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Cardiopulmonary function studies in workers dealing with asbestos and glasswool¹

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Pulmonary fibrosis is thought to be a common complication of exposure to asbestos dust. The inhaled asbestos fibres are supposedly not transported by the pulmonary lymphatics, and thus one single massive exposure might lead to the same stage of fibrosis as a prolonged but less intense exposure.

This industrial hazard has led to the search for substitutes for asbestos in insulation work, and at present glasswool and rockwool are often used. The fragmentation of these materials may give rise to fibre particles which can be inhaled and deposited in the alveoli. The possible effect on cardiopulmonary function in a group of men doing insulation work, with prolonged exposure to glasswool and rockwool dust, is the subject of the present paper, and a similarly exposed group of asbestos workers was studied for comparison.

MATERIAL

These men have regular routine medical examinations. All the subjects in this study, which formed part of a general survey, were gainfully employed male insulators who volunteered. Their employment records were carefully studied in an effort to evaluate the kind of dust to which they had been exposed. Group A consisted of eight subjects whose exposure to asbestos dust comprised at least 50% of their employment time. In all subjects the chest radiographs suggested asbestosis, and two patients complained of cough and exertional dyspnoea. Six subjects were selected who had had prolonged exposure to glasswool and rockwool but only minimal exposure to asbestos dust (group B). They had no history of cardiopulmonary disease. Physical findings and chest radiographs were considered normal.

Clinical, radiological, and occupational data are recorded in Table I.

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METHODS

Dynamic spirometry was performed, as described by Berglund, Birath, Bjure, Grimby, Kjellmer, Sandqvist, and Söderholm (1963).

Functional residual capacity (F.R.C.) was determined in the supine position, using an open-circuit nitrogen wash-out technique (Lundin and Åkesson, 1954). The volume required to wash out the nitrogen from 1 litre F.R.C. to an end-tidal concentration of 2%, lung clearance index (L.C.I.), was calculated from these records (Becklake, 1952).

Electrocardiography was performed using five chest electrodes (CR) and the conventional limb leads as well as aVR, aVL, and aVF. Physical performance was studied on a bicycle ergometer as described by Sjöstrand (1947). The heaviest work load which could be maintained in a steady state, as judged from the heart rate, was used as an index of the physical performance (Grimby and Söderholm, 1963).

Heart catheterization was performed in the morning after a light meal. A double-lumen catheter (no. 9) was wedged in a pulmonary artery (P.C.V. position) with the proximal lumen in the pulmonary artery. Brachial artery pressure was recorded from an indwelling polythene tube. Pressures were recorded with strain-gauge manometers on a six-channel direct-writing recorder. A point 5 cm. dorsal to the sternal angle was used as zero reference level. Mean pressures were measured by electrical integration. Cardiac output was estimated according to Fick's direct principle.

Gas analyses and measurements of oxygen saturation and oxygen capacity were performed as described by Holmgren and Pernow (1959). The oxygen tension in arterial blood was determined by the potentiometric method described by Gleichmann and Lübbers (1960). The alveolo-arterial difference in oxygen tension was calculated from the alveolar air equation and the arterial oxygen tension. Venous admixture to arterial blood was calculated in per cent of cardiac output, assuming an end-capillary oxygen saturation of 98%.

After introduction of the catheters the subjects were allowed to rest for 30 minutes. Pressures and flows were then studied in the supine position. All measure-

