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PULMONARY FUNCTION IN ASBESTOSIS: SERIAL TESTS IN A LONG-TERM PROSPECTIVE STUDY*

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INTRODUCTION

Studies of pulmonary function in asbestosis of the lung have been previously reported.¹⁻⁴ There is good agreement that the principal findings include reduced vital capacity, fairly well preserved maximum breathing capacity, hyperventilation at rest and particularly on exercise, decreased diffusing capacity of the lung, impaired oxygenation of the arterial blood, and reduced pulmonary compliance. No significant incidence of pulmonary emphysema has been reported.

All who did studies have had the same difficulty assessing the degree of exposure to asbestos dust, and both clinical and physiological data have varied with respect to duration of exposure. There is a lack of serial observations in asbestos workers. The present study was undertaken to follow several parameters of pulmonary function in a group of workers who had been exposed to asbestos dust and then had been withdrawn from further industrial exposure. Data were collected over a ten-year period, during which time clinical and radiological features were also followed. In 1954-1955 17 workers were made the subject of careful pulmonary function studies¹, and follow-up studies, varying from 1 to 3 subsequent studies, were made in 13. Additional observations on 21 asbestos workers were made with reference to pulmonary compliance to obtain information relative to vital capacity independent of patient performance. These data will be presented also.

MATERIALS AND METHODS

In 1954-1955 (see TABLE 1 for date of initial study), 17 workers from asbestos factories were studied.¹ Clinical symptomatology and lung involvement on radiographic examination varied. All patients had been exposed to asbestos dust for years (range 4 to 24 years; average 11½ years at that time).

In each case, a detailed history was elicited with particular reference to occupational exposure to asbestos dust or other offending agents which included the intimacy of contact with dust, duration of contact, degree of exertion (increased ventilation) of the workers, and concentration of dust in the inspired air. Severity of exposure was graded 1 to 4.¹

In addition to routine laboratory tests, search was made for asbestos

*Supported by the Robert S. Clark Foundation, New York, N. Y.

TABLE 1
SERIAL OBSERVATIONS OF PULMONARY FUNCTION

Case #	Date of Study Mo./Year	Vital Capacity %	Maximum Breathing Capacity %	Arterial O ₂ Saturation %		Air Velocity Index	Arterial pCO ₂ mm.Hg	pH
		Predicted	Predicted	Rest	Exercise			
1. J.P.	12/54	56	100	90	71	1.79	40	7.40
	10/61	46		93	82	1.76	40	7.41
	9/62	50	88	93	81		41	7.42
	12/63	43	85	93		1.98	42	7.40
2. R.J.	10/56	65	113	93	78	1.74	41	7.40
	11/61	34	62	87	65	0.94	36	7.40
3. N.C.	7/55	53	81	95	83	1.53	41	7.40
	2/61	42	63	92	80	1.50	45	7.39
	1/64	37	65	92	84	1.76	41	7.39
4. R.B.	8/55	86	131	93	36	1.49	42	7.40
	2/60			92	81		40	7.41
	9/62	72	141	91	80	1.96	42	7.40
5. M.G.	12/54	117	120	95	88	1.02	37	7.39
	12/59	100	94	94	92	0.94	43	7.39
	2/60	118	124			1.03		
	11/61	104	106	97	91	1.02	35	7.43
	11/62	63	112	97	86	1.79	36	7.43
	11/63	63	92	94	82	1.47	39	7.42
6. M.R.	12/54	77	120	93	88	1.56	43	7.41
	2/60	77	100	94		1.30	38	7.42
	2/62	65	59			1.33		
7. S.Mc.	12/54	71	113	94	90	1.39	41	7.41
	1/60	56	79	95	91	1.41	39	7.40
8. T.H.	10/55	97	98	96	91	0.91	43	7.39
	1/60	79	93	94	91	1.18	41	7.40
	11/62	81	77	94	92	0.95	39	7.42
9. A.C.	2/55	98	88	97	92	0.90	38	7.41
	2/60	81	124	94	92	1.53	36	7.42
	11/62	77	78	97	91	1.01	36	7.42
	9/64	70	79			1.13		
10. T.W.	10/56	90	106	95	92	1.18	40	7.39
	6/63	81	89	94	94	1.11	40	7.40
12. H.S.	8/55	65	101	95	95	1.55	40	7.40
	10/62	74	88	96	94	1.08	40	7.40
13. A.F.	5/55	107	87	98	95	0.81	40	7.38
	4/59	61	87			1.43		
	2/60	82	81			0.69		
15. J.P.	10/55	81	118	96	95	1.46	42	7.41
	10/62	72	73	96	92	1.02	37	7.42

