LABILITY OF PULMONARY PRESSURE/FLOW CURVES DURING EXERCISE IN CLINICALLY MILD BRONCHITIS; EVIDENCE FOR A PULMONARY VASCULAR SLUICE IN MAN

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SUMMARY

1. Pulmonary arterial mean pressure, cardiac output and other variables have been measured at rest and during exercise breathing air and oxygen in eight selected working coalminers with pneumoconiosis; four of the subjects had no respiratory symptoms and four had chronic cough and sputum but a well maintained ventilatory capacity.

2. The relationship of cardiac output to cardiac frequency during exercise was used to estimate cardiac output by interpolation with a residual standard deviation of 0.28 l/min. Used in this way the curves provided additional points for construction of mean pressure/flow curves.

3. In the subjects without respiratory symptoms the pulmonary arterial mean pressure when breathing air was similar to that in normal subjects. In the subjects with respiratory symptoms the pressure was normal at rest but consistently increased on exercise, although the arterial oxygen tension was relatively normal. The findings are interpreted as evidence for an increase in pulmonary vasomotor tone in patients with clinically mild chronic bronchitis.

4. Breathing oxygen during exercise led to a reduction in pulmonary arterial mean pressure in all subjects but not to a change in slope of the mean pressure/flow curve; a similar displacement of the curve was observed in some bronchitic subjects on repetition of the exercise breathing air. The response may be due to the small pulmonary vessels acting as a vascular sluice rather than to a change in calibre of the resistance vessels.

In clinical studies of the pulmonary circulation it is difficult to obtain sufficient measurements of cardiac output for construction of mean pressure/flow curves. This has led to changes in pulmonary arterial pressure being attributed to variation in pulmonary vascular resistance, despite evidence from animal studies that the effective outflow pressure at the distal end of

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the resistance vessels may be a more important variable; the literature is reviewed by Caro
(1966). However, during steady state exercise the cardiac output is mainly dependent on
cardiac frequency; in addition, we have shown that the stroke volume is relatively independent
of the duration of exercise between the second and sixth minutes whether or not the inspired
gas is air or oxygen (Cotes, Pisa & Thomas, 1963). This suggests to us that the number of
estimates of output may be increased by interpolation from the relationship of cardiac output
to cardiac frequency. In addition, the number of pressure measurements may be increased
by use of a pulmonary catheter of small diameter (Bradley, 1964). We have used these tech-
niques to study the effects upon the pulmonary circulation during exercise of bronchitis,
pneumoconiosis and replacement of inspired air by 100% oxygen.

METHODS

The subjects were working coalminers with early progressive massive fibrosis for whom annual
records of their respiratory symptoms were available over the previous 5 years as a result of
their taking part in a controlled trial of therapy (Ball et al., 1969; Cotes & Gilson, 1967).
They were allocated into two groups, mild chronic bronchitis and no chronic bronchitis, on the
basis of their answers to Question 6 of the M.R.C. Questionnaire of Respiratory Symptoms
(1966) which takes the form 'do you bring up phlegm like this (i.e. first thing in the morning,
during the day or at night) on most days (or nights) for as much as 3 months each year'? 
Administration of the questionnaires and allocation of the subjects were performed separately
from the main investigation; the latter was undertaken without knowledge of the groups to
which the subjects had been allocated.

All the subjects had normal systemic blood pressure and were free from symptoms referable
to the cardiovascular system. Their relevant clinical features are listed in Table 1. They received
a full account of the nature, purpose and possible risks of the proposed investigation and these
aspects were also discussed with a group of informed physicians and the patient's general
practitioner. Provisional agreement to participate was given to a third party subject to a
satisfactory result from further screening tests; these included electrocardiography during
a trial of the exercise procedure. It was made clear to the subject that he was then free to
withdraw if he wished to do so. The time off work was 3 to 7 days except in one instance when
the subject developed a haematoma at the site of the arterial cannulation 48 hr after completion
of the investigation. He was then off work for 2 weeks. Subjects were fully compensated for
loss of earnings. Sixteen subjects were submitted for investigation and in twelve it was possible
to position all catheters. Complete data were obtained in eight. There is no evidence that those
lost from the study differed materially from those in whom the procedure was completed
successfully.