⁴ Mingograph, Elma

TABLE I

Subject No.	Age	Height (cm.)	Pleural Thickening	Streaking Mottling	Dyspnoea	Working Capacity (kpm./min.)	Pulse Rate	Respiratory Rate	Occupational History
1	29	167	—	—	—	600	124	30	11 yr. almost exclusively rockwool and glasswool; minimal exposure to asbestos
2	37	191	—	—	—	1,200	157	30	22 yr. exclusively rockwool and glasswool; no exposure to asbestos
3	41	171	—	—	—	600	128	20	25 yr. almost exclusively rockwool and glasswool; minimal exposure to asbestos
4	37	177	—	—	—	900	150	28	8 yr. exclusively rockwool and glasswool
5	43	187	—	—	—	1,200	162	28	29 yr. Since 15 yr. no exposure to asbestos but has earlier been moderately exposed to asbestos
6	45	178	—	—	—	900	172	28	11 yr. almost exclusively rockwool and glasswool; minimal exposure to asbestos
7 ¹	48	180	+	+	—	900	154	35	30 yr. exposure to both asbestos and rockwool
8	50	168	+	+	+	950	152	40	25 yr. exposure to both asbestos and rockwool
9	40	188	+	+	—	600	120	28	10 yr. mostly exposure to asbestos but has used face mask
10	33	173	+	—	—	1,200	180	44	11 yr. mostly exposure to asbestos but has used face mask
11	51	172	+	—	—	900	165	28	30 yr. mostly exposure to asbestos
12	49	165	+	+	—	900	165	30	22 yr. mostly exposure to asbestos
13	47	168	+	+	+	600	130	36	7 yr. mostly exposure to asbestos
14	46	164	+	+	—	600	115	28	9 yr. mostly exposure to asbestos (mattresses)

¹ Scoliosis of thoracic spine. + Pleural and/or diaphragmatic calcifications.

TABLE II
PULMONARY FUNCTION STUDIES

Subject No.	V.C. (l.)		F.E.V. ₁₋₂ (l.)		F.E.V.%		N ₂ Difference	F.R.C.	L.C.I.	D _{lco}
	Found	Predicted	Found	Predicted	Found	Predicted				
Group B										
1	4.68	4.67	3.96	3.84	85	81	0.9	—	—	19.6
2	5.76	5.64	3.83	4.37	66	75	1.8	3.02	9.0	30.1
3	4.55	4.55	3.44	3.31	76	77	0.9	1.76	7.8	21.7
4	4.86	4.97	2.92	3.58	60	78	2.1	1.98	6.3	20.2
5	4.76	5.29	3.39	3.97	71	75	2.5	2.59	9.0	29.4
6	4.52	4.88	3.44	3.69	76	76	1.4	2.44	7.8	22.2
Group A										
7	4.42	4.89	2.92	3.63	66	74	1.8	2.36	10.6	9.4
8	2.69	4.27	1.96	3.14	73	73	—	—	—	15.2
9	4.03	5.44	3.31	4.17	82	77	6.5	3.31	8.3	17.3
10	3.08	4.84	2.69	3.61	87	79	0.9	1.99	10.2	21.2
11	3.83	4.43	2.22	3.22	58	73	5.4	3.07	11.8	11.8
12	3.35	4.29	2.64	3.18	78	74	0.8	2.76	7.0	15.0
13	3.44	4.31	2.07	3.21	86	74	1.5	1.88	11.3	11.5
14	2.90	4.16	2.30	3.14	79	75	6.3	2.05	8.8	21.9
Mean values										
Group B	4.86	101%	3.50	90%	72	78	1.6	2.36	7.6	23.9
Group A	3.47	76%	2.63	76%	76	75	3.3	2.45	9.71	14.2
P-values for difference A-B	<0.01		<0.01		>0.05		>0.05	>0.05	>0.05	<0.01

V.C. = vital capacity (l. A.T.P.S.) sitting. F.E.V.₁₋₂ = forced expired volume in 1 sec. (l. A.T.P.S.) sitting. F.E.V.% = forced expired volume in 1 sec. in per cent of vital capacity. N₂ difference = 'single breath' difference in expired N₂ content between 750 and 1,250 ml. F.R.C. = functional residual capacity (l. B.T.P.S.) supine. L.C.I. = lung clearance index (litres of total ventilation per litre of F.R.C.). D_{lco} = pulmonary diffusing capacity for carbon monoxide (ml./min. × mm. Hg).

ments were made under steady-state conditions, as judged by pulse rate and pressures. Haemodynamic data were studied during rest only in group B and during rest and exercise in group A.

The diffusing capacity of the lung was determined at rest using the steady-state carbon monoxide method described by Filley, Macintosh, and Wright (1954), modified according to Linderholm (1957). Carbon monoxide was analysed in a hopcalite apparatus (Silex). The carbon monoxide content of arterial blood was determined after release of CO by sulphuric acid in an extraction chamber.