TABLE 2
CLINICAL STATUS, X-RAY FEATURES, AND COURSE IN 17 PATIENTS WITH
PULMONARY ASBESTOSIS

Patient	Status 1954-1955					1964			Comment
	Years onset	Age	X-ray	DOE*	Club†	X-ray PROG‡	DOE PROG	Club PROG	
1. J.P.	14	48	3	2	3	1 (1959)	1 (1959)	0	Working regularly 1964 no significant change 1959-1964
2. R.J.	12	43	4	3	3	2	2	0	Died cor pulmonale 1962
3. N.C.	11	35	3	3	3	0 (1963)	1 (1963)	0	Not able to work now
4. R.B.	10	66	3	0	0	1	0	0	Died 1963; Carcinoma of stomach
5. M.G.	13	42	1	2	3	2 (1964)	2 (1964)	0	Carcinoma of lung- segmental resection; recent progression other side with increase DOE.
6. M.R.	11	67	2	2	0	0	0	0	Died Carcinoma of lung 1963
7. S. Mc.	10	62	1	4	2	2	1	0	Died Asbestosis 1961
8. T.H.	24	46	1	1	1	0	0	0	Working regularly
9. A.C.	13	36	2	0	1	0	0	0	Working regularly
10. T.W.	6	51	2	1	0	0	0	0	Working regularly
11. G.R.	13	48	2	3	3	-	-	-	Died 1958 Carcinoma of lung
12. H.S.	13	63	1	0	0	0	0	0	Coronary; DOE now 2+
13. A.F.	11	67	3	0	0	0	2	0	Died coronary 1962
14. W.S.	7	37	0-1	1	0	-	0 No change to 1959 in X-ray	-	Not seen since 1959 but known to be well
15. J.P.	4	38	0-1	0	0	0	0	0	Working regularly
16. C.D.	10	62	1	4	2	2	1	0	Died Mesothelioma (Carcinoma 1959)
17. J. Pet.	12	58	0-1	0	0	Deceased			Died 1956 of carcinoma of stomach

*DOE = Dyspnea of Exertion.

†CLUB = Clubbing.

‡PROG = Progression.

Numbers in the columns labeled X-ray and DOE are based on a grading of 1 to 4.1

bodies in 14 of the 17, at least once, and all sputa were cultured for tubercle bacilli. A routine electrocardiogram and PA chest film were obtained. The latter were graded from 1 to 4+ based on criteria previously reported.¹ Measurement of lung volumes, maximum breathing capacity, index of intrapulmonary mixing, arterial oxygen saturation, and carbon dioxide content were carried out according to the methods of Baldwin, Cournand, and Richards.² The partial pressure of oxygen in the arterial blood was measured by the direct technique of Riley, Proemmel, and Franke,¹⁰ and the ventilation perfusion relations and diffusing capacity of the lung were determined by the method of Riley and Cournand.^{11,12} From the analysis, data for physiological dead space, venous admixture, and diffusing capacity of the lung were obtained.

Of these 17 men, follow-up studies were obtained on 12, listed by number in TABLE 1. The status in terms of X-ray, dyspnea on exertion and clubbing are listed in TABLE 2, with any changes between 1954-1955 and 1964 noted. The clinical fate and reason for loss to follow-up are shown in the right-hand column of the Table. As may be seen, eight are now dead — one of cor pulmonale, two of carcinoma of the lung, two of carcinoma of the stomach, one of asbestosis, one of coronary occlusion, and one of pleural mesothelioma. Of the living, six are working, one had surgery for carcinoma of the lung, one had a coronary occlusion, and one is unable to work.