Measurements of the lung function including the single breath transfer factor for carbon
monoxide and its subdivisions (the diffusing capacity of the alveolar membrane and the volume
of blood in the lung capillaries), were made on the day preceding the haemodynamic studies
using standard methods (Cotes, 1968). In the ward on the morning of the study a 4 cm teflon
catheter, internal diameter 1.0 mm (Longdwel, Becton, Dickinson) was inserted percutaneously
into the left brachial artery. A 30 cm polyethylene catheter internal diameter 1.5 mm was
inserted by the Seldinger technique into the left median cubital vein. This was connected to a
single side-arm Straube tip-occluder assembly (US Catheter and Instrument Co.) modified to
allow a seal to be made around a catheter passed through its main arm. A gamma-ray sterilized Bradley miniature catheter of internal diameter 0.5 mm (Bradley, 1964) was inserted along this venous catheter and thence floated into position in the main pulmonary artery about 6 cm above the pulmonary valve. The chuck of the tip-occluder assembly was then tightened to make a seal around the catheter and hold it in place. The progress of the catheter was assessed from the pressure tracing which was monitored continuously on an oscilloscope during the insertion. Great care was taken to exclude from the catheter bubbles of air which if present would have resulted in a ‘damped’ trace. After these procedures the subject rested and then ate a light lunch.

### Table 1. Summary of clinical features

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age (m)</th>
<th>Ht (kg)</th>
<th>Job activity</th>
<th>Clinical grade*</th>
<th>Cough and sputum</th>
<th>Chest illness†</th>
<th>Smoking</th>
<th>X-ray‡</th>
<th>Past illness</th>
</tr>
</thead>
<tbody>
<tr>
<td>S.D.</td>
<td>49</td>
<td>1.71</td>
<td>68</td>
<td>Moderate</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>25/day</td>
<td>3m/A2/1-</td>
</tr>
<tr>
<td>T.R.</td>
<td>55</td>
<td>1.72</td>
<td>81</td>
<td>Light</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>10/day</td>
<td>2m/A1/-</td>
</tr>
<tr>
<td>A.P.</td>
<td>50</td>
<td>1.73</td>
<td>79</td>
<td>Heavy</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>Ex-smoker</td>
<td>3p-m/B2/1</td>
</tr>
<tr>
<td>D.M.</td>
<td>50</td>
<td>1.70</td>
<td>86</td>
<td>Heavy</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>Non-smoker</td>
<td>2m/A2/2</td>
</tr>
<tr>
<td>A.W.</td>
<td>54</td>
<td>1.78</td>
<td>77</td>
<td>Light</td>
<td>3</td>
<td>+</td>
<td>0</td>
<td>Ex-smoker</td>
<td>3p-m/A2/0</td>
</tr>
<tr>
<td>A.C.</td>
<td>55</td>
<td>1.83</td>
<td>63</td>
<td>Moderate</td>
<td>2</td>
<td>+</td>
<td>1</td>
<td>10/day</td>
<td>2m/B2/2</td>
</tr>
<tr>
<td>R.G.</td>
<td>54</td>
<td>1.62</td>
<td>54</td>
<td>Heavy</td>
<td>2</td>
<td>+</td>
<td>1</td>
<td>15/day</td>
<td>2m/A1/1</td>
</tr>
<tr>
<td>R.J.</td>
<td>57</td>
<td>1.63</td>
<td>53</td>
<td>Heavy</td>
<td>1</td>
<td>+</td>
<td>0</td>
<td>2 oz/week</td>
<td>2m/B2/2</td>
</tr>
</tbody>
</table>

* Clinical grade of breathlessness (Fletcher, 1952).
† In last 3 years = question 21b of M.R.C. Questionnaire.
‡ Classification of International Labour Office (1959).

In the laboratory pulmonary arterial pressures were measured from a reference point at the anterior insertion of the fourth rib using a low compliance pressure transducer (Statham P23GB). This was coupled to a Devices amplifier and Mingograf recorder. Calibration was performed with a water manometer before and after each stage of the study. Mean pressures were obtained by electrical damping of the transducer signal; a mean line was fitted by eye to the small residual respiratory fluctuations. In four instances for each subject the mean pressure was also obtained by planimetry. The mean results were for practical purposes identical and the coefficient of variation about the line of identity was less than 5%.