RESULTS

Table II gives details of the pulmonary function studies. The predicted values have been calculated according to Berglund *et al.* (1963). Group B showed completely normal values in all respects.

In group A the dynamic function tests revealed a marked restriction, and the diffusing capacity for carbon monoxide was reduced. However, there were no signs of increased airway resistance, as judged from F.E.V.% nor any indications of

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impaired distribution of the inspired air, as judged from the lung clearance index and single-breath N_2 test.

Physical performance (Table I) was comparable in the two groups. In only one subject (no. 13) in group A was there any reason to suspect a limitation of the working capacity because of impaired ventilation. However, all subjects in group A had a tendency to use a higher respiratory rate at a given work load than the subjects in group B.

Table III shows the haemodynamic data. Also from this table it is evident that the abnormal findings are confined to group A. Even though the average pulmonary artery pressure is not definitely raised for the whole group, the difference between groups is significant, as is the difference in calculated pulmonary vascular resistance.

The respiratory data are given in Table IV. When comparing the two groups there is a significant difference only in the arterial oxygen tension and the alveolo-arterial oxygen tension difference. However, the lowest oxygen saturations, as well as the highest V_D/V_T and Q_2/Q_1 , are found in group A.

In both groups some subjects (nos. 4, 6, 7, and 12) had a low arterial PCO_2 at rest. This has been interpreted as being due to anxiety. The normal value during exercise in subject 12 gives some support to this interpretation.

In subject 8 essential hypertension might be suspected because of the increased brachial artery pressure and systemic vascular resistance.

Electrocardiography revealed in group B only one subject with signs suggestive of right ventricular hypertrophy (R.V.H.) but here the pulmonary artery (P.A.) pressure was normal. In group A two subjects had the E.C.G. pattern of R.V.H.; one had a normal P.A. pressure at rest whereas the other had pathologically raised pressures both at rest and on exercise. Three other subjects had signs suggestive only of R.V.H. Of these only one had an abnormally raised P.A. pressure at work. One subject with pulmonary hypertension at rest had a normal E.C.G.

In view of the difference between the two groups these findings indicate that electrocardiographic signs of right ventricular hypertrophy in a subject exposed to asbestos dust would indicate the necessity for further cardiopulmonary function studies.

TABLE III
HAEMODYNAMIC DATA

Subject No.	Brachial Artery			P.C.V.	Pulmonary Artery			R.A.	S.V.R.	P.V.R.	(a-v) O_2	C.O.	H.R.	S.V.
	Systolic	Diastolic	Mean		Systolic	Diastolic	Mean							
Group B														
1	122	73	92	—	—	—	—	—	—	—	—	—	69	—
2	128	77	101	13	27	13	18	—	17.1	0.8	51	5.9	64	92
3	117	72	93	4	15	7	8	0	20.7	0.9	44	4.5	63	66
4	110	61	81	5	15	4	9	—	13.5	0.5	45	6.0	65	88
5	130	76	93	5	20	8	13	1	11.1	1.0	40	8.4	73	115
6	130	81	104	3	16	4	8	2	15.8	0.8	36	6.6	70	94
Group A														
7	135	79	106	6	25	7	15	1	15.6	1.3	41	6.8	54	126
8	172	104	132	13	38	17	25	4	29.3	2.7	47	4.5	63	66
9	147	73	90	5	27	3	13	1	7.7	0.7	25	11.7	98	119
10 R	117	62	93	7	25	6	16	0	14.8	1.4	37	6.3	80	74
10 E	141	77	96	5	44	14	23	0	8.9	1.7	79	10.8	103	100
11 R	134	76	100	4	29	7	15	0	17.5	2.0	44	5.7	78	75
11 E	166	91	123	7	35	11	21	0	14.5	1.7	101	5.5	110	125
12 R	128	84	103	3	22	9	16	2	18.1	2.3	48	5.7	82	70
12 E	160	100	123	3	20	22	33	2	13.5	—	102	9.5	114	81
13 R	129	76	96	5	22	7	13	0	16.3	1.4	37	5.9	65	83
13 E	143	81	105	10	32	10	19	0	9.5	0.8	78	11.1	102	107
14 R	143	84	113	12	32	11	21	4	21.6	1.8	42	5.2	64	82
14 E	190	109	150	17	60	23	33	—	14.3	2.0	92	10.5	102	103
Mean values at rest														
Group B	123	73	94	6	19	7	11		15.6	0.5	43.2	6.3	67	92
Group A	139	81	104	7	28	8	17		17.6	1.7	40.1	6.5	74	88
P-values for difference A-B			>0.05	>0.05			<0.05		>0.05	<0.05	>0.05	>0.05	>0.05	>0.05