It was decided to follow these patients with ventilometric measurements and arterial blood gas studies. In 4 of the 13 cases followed, residual volume measurements were repeated. Data on the 13 patients are listed in TABLE 1.

In 21 cases of asbestosis dynamic pulmonary compliance was measured 22 times by the method of Mead and Whittenberger.¹³ No serial data are presented on these parameters.

RESULTS

Initial Observations

Initial observations carried out in 1954-1955 on the 17 patients have been reported in detail.¹ For convenience the data are shown in FIGURES 1 and 2. These results may be summarized as follows: Vital capacity was well preserved in half the patients and moderately reduced in the remainder. Residual volume was not significantly altered except for a slight increase in six patients. The ratio of residual volume to total capacity was normal in all but two patients. Maximum breathing capacity was well preserved in all cases. Analysis of ventilation-perfusion relationships revealed normal intrapulmonary mixing of gases (by the residual nitrogen technique) in all but three subjects, in whom it was reduced. Hyperventilation was present at rest and exercise in the majority of patients. Arterial

oxygen saturation was slightly reduced in 6 patients at rest and lower than 92 per cent on exercise in 10 patients. While dead space ventilation (expressed as per cent of minute ventilation) exceeded the upper limits of normal in 12 patients, alveolar ventilation was increased in absolute terms, and in no case was it decreased. The diffusing capacity of the lung for oxygen was measured in five patients at rest. In four of these, it was reduced. In addition, in four of these five subjects venous admixture was increased. The abnormalities correlated poorly with intimacy and duration of exposure. A better correlation was found when compared with radiological findings.

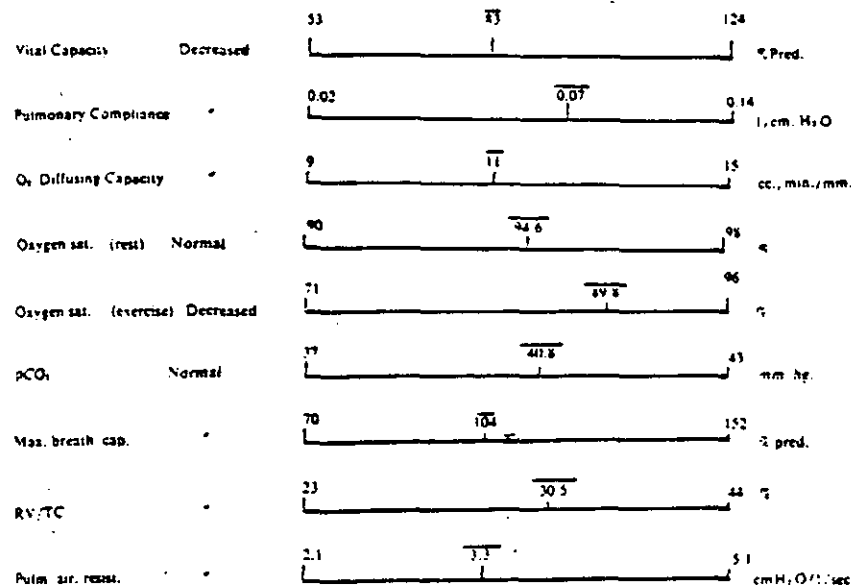


FIGURE 1. Summary of initial observations of pulmonary function in 17 cases of asbestosis.

Follow-up Studies

These are observations made after withdrawal of the patient from industrial exposure, and reflect the natural history of the asbestosis of the lung already present.

