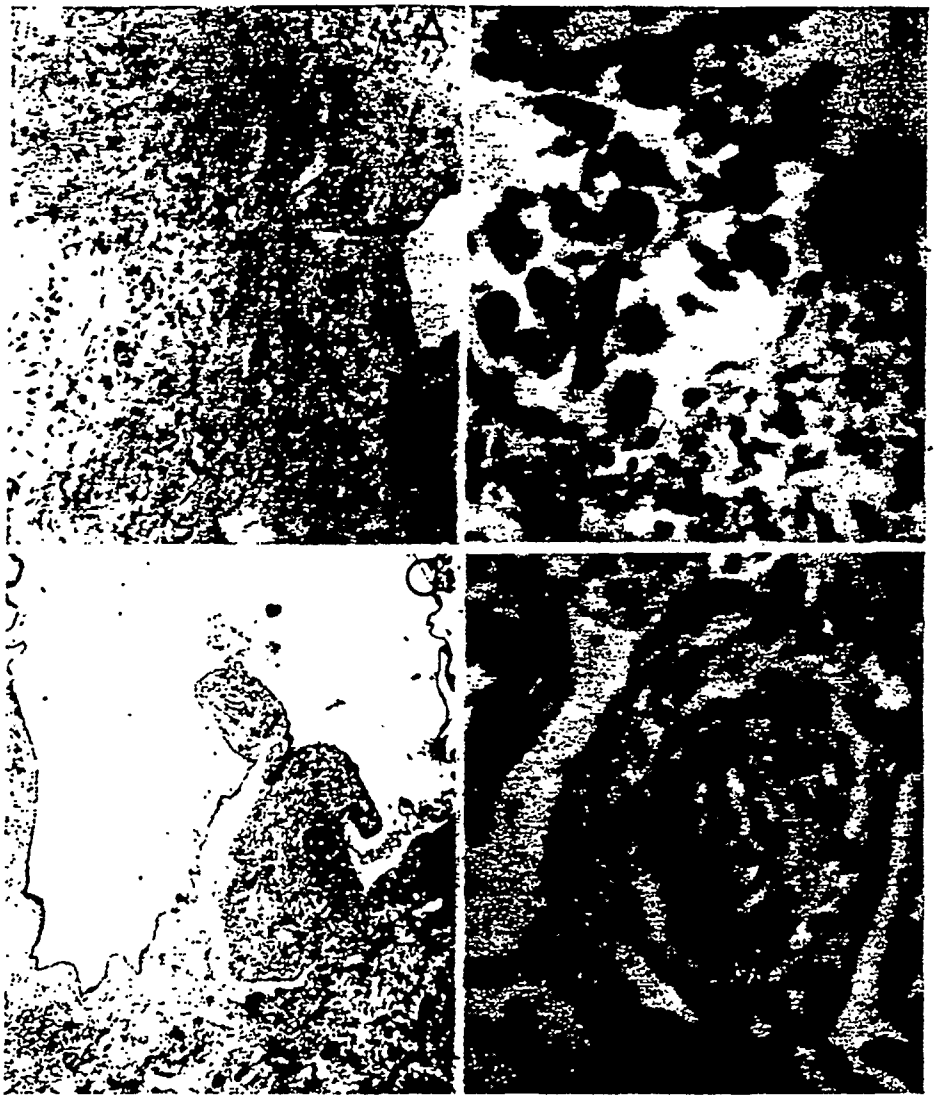

Fig 2.—Histological findings in a deceased 61-year-old asbestos insulator exposed to asbestos dust for 18 years: (*A*) Interstitial fibrosis with dust particles absorbed into the macrophages (×645). (*B*) Asbestos bodies located in the alveoli and interstitially (×645). (*C*) Bronchiolectasia (×52.5). (*D*) Endarteritis (×645).

more diffuse reticulonodular infiltration involving more than 50% of the total lung area. In addition to the pulmonary infiltration there was also a varying degree of obliteration of the costophrenic sinuses in 16 individuals and/or the cardiac borders in 10. Pleural calcification was observed in five instances. Two individuals showed emphysema which was localized to the left upper lobe in one and the right lower lobe in the other. There was no cardiac enlargement found in any of the cases.