All pressures are given in mm. Hg. P.C.V. = pulmonary artery wedge pressure. R.A. = right atrium pressure. S.V.R. = systemic vascular resistance ($\frac{P_{S.A.} - P_{C.V.}}{CO}$, mm. Hg./l./min.). P.V.R. = pulmonary vascular resistance ($\frac{P_{P.A.} - P_{C.V.}}{CO}$, mm. Hg./l./min.). (a-v) O_2 = arterio-venous oxygen difference (ml./l.). C.O. = cardiac output (l./min.). H.R. = heart rate. S.V. = stroke volume (ml.).

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TABLE IV
RESPIRATORY DATA

Subject No.	S_{aO_2}	O_2 cap.	$\dot{V}_{O_2}$	$\dot{V}_E$	$\dot{V}_D/\dot{V}_T$	P_{aCO_2}	P_{aO_2}	$(A-a)O_2$	Q_3/Q_1
Group B									
1	97	17.8	240	6.8	35	40	96	8	5.5 ¹
2	97	17.8	300	7.9	33	39	92	4	5.2
3	97	18.7	199	6.4	25	32	92	16	5.6
4	98	17.5	270	14.3	32	24	121	5	0
5	96	18.5	334	10.1	32	36	86	23	8.5
6	98	18.2	239	8.0	27	30	105	6	2.5
Group A									
7	98	17.3	278	11.7	34	30	91	27	0
8	98	19.4	215	6.9	27	35	85	27	1.2
9	97	17.6	293	9.0	46	39	79	19	6.6
10 R	96	17.7	243	7.5	65	41	88	(9)	7.5
E	96	18.6	852	17.1	22	42	92	(10)	4.5
11 R	92	19.8	252	9.5	43	36	72	35	21.3
E	94	19.9	850	25.1	21	36	89	20	6.6
12 R	97	20.2	272	13.1	23	19	104	20	2.9
E	97	19.5	971	22.9	18	37	83	21	2.4
13 R	93	17.2	219	6.5	31	34	83	22	19.2
E	94	17.6	867	25.6	27	36	83	24	7.5
14 R	96	18.1	220	7.7	40	35	82	26	6.8
E	96	19.8	964	31.4	24	33	79	34	4.7
Mean values at rest									
Group A	97.0	18.4	264	8.9	30.7	33.5	101.5	10.3	4.6
Group B	95.9	18.4	249	9.0	36.1	33.6	85.5	23.1	8.2
P-values for difference A-B									
	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	<0.02	<0.01	>0.05

¹ $(A-a)O_2$ difference assumed to be 4.30 vol.%. Figures in parentheses indicate P_{aO_2} calculated from Dill curve.

S_{aO_2} = arterial oxygen saturation (%). O_2 cap. = oxygen capacity (ml./100 ml). $\dot{V}_{O_2}$ = oxygen consumption (ml./min. S.T.P.D.). $\dot{V}_E$ = total ventilation (l./min. B.T.P.S.). $\dot{V}_D/\dot{V}_T$ = dead space ventilation in per cent of total ventilation. P_{aCO_2} = arterial carbon dioxide tension (mm. Hg). $(A-a)O_2$ = alveolo-arterial oxygen tension difference (mm. Hg). P_{aO_2} = arterial oxygen tension (mm. Hg). Q_3/Q_1 = venous admixture in per cent of cardiac output.