Vital Capacity

Vital capacity data expressed as per cent of predicted are presented for

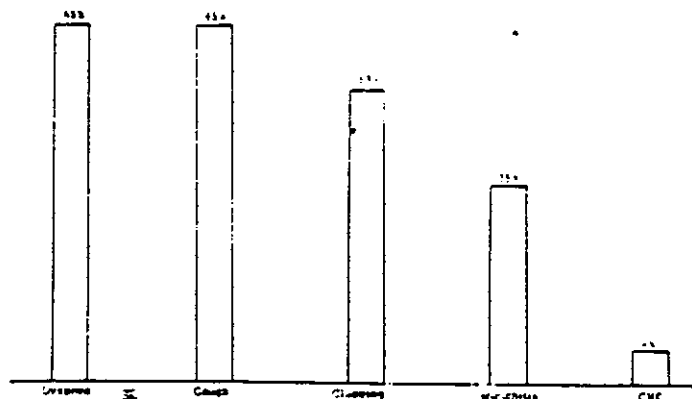


FIGURE 2. Clinical features in 17 patients with pulmonary asbestosis.

the 13 patients available to follow-up in TABLE 1, and in FIGURE 3. In 12 of the 13 there was a fall in vital capacity ranging from 9 to 31 per cent expressed as per cent of predicted. In one case, it rose 9 per cent. The average fall was 18 per cent, which is in excess of what may be expected from aging alone. In the original study, nine patients had a vital capacity above 80 per cent of predicted (maximum 117 per cent), six ranged between 60 and 80 per cent, and two had less than 60 per cent. In the last follow-up studies, only three had volumes in excess of 80 per cent, and four below 60 per cent.

Maximum Breathing Capacity

Maximum breathing capacity data expressed as per cent predicted are presented in TABLE 1 and FIGURE 4. Of the 13 patients followed, the maximum breathing capacity fell in 12. The fall ranged 6 to 51 per cent (average 21 per cent) with a rise in one patient of 10 per cent. In the original 17 patients, the maximum breathing capacity exceeded predicted figures in 10, and ranged between 88 and 150 per cent in the remaining 7 cases. In the last obtained serial studies, maximum breathing capacity exceeded predicted in only one, ranged between 80 and 99 per cent in six, between 60 and 80 per cent in another six.

Air Velocity Index

Because of the fall in maximum breathing capacity (see TABLE 1 and FIGURE 5), calculation was made of the air velocity index $\left(\frac{\% \text{ MBC}}{\% \text{ VC}}\right)$ to determine if there was evidence of a fall in this index, and in how many cases

it fell below one. In the 13 patients serially studied, the original air velocity index was greater than one in ten patients, and less than one in three. Of the three with air velocity indices of less than one, all rose — two to greater than one, and one remained below one with an insignificant rise. Of the 10 patients with air velocity indices greater than 1 it rose in 4, and fell in 6 (only in one case did it fall below 1).

Arterial Blood Gases

1. *Arterial oxygen saturation at rest* (see TABLE 1, FIGURE 6). There was no significant trend in oxygen saturation at rest. Of the 13 patients, 8 had an initial value of 95 per cent or greater, one of 94 per cent, three of 93 per cent, and one of 90 per cent. On follow-up study, there was a fall in seven, but the only noteworthy ones were 93 to 87 per cent (patient died of cor pulmonale), 93 to 91 per cent, and 95 to 92 per cent. All others were insignificant. In the remaining six, arterial oxygen saturation at rest either

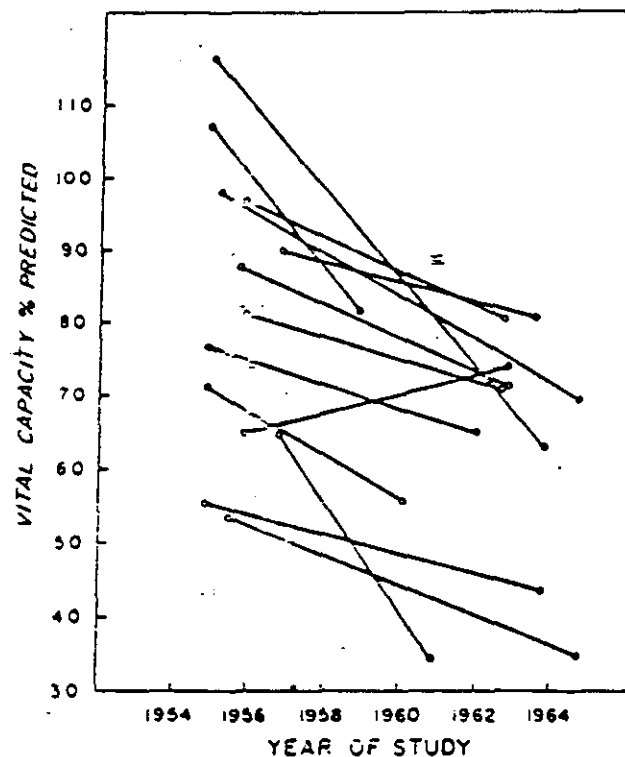


FIGURE 3. Changes in vital capacity of 10 year period.