Physiologic.—The values within the normal range for each parameter of pulmonary function studied are indicated by the *circles* within the *rectangles* shown in Fig 3. Those circles above and below the rectangles for both the control and asbestos groups lie outside the 95% confidence interval. Low values for vital capacity (less than 74.0% predicted) were found in 14 of the 21 asbestos workers. None in the control group had a value below 74.0%. The low values in the asbestos group ranged from 42.9% to 72.1%. Five of the asbestos workers had a one-second vital capacity less than 65.7% with a range of 57.8% to 65.2%. Only one in the control group had a low value, namely

TABLE 3.—*Clinical and Physiological Findings in Control and Asbestos Worker Groups*

	Controls		Asbestos Workers		Probability
No. in group	50		21		
Age (yr)					
Mean	49.2		54.5		NS
Range	35-63		39-77		
Clinical	No.	%	No.	%	
Cough	3	6.0	10	47.6	<0.01
Dyspnea	5	10.0	7	33.3	<0.05
Lung crepitations	0	0.0	8	38.1	<0.01
Clubbing	0	0.0	6	28.6	<0.05
Physiologic *					
VC (% pred)	101.1±1.9		69.2±3.8		<0.01
VC_1 (% VC)	78.7±0.9		76.3±2.2		NS
RV (% pred)	90.1±2.7		91.5±4.9		NS
TLC (% pred)	93.0±1.6		73.4±3.0		<0.01
RV/TLC (% pred)	93.6±2.0		120.2±4.4		<0.01
$D_{L_{CO}}$ (cc/mm Hg/min)	31.6±1.0		19.6±1.7		<0.01

* Expressed as mean values ± standard errors.

60.7%. Values for residual volume above 128.5% predicted were found in two of the asbestos group and in one individual of the control group. The two high values in the asbestos group were 129.3% and 139.5%. The single high value in the control group was 156.9%. Values for total lung capacity less than 69.8% predicted were found in eight of the asbestos workers. The low values ranged from 50.3% to 68.9%. Only one in the control group had a low value, namely, 69.4%. The ratio of residual volume to total lung capacity was above 122.2% predicted in eight of the asbestos group; the high values ranging from 126.2% to 180.5%. Two of the controls had abnormal values of 122.3% and 123.3%. Thirteen of the asbestos workers had a $D_{L_{CO}}$ less than 20.0 cc/mm Hg/min, and none of the controls had a value below this figure. Among the asbestos workers the low values ranged from 8.3 to 19.9 cc/mm Hg/min. The differences between the control and the asbestos worker groups are statistically significant for VC, TLC, RV/TLC, and $D_{L_{CO}}$, but not for VC_1 and RV.

Environmental.—The asbestos dust to which these workers were exposed was chrysotile and amosite asbestos. The only exposure data available were those on the duration of exposure in each instance. The minimum exposure was 14 years (case 8) and the maximum 55 years (case 2). The mean duration of exposure for the group was 29.2 years.

The data in Table 3 show that the asbestos workers as a group have a greater incidence of abnormal clinical and physiological findings referable to the respiratory system than do the persons in control group. The clinical picture characterized by cough, dyspnea, lung crepitations, and clubbing, although not diagnostic, is consistent with sustained exposure to asbestos dust. The positive radiological changes in the chest roentgenogram, characterized by reticulonodular shadowing, obscuration of the cardiac borders or costophrenic sinuses, or both, and the presence of pleural calcification are similar to what has been observed in previous studies of asbestos workers [1,3] and talc millers.[7]

It is of interest that none of the electrocardiograms or chest roentgenograms showed evidence of cor pulmonale even though a certain number of individuals had a long duration of exposure to asbestos dust, dyspnea, basal crepitations, and severe pulmonary infiltration on chest roentgenogram (cases 2, 11, and 21). In the absence of data on pulmonary artery pressures, cor pulmonale cannot be ruled out with certainty. Instances of high pulmonary artery pressure are found where the electrocardiogram is normal. It is noteworthy that Lavenne found no indications of cor pulmonale by electrocardiogram when there were no roentgenographic signs of cor pulmonale in coal workers pneumoconiosis.[8] With regard to pneumoconiosis, cor pulmonale usually occurs as a relatively late event.