DISCUSSION

The subjects studied were selected from a larger group of insulation workers. They all had similar working conditions and employment times, the main difference being the insulating material used. A positive diagnosis of asbestosis was made in the presence of prolonged exposure to asbestos dust or radiological findings suggestive of asbestosis.

To exclude any exposure to asbestos dust in the group of glasswool workers proved impossible. However, the time of exposure to asbestos was much shorter, and no one had been employed in the production of mattresses etc., where the exposure to dust is known to be severe. The absence of radiological findings was considered confirmative. Nevertheless any patho-physiological findings in group B should be judged with caution since asbestosis might occur even without radiological changes (Williams and Hugh-Jones, 1960; Leathart, 1960). In spite of prolonged exposure to glasswool and rockwool dust no subjects in group B have shown impairment of those cardio-pulmonary functions studied. Thus it seems safe to conclude that prolonged exposure to this type of dust does not initiate any fibrosis of the lungs.

This is in agreement with studies performed on different animal species by Schepers, Durkan, Delahant, Redlin, Schmidt, Creedon, Jacobson, and Bailey (1958) and by Schepers (1959). They found an essentially cellular reaction to glasswool particles while the deposition of collagen in the lungs is very slight compared to that in asbestosis. The main patho-anatomical findings have been peribronchiolar and perivascular infiltrations sometimes combined with proliferative cell masses obliterating the alveolar lumen. No signs of fibrosis have been observed and all the changes described have been reversible on cessation of exposure.

There are few patho-anatomical studies performed on human lungs, but Kahlau (1947) reports on a patient who died with pneumonia after a relatively short period of exposure to glasswool. Microscopy revealed foreign bodies, supposedly glasswool particles, but no fibrotic reaction. Murphy (1961) describes multiple focal abscesses arising from terminal bronchi and bronchioles containing glass fibres and only slight fibrosis.

Patho-anatomical studies of the lungs in cases of asbestosis have shown dense fibrosis of the

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pleura, often with calcifications and a more or less generalized fibrosis of the lung parenchyma (Vorwald, Durkan, and Pratt, 1951; Heard and Williams, 1961). These patho-anatomical findings should be compared with the physiological alterations observed.

There are several findings in asbestosis which have been attributed to the induced fibrosis.

DECREASED VITAL CAPACITY This is a common finding (Leathart, 1960; Bastenier, Denolin, de Coster, and Englert, 1955; Williams and Hugh-Jones, 1960) and in our subjects the V.C. averaged 76% of predicted normal. There was a poor correlation between the radiological findings and a decrease in V.C. Calcifications were found both in cases with a markedly reduced and an almost normal V.C. On the other hand, those subjects with the lowest V.C. also had an elevated pulmonary artery pressure at rest or during exercise. Similar observations have been made by Söderholm (1957) in patients with pulmonary tuberculosis where a good correlation was found between a reduced maximum voluntary ventilation and increased pulmonary artery pressure during standardized exercise. This observation might be of importance as a simple screening test.

LOW COMPLIANCE OF THE LUNG Leathart (1960) found a markedly reduced dynamic compliance which was closely correlated to the reduction in vital capacity. Similar findings have been reported by Rubino, Garbagni, Scansetti, and Carelli (1961).

DECREASED PULMONARY DIFFUSING CAPACITY This has been found by several authors (Leathart, 1960; Williams and Hugh-Jones, 1960; Thomson, McGrath, Smither, and Shepherd, 1961).

In our group A six of eight subjects had both a reduced diffusing capacity and an increased pulmonary vascular resistance (Fig. 1). Such an increased vascular resistance in the absence of any indications of obstructive lung disease fits well with the concept of a reduced pulmonary vascular bed due to pulmonary fibrosis. There is no direct relation between vascular resistance and diffusing capacity even if an increased resistance is usually found in cases with a reduced diffusing capacity. Thus the impairment of diffusing capacity might be due to both a reduction in the pulmonary capillary bed and alterations in the alveolar membrane and/or uneven distribution of the diffusion to perfusion ratios. Measurement of the end-capillary oxygen tension is not possible, but some deductions can be made since the mean