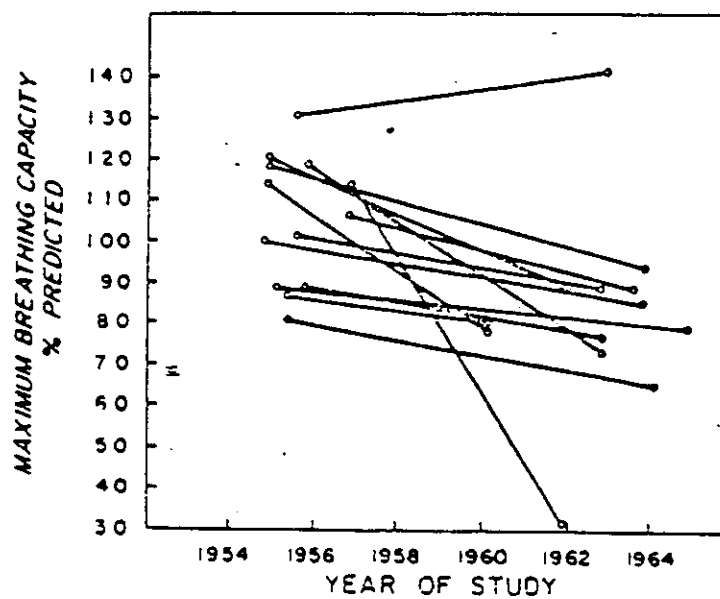


FIGURE 4. Changes in maximum capacity over 10 year period.

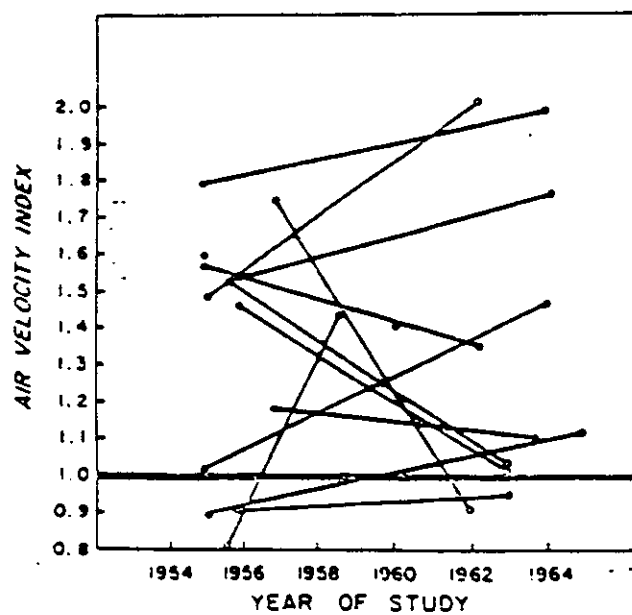


FIGURE 5. Changes in air velocity index over 10 year period.

rose or remained unchanged, the only noteworthy rise being 90 to 93 per cent.

2. *Arterial oxygen saturation on exercise.* Of the original 17 patients, in 10 the arterial oxygen saturation on exercise was 92 per cent or less. At the conclusion of the initial study¹, it was thought that this would be