With respect to the lung function parameters, the data in Table 2 show that the abnormal values are indicative of a restrictive breathing disorder and impairment in diffusion capacity. This is consistent with the observations reported by others in workers exposed for long periods of time to asbestos dust.[3,9] Other diseases, including scleroderma, sarcoidosis, and the Hamman-Rich syndrome can cause a similar functional impairment. The finding of such a functional lesion, coupled with a consistent chest roentgenogram and history of sustained exposure to asbestos dust, is strong evidence of asbestosis. Although the mean values of the lung function parameters, with the exception of vital capacity and diffusion capacity for the group of asbestos workers, fall within the 95% confidence limits for the control group, it can be seen from Fig 3 that an ap-

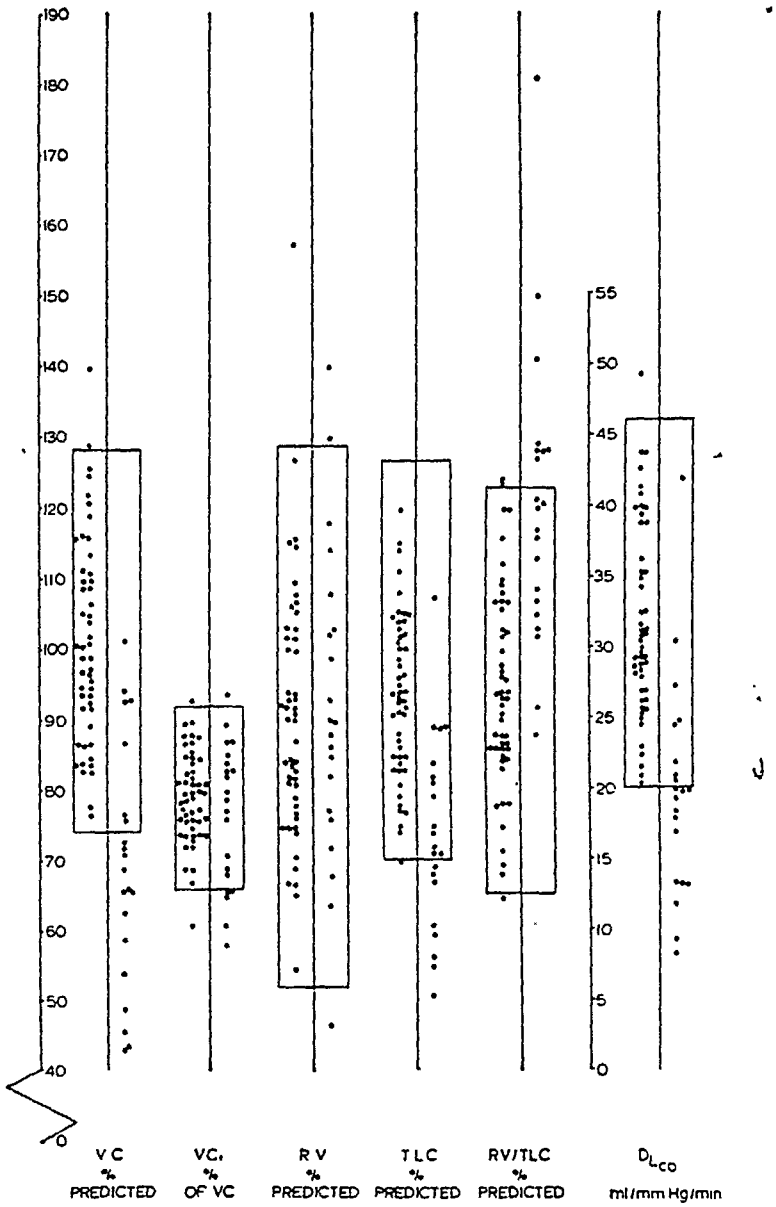

Fig 3.—The pulmonary function data observed in control and asbestos worker group are summarized. The values within the 95% confidence interval for each parameter of pulmonary function are indicated by the *circles* within the *rectangles*. Those *circles* above and below the *rectangles* represent abnormally high or low values respectively. The *shaded circles* identify the control group and the *open circles* the asbestos group.

preciable number of asbestos workers fall outside these limits. This is particularly evident for vital capacity, total lung capacity, ratio of residual volume to total lung capacity, and diffusion capacity. To a lesser extent, this is also observed in the one-second vital capacity. The high incidence of smokers probably accounts for this finding.

Relating the changes in lung function to the clinical and radiological findings it was observed that those with dyspnea and lung crepitations had a significantly lower mean vital capacity and total lung capacity than those in whom these findings were absent. The diffusion capacity was also appreciably lower in the group with lung crepitations. No relationship could be established between clubbing and changes in pulmonary function. It is of interest that Williams and Hugh-Jones [3] did find a good correlation between reduction in diffusion capacity and the grade of finger clubbing. These authors also noted a strong correlation between reduction in diffusion capacity and degree of pulmonary infiltration. Vital capacity and total lung capacity were also related to the severity in

radiological change but at lower levels of significance. Our study showed only a weak correlation between these lung function parameters and degree of pulmonary infiltration. In an extension of our study 16 of the 21 workers were compared with a group of 20 asbestos workers of statistically comparable mean and range of age and duration of exposure but having negative radiological findings. There were no significant differences in the clinical findings between the two groups, however, the lung function parameters showed an appreciably lower vital capacity, total lung capacity, and diffusion capacity in those with positive radiologic findings.[10]