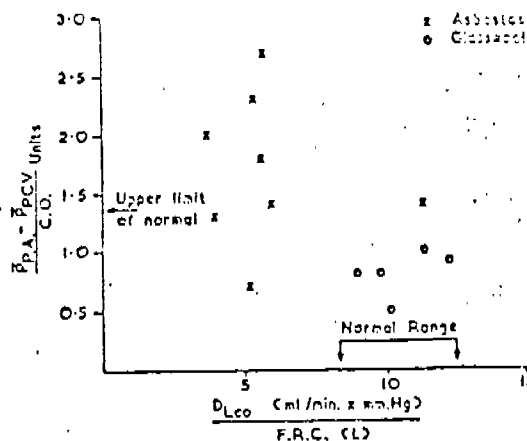


FIG. 1. Pulmonary diffusing capacity per litre functional residual capacity ($DL_{coll. F.R.C.}$) in comparison with the pulmonary vascular resistance (P.V.R.) at rest. The normal limits are derived from subjects studied with the same techniques in this laboratory: $DL_{coll. F.R.C.}$: 12 subjects 20–25 years of age. P.V.R.: 12 subjects 21–50 years of age.

diffusion gradient for oxygen is readily calculated from the $DL_{coll.}$. In the two groups the average mean diffusion gradient was 15 mm. Hg in group A and 9 mm. Hg in group B, when the total alveolo-arterial O_2 difference was 23 and 10 mm. Hg, respectively. As the average arterial O_2 tension was 86 and 102 mm. Hg in the two groups, the end-capillary oxygen tension must have exceeded 95 mm. Hg. It is thus reasonable to assume an end-capillary oxygen saturation of 98% and an end-capillary O_2 gradient of less than 5 mm. Hg. The contribution of venous admixture to the over-all alveolo-arterial oxygen difference approximates 5 and 18 mm. Hg in groups B and A respectively. These figures agree closely with the Q_v/Q_t of 5% and 8% calculated otherwise. It is a matter of conjecture whether this admixture of poorly oxygenated blood is considered a result of perfusion of poorly ventilated alveoli or the interposition of an enormously thickened alveolar wall between normally ventilated and perfused alveoli (*cf.*, Piiper, 1961). When calculating the effect of increasing alveolo-capillary membrane thickness on the O_2 diffusing capacity, Finley, Swenson, and Comroe (1962) found that a six- to eight-fold increase of the membrane must occur before the alveolo-arterial O_2 tension difference is measurable (1 mm. Hg). Thus uneven distribution of ventilation in relation to blood flow is a more probable cause of hypoxaemia even in cases with advanced impairment of diffusion.

Thus our data indicate a mixed impairment of the gas transport mechanisms where both an impaired diffusion and a disturbance of the ventilation-perfusion ratio coexist. This is in agreement with the observations of Williams and Hugh-Jones (1960) and of Bader, Bader, and Selikoff (1961).

No relation was found between physical performance or radiological findings and diffusing capacity. This might indicate that an impaired diffusing capacity is a sensitive index of asbestosis, which Williams and Hugh-Jones have already stated. Leathart showed that among asbestos workers those with radiological changes had a significantly lower diffusing capacity.

In three of eight subjects a pathologically increased pulmonary artery pressure at rest and/or during light exercise was found. Bearing in mind that all subjects were gainfully employed and symptom-free and that the investigation was performed as part of a routine health check up, this is a surprisingly high incidence. Presumably they represent moderately advanced cases of asbestosis and yet their cardiopulmonary function studies have shown marked deviations from normal.

These findings put further emphasis on the importance of preventive medical supervision of workers exposed to asbestos dust.

It is concluded that even prolonged exposure to glasswool and rockwool does not cause any significant impairment of cardiopulmonary function. On the other hand, similar exposure to asbestos does cause such impairment even if the subjects are symptom-free and fit for work.

SUMMARY

Cardiopulmonary function studies have been performed in insulators exposed to glasswool or asbestos.

With a similar time of exposure glasswool did not cause any detectable functional impairment. Exposure to asbestos gave rise to a marked restriction in dynamic lung function, a reduced diffusing capacity, and, in three out of eight subjects, a pathologically raised pulmonary artery pressure at rest or during exercise.

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