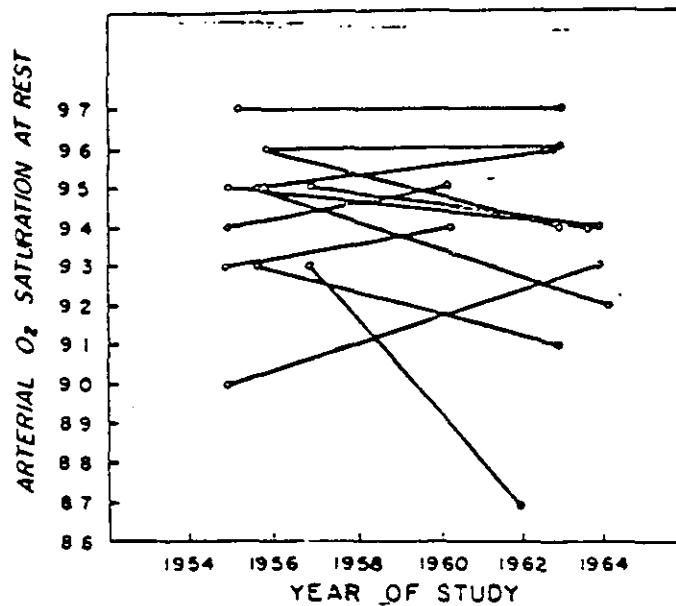


FIGURE 6. Changes in arterial oxygen saturation at rest over 10 year period.

perhaps a valuable and sensitive index of progression of the disease. In TABLE 1 and FIGURE 7 one can see that 7 (of 13) had no significant change, three fell (88 to 82 per cent, 86 to 81 per cent, and 78 to 65 per cent, the last dying of cor pulmonale shortly after the study). In one there was a significant rise from 71 per cent to a still quite abnormal 81 per cent. In the time period of the study there was no distinct downward trend of the arterial oxygen saturation on exercise.

3. *Arterial carbon dioxide tension* (see TABLE 1). There was no significant hypercapnia in these patients originally or in final study. $p\text{CO}_2$ values did not change significantly in the initial and final studies.

4. *Arterial pH* (see TABLE 1). Arterial pH remained essentially unchanged throughout the study.

Residual Volume

In the original studies on 17 patients, the residual volume did not differ

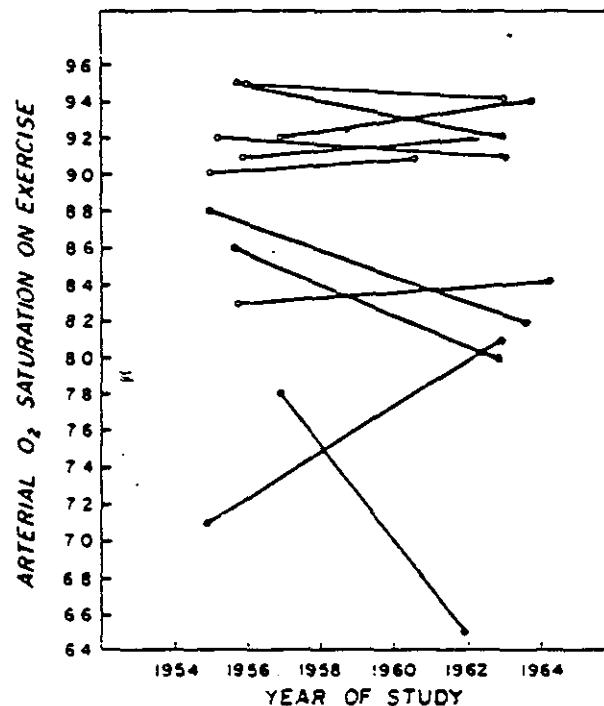


FIGURE 7. Changes in arterial oxygen saturation on exercise over 10 year period.

significantly from the predicted figure in 10 cases. In six, it exceeded the predicted figure by 20 per cent or more. The ratio of residual volume to total capacity, however, was within normal limits in all but two patients. In four cases (#1, #5, #7, #9) studied serially, residual volume increased in two. The ratio RV:TC, increased in all four. Indeed in only one was it within normal limits on the final follow-up study. It should be noted that in only one (case #1) was there a marked increase in residual volume to account for the increase in RV:TC ratio. The changes in RV:TC ratio were markedly influenced by the fall in VC, rather than by a rise in residual volume.

Pulmonary Compliance

In 21 asbestos workers, measurements were made of pulmonary compliance 30 times. On the same visit, vital capacity was measured. Compliance

is compared with vital capacity in FIGURE 8. Inspection of FIGURE 8 reveals a linear relation between vital capacity and pulmonary compliance.

