*Thorax* (1964), 19, 22

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# Cardiopulmonary function studies in workers dealing with asbestos and glasswool[1]

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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.

## 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.[4] 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-

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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 | – | – | – | 1,800 | 124 | 30 | 11 yr. almost exclusively rockwool and glasswool; minimal exposure to asbestos |
| 2 | 37 | 191 | – | – | – | 1,200 | 137 | 30 | 23 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 | 160 | 28 | 8 yr. exclusively rockwool and glasswool |
| 5 | 45 | 187 | – | – | – | 1,200 | 162 | 28 | 29 yr. Since 15 yr. no exposure to asbestos but less earlier been moderately exposed to asbestos |
| 6 | 45 | 178 | – | – | – | 900 | 172 | 28 | 11 yr. almost exclusively rockwool and glass wool; minimal exposure to asbestos |
| 7[1] | 48 | 180 | +[2] | + | – | 900 | 154 | 36 | 30 yr. exposure to both asbestos and rockwool |
| 8 | 50 | 168 | +[2] | + | + | 900 | 152 | 40 | 23 yr. exposure to both asbestos and rockwool |
| 9 | 40 | 188 | + | + | – | 600 | 150 | 28 | 19 yr. mainly exposure to asbestos but less used from work |
| 10 | 33 | 173 | + | – | – | 1,200 | 190 | 44 | 11 yr. mainly exposure to asbestos but less used from work |
| 11 | 51 | 172 | +[2] | – | – | 900 | 165 | 28 | 30 yr. mainly exposure to asbestos |
| 12 | 49 | 168 | + | + | – | 900 | 165 | 28 | 22 yr. mainly exposure to asbestos |
| 13 | 47 | 168 | +[2] | + | + | 600 | 130 | 36 | 7 yr. mainly exposure to asbestos |
| 14 | 46 | 164 | + | + | – | 600 | 115 | 22 | 9 yr. mainly exposure to asbestos (insulation) |

[1] Scoliosis of thoracic spine. [2] Pleural and/or diaphragmatic calcifications.

TABLE II
PULMONARY FUNCTION STUDIES

| Subject No. | V.C. (l.) | | $F.E.V._{1\cdot0}$ (l.) | | F.E.V.% | | $N_2$ Difference | F.R.C. | L.C.I. | $D_{L_{CO}}$ |
|---|---|---|---|---|---|---|---|---|---|---|
| | Found | Predicted | Found | Predicted | Found | Predicted | | | | |
| *Group B* | | | | | | | | | | |
| 1 | 4·68 | 4·67 | 3·96 | 3·84 | 85 | 82 | 0·9 | — | — | 19·6 |
| 2 | 5·76 | 5·64 | 3·83 | 4·37 | 66 | 78 | 1·8 | 3·82 | 9·0 | 30·1 |
| 3 | 4·55 | 4·53 | 3·44 | 3·51 | 76 | 77 | 0·9 | 1·76 | 7·8 | 21·7 |
| 4 | 4·86 | 4·97 | 2·92 | 3·88 | 60 | 78 | 2·1 | 1·98 | 6·3 | 30·2 |
| 5 | 4·76 | 5·29 | 3·39 | 3·97 | 71 | 75 | 2·5 | 2·30 | 9·0 | 25·4 |
| 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 | 3·86 | 87 | 79 | 0·9 | 1·89 | 10·2 | 21·2 |
| 11 | 3·83 | 4·43 | 2·22 | 3·22 | 58 | 73 | 5·4 | 3·07 | 11·6 | 11·8 |
| 12 | 3·36 | 4·29 | 2·64 | 3·18 | 78 | 74 | 0·8 | 2·76 | 7·0 | 19·0 |
| 13 | 3·44 | 4·31 | 2·97 | 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 | 11·9 |
| Mean values Group B | 4·86 | 101% | 3·50 | 90% | 72 | 78 | 1·6 | 2·36 | 7·76 | 23·9 |
| Group A | 3·47 | 76% | 2·63 | 76% | 76 | 75 | 3·3 | 2·48 | 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. $F.E.V._{1\cdot0}$ = 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. $N_2$ difference = 'single breath' difference in expired $N_2$ 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.). $D_{L_{CO}}$ = pulmonary diffusing capacity for carbon monoxide (ml./min. x 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 (Stälex). 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

TABLE IV
RESPIRATORY DATA

| Subject No. | $S_{a_{O_2}}$ | $O_2$-cap. | $\dot{V}_{O_2}$ | $\dot{V}_E$ | $V_D/V_T$ | $P_{a_{CO_2}}$ | $P_{a_{O_2}}$ | $(A-a)_{O_2}$ | $\dot{Q}_s/\dot{Q}_t$ |
|---|---|---|---|---|---|---|---|---|---|
| *Group B* | | | | | | | | | |
| 1 | 97 | 17·8 | 240 | 6·8 | 35 | 40 | 96 | 8 | 5·8[1] |
| 2 | 97 | 19·8 | 300 | 7·9 | 33 | 39 | 99 | 4 | 5·2 |
| 3 | 97 | 18·7 | 199 | 6·4 | 25 | 32 | 99 | 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 | 108 | 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 | 245 | 7·5 | 45 | 41 | 88 | (9) | 7·5 |
| E | 96 | 18·6 | 852 | 19·1 | 22 | 42 | 92 | (10) | 4·5 |
| 11 R | 92 | 19·8 | 252 | 9·5 | 43 | 36 | 72 | 35 | 21·3 |
| E | 94 | 19·9 | 820 | 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 | 25·8 | 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 B | 97·6 | 18·4 | 264 | 8·9 | 30·7 | 33·5 | 101·5 | 10·3 | 4·6 |
| " A | 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] $(a-\bar{v})_{O_2}$ difference assumed to be 4·30 vol.%. Figures in parentheses indicate $P_{a_{O_2}}$ calculated from Dill curve.

$S_{a_{O_2}}$ = 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.). $V_D/V_T$ = dead space ventilation in per cent of total ventilation. $P_{a_{CO_2}}$ = arterial carbon dioxide tension (mm. Hg). $(A-a)_{O_2}$ = alveolo-arterial oxygen tension difference (mm. Hg). $P_{a_{O_2}}$ = arterial oxygen tension (mm. Hg). $\dot{Q}_s/\dot{Q}_t$ = 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 cardiopulmonary 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

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

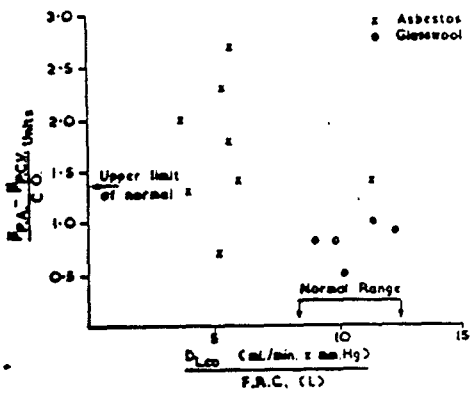


FIG. 1. *Pulmonary diffusing capacity per litre functional residual capacity ($DL_{CO}$/l. F.R.C.) in comparison with the pulmonary vascular resistance (P.V.R.) at rest. The normal limits are derived from subjects studied with the same techniques in this laboratory: $DL_{CO}$/l. F.R.C.: 12 subjects 20–25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

diffusion gradient for oxygen is readily calculated from the $DL_{CO}$. 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 $Q_s / Q_t$ 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.