Summary and Conclusions

Clinical, electrocardiographic, and physiological observations were made of 21 asbestos workers who had an average exposure to asbestos dust of 29.2 years and who had radiological findings compatible with asbestosis. Ten of the 21 workers had chronic cough, and seven evidenced exertional dyspnea. Basilar crepitations were found in eight, and six had clubbing. Electrocardiographic findings were abnormal in six but in none of these were the abnormalities consistent with the criteria of cor pulmonale. In eight individuals the pulmonary infiltration was minimal, in nine it was moderate, and in four it was classified as severe. Varying degree of obliteration of the costophrenic sinuses was observed in 16 and/or cardiac borders in 10. Pleural calcification was observed in five. Two individuals showed emphysema which was localized. The abnormal lung function findings were consistent with a restrictive breathing and diffusion capacity impairment. This was characterized by low values in vital capacity (14 persons), in total lung capacity in (8), and in diffusion capacity (13). The workers with dyspnea and lung crepitations had a significantly lower mean vital capacity and total lung capacity than those without these clinical findings. In addition, the group with pulmonary crepitations had a lower mean $D_{L_{CO}}$. There was a poor correlation between clubbing and vital capacity, total lung capacity, and diffusion capacity. There was a weak correlation between these lung function parameters and the degree of pulmonary infiltration. When 16 of the 21 asbestos workers were compared with a group of 20 asbestos workers of similar age and duration of asbestos exposure, but having negative radiological findings, there were no significant differences in the clinical findings between the two groups. There was, however, a significantly lower vital capacity, total lung capacity, and diffusion capacity in the group with positive radiological signs as compared with the group with negative roentgenograms.

Dr. Emanuel Levin of Maimonides Hospital of Brooklyn and the State University of New York, Downstate Medical Center, Brooklyn, NY, reviewed the chest roentgenograms. Dr. Harold Lepow of Lincoln Hospital and Albert Einstein College of Medicine, Bronx, NY interpreted the histological data. Mr. Jay Sarfaty of this Division assisted in the technical aspects of the program.

REFERENCES

1. Oosthuizen, S.F.; Theron, C.P.; and Sluis-Cremer, G.K.: Calcified Pleural Plaques in Asbestosis: An Investigation Into Their Significance, *Med Proc* (Mediese Bydroes) 10:496-501, 1964.

2. Heard, B.E., and Williams, R.: The Pathology of Asbestosis With Reference to Lung Function, *Thorax* 16:264-281, 1961.

3. Williams, R., and Hugh-Jones, P.: The Significance of Lung Function Changes in Asbestosis, *Thorax* 15:109-119, 1960.

4. Wright, G.W., and Gilford, S.R.: A Method for the Simultaneous Measurement of Maximum Breathing Capacity, Pulmonary Volumina and Effective Lung Ventilation, *J Thorac Cardiov Surg* 38:643-651, 1959.

5. Ogilvie, C.M., et al: A Standardized Breath Holding Technique for the Clinical Measurement of the Diffusing Capacity of the Lung for Carbon Monoxide, *J Clin Invest* 36(pt 1):1-17, 1957.

6. Needham, C.D.; Rogan, M.C.; and McDonald, I.: Normal Standards for Lung Volumes, Intrapulmonary Gas Mixing and Maximum Breathing Capacity, *Thorax* 9:313-325, 1954.

7. Kleinfeld, M., et al: Effect of Talc Dust Inhalation on Lung Function, *Arch Environ Health* 10:431-437, 1965.

8. Lavenne, F.: "Correlation Between E.C.G. Criteria, Clinical Manifestations and Necropsy Findings in Coal Miners' Pneumoconiosis," in Orenstein, A. J. (ed.): *Proceedings of the Pneumoconiosis Conference*, University of Witwatersand, Johannesburg, Feb 9-24, 1959, Boston: Little, Brown & Co., 1959, pp 237-241.

9. Bader, M.E.; Bader, R.A.; and Selikoff, I.J.: Pulmonary Function in Asbestosis of the Lung, an Alveolar-Capillary Block Syndrome, *Amer J Med* 30:235-242, 1961.

10. Kleinfeld, M., et al: The Effect of Asbestos Dust Inhalation on Lung Function, unpublished data.