DISCUSSION

Pathologically,¹⁴ asbestos particles lodge particularly in the vestibular area of the lobules and elicit a fairly uniformly distributed diffuse (non-nodular) fibrosis. It is not surprising, therefore, that previous investigation has established that the physiological changes encountered are those of the alveolar-capillary block syndrome.^{1,4,15} Almost all reports have demonstrated decreased vital capacity,^{1,16} fairly well preserved breathing capacity,^{1,2,1} impaired oxygenation of the blood^{1,4} due to decreased diffusing capacity,^{1,4} and increased rigidity of the lung as measured by decreased pulmonary compliance.^{3,3,16} What have been lacking are data on patients followed over a several year period in which there was no industrial exposure.

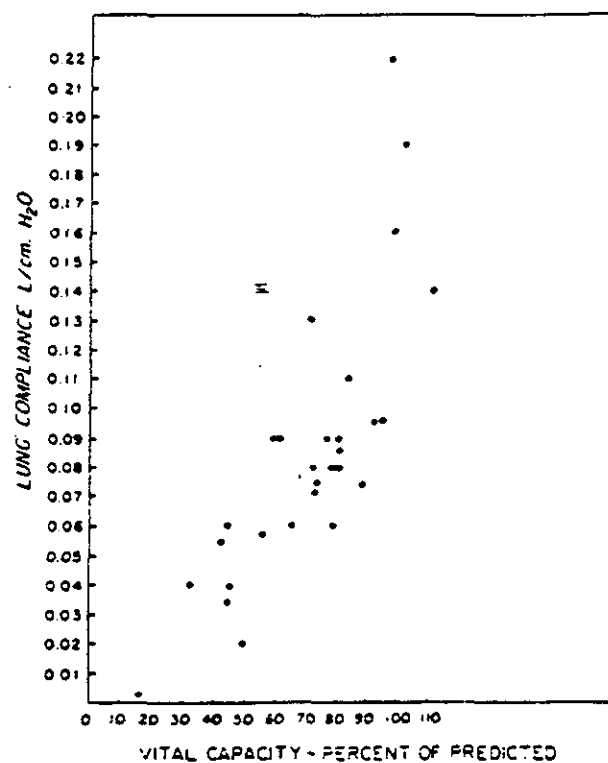


FIGURE 8. Correlation of vital capacity and pulmonary compliance in patients with asbestosis of the lung.

The principal change encountered in the present study was the uniform finding of a significant reduction in vital capacity compared with initial studies in 1954-1955. It was previously demonstrated that the reduction in vital capacity correlated poorly with intimacy of exposure.¹ Better correlation existed with regard to radiological findings.¹ Analysis of the data in TABLES 1 and 2, comparing the reduction in vital capacity in the initial and final studies with X-ray progression, reveals good correlation in six, fair in two, and poor in five. Poor correlation in almost every case meant a reduction in vital capacity without evidence of X-ray progression. Similarly, about half of the patients had good correlation with progression of dyspnea on exertion but fair or poor correlation in the remainder, vital capacity again being reduced without significant progression of dyspnea.

There are two possible explanations of the fall in vital capacity without significant change in the radiological or clinical picture in half these cases of asbestosis of the lungs: (1) It is a more sensitive index of pulmonary involvement than either the X-ray or clinical symptoms and (2) the data may reflect poor patient cooperation.

Taking the first possibility, it has been previously shown that correlation of reduced vital capacity with X-ray is only fair.¹ Furthermore, significant pathological alteration may exist without evident radiological changes.¹² Indeed roentgenographic diagnosis and differential diagnosis can be very difficult.¹² With regard to the second possibility, the data on the 21 patients in whom pulmonary compliance data are available demonstrate a good correlation between vital capacity and dynamic pulmonary compliance. The latter test does not involve patient performance cooperation, other than breathing differing tidal volumes. This lends great weight to the validity of the vital capacity measurements and suggests the view that it is an accurate and more sensitive index of pulmonary involvement than the clinical or radiographic features.

Arterial oxygen saturation on exercise in the original studies on 17 patients,¹ although found to be a sensitive index of impairment, did not show a uniform pattern of change in follow-up studies despite fair correlation with X-ray and dyspnea on exertion in about half the patients. Furthermore, vital capacity fell much more often than the oxygen saturation on exercise. Needless to say the vital capacity is a simpler and more convenient test to perform.

With regard to the question of the development of ventilatory changes, it is clear that the maximum breathing capacity values, while reduced compared to the initial observations in 1954-1955, are in the range expected in alveolar-capillary block cases. Other studies have also stressed the maintenance of the maximum breathing capacity. In our series the only marked fall was in one patient who died of cor pulmonale shortly after the study. Analysis of the air velocity index (AVI) reveals that the majority rose

be uniform with initial reduction or correlation of the data the initial fall in six cases meant less reduction. Similar reduction of arterial oxygen saturation, vital capacity, and dyspnea without change in these cases of pulmonary function the data

correlation significant changes.¹⁷ can be very good correlation. The other than the validity of it is an initial

on 17 patients not show correlation. Further reduction on convenient

changes, reduced compared expected the main marked the study. only rose

during the follow-up period and that only one patient had an AVI of less than one in the final studies. Further evidence against emphysematous changes is available in the large number of studied cases in whom evidence against an emphysematous pattern of pulmonary function is presented.^{12,13} The only significant exception is the report of Bastenier *et al.*,¹⁸ but five of these nine patients had chronic bronchitis. Finally in none of our cases did any significant hypercapnia or acidosis appear.

No serial measurements were made of the diffusing capacity of the lung in our series, and it is impossible for us to conclude that the vital capacity is superior to the diffusing capacity as an index of progression of asbestosis of the lung. The finding, however, that the arterial oxygen saturation on exercise showed no significant downward trend would support the view that if changes in diffusing capacity did occur as frequently as the reductions in vital capacity, they were not sufficient to be reflected in oxygenation of the arterial blood on exercise. We can conclude that the vital capacity is the most sensitive index of progression of the parameters we studied. Needless to say, the vital capacity is the most accessible, easily applied, and repeatable technique available.

SUMMARY AND CONCLUSIONS

1. In 1954-1955, pulmonary physiological studies in 17 asbestos workers revealed the characteristic pattern of alveolar-capillary block syndrome. These patients were withdrawn from industrial exposure.

2. Of these 17 patients, 13 were available to follow-up study up to 10 years after the initial observation. Eight are now dead — one of cor pulmonale, two of carcinoma of the lung, two of carcinoma of the stomach, one of asbestosis, one of coronary occlusion, and one of mesothelioma. Of the living, six are working, one had surgery for carcinoma of the lung, one had a coronary occlusion and is unable to work.

3. Follow-up measurements were made in 13 patients. These included vital capacity, maximum breathing capacity, arterial oxygen saturation at rest and with exercise, and arterial pCO_2 and pH .

4. During the period of the study, vital capacity was found to be reduced significantly in 12 of the 13 patients. There was also a fall in maximum breathing capacity, but in general they remained relatively well preserved. Air velocity indices showed an upward trend in more than half, and in only one was the air velocity index slightly less than one.

5. There was no significant trend in the arterial oxygen saturation at rest or on exercise. Arterial pCO_2 and pH remained essentially unchanged.

6. The fall in vital capacity correlated well in about half of the cases with progression of X-ray findings and progression of dyspnea on exertion. In the remainder, vital capacity fell in almost all, without significant progression of radiological features or clinical symptoms.

7. The reduction in vital capacity correlated well with reduction in pulmonary compliance in 30 observations on 21 patients with asbestosis. This would indicate that the reduction in vital capacity is not a consequence of poor patient performance.

8. While diffusing capacity was not measured, the arterial O_2 saturation on exercise did not demonstrate changes parallel to the fall in vital capacity observed.

9. It is concluded that of the parameters here studied, vital capacity was the most sensitive index of progression of the disease. Its ease of application, availability, and repeatability all recommend it for use in the frequent assessment of workers exposed to asbestos dust.

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