Cardiac output was measured by a dye-dilution technique using indocyanine green (Cotes et al., 1963). The dye was injected into the subclavian vein through the side-arm of the tip-occluder assembly attached to the venous catheter; this was then immediately flushed through with saline. Arterial blood was withdrawn at a constant rate via a heparinized motor driven syringe from which air bubbles were excluded, and subsequently returned through the venous catheter. Calibration of the densitometer used to determine the concentration of dye was performed on a sample of the subject’s blood at the end of each study. Correction of the record for recirculation was made by extrapolation of the exponential part of the curve.
Arterial blood samples were taken anaerobically into 10 ml ungreased glass syringes previously lubricated with heparin solution. Analysis for \( \text{Po}_2 \) and \( \text{PCO}_2 \) were made within 10 min using an EIL electrode system calibrated before and after each measurement with gas mixtures analysed by the Scholander technique. A predetermined correction factor of 1.075 was applied to readings of \( \text{Po}_2 \) to allow for the blood–gas difference of the oxygen electrode.

Ventilation was measured using a dry gas meter (Parkinson & Cowan) fitted with an optical integrator and counter which was read and reset each minute (Reynolds, 1968); the gas meter was positioned on the inspiratory side of the valve box and mouthpiece and was supplied with compressed air through a low-pressure demand system. On inspiration the suction required for a flow rate of 100 l/min was 1.5 cm H\( _2 \)O and on expiration at the same flow rate the back pressure was 3.7 cm H\( _2 \)O. The mean oral pressure at a ventilation minute volume of 30 l/min was 0.4 cm H\( _2 \)O. Expiration was to atmosphere via a gas mixing chamber (capacity 4 litres) and an exit pipe from which a sample of mixed expired gas was drawn continuously through the gas analysers; these were, for oxygen, a Servomex OA 137 paramagnetic analyser and, for carbon dioxide, a Hartmann and Braun URAS 3 infra red analyser. The accuracy of analysis was that expected using these methods (Cotes & Woolmer, 1962). Respiratory frequency was recorded on one channel of a Mingograf recorder using a thermistor mounted in the valve box; another channel of the recorder was used to monitor the cardiac frequency from electrodes applied to the chest.

Measurements were made with the subjects seated upright on a bicycle-ergometer. Exercise was performed by all subjects at 40 and 80 W. The subjects without, but not those with, respiratory symptoms were also studied at 100 or 120 W. Air was breathed at rest and all levels of exercise; oxygen at rest and the highest level of exercise. The order of administration of air and oxygen was random at rest and this was also planned for the highest level of exercise; however, amongst the subjects excluded from the study on account of incomplete data the majority breathed oxygen first, so that for seven of the eight subjects for whom complete data were available the last period of measurement was that on oxygen.

At least 10 min was allowed between each period of measurement. In addition, when breathing oxygen the mixed expired nitrogen concentration was required to be less than 1% before resting measurements were made or exercise commenced. Following oxygen the next stage of the study was not begun until the mixed expired oxygen concentration had fallen to its initial value.

Pulmonary arterial pressure and cardiac frequency were recorded continuously during each stage of the study. Duplicate measurements of cardiac output, ventilation and blood gas tensions at rest were made between the eighth and the twelfth minute after connecting the subject to the mouthpiece. During exercise, which was of 6 min duration, the cardiac output was measured at the beginning of the third and end of the fifth min and a sample of blood taken for blood gas estimations immediately after each measurement.

**RESULTS**

*Lung function, gas exchange and performance during exercise*

The findings on assessment of lung function are given in Table 2. Group 1 comprises subjects without bronchitis, Group 2 those with bronchitis. With the exception of the forced expiratory volume, which is reduced in Group 2, all the findings are within the normal range.
Table 2. Findings on assessment of lung function

<table>
<thead>
<tr>
<th>Subject</th>
<th>FEV₁.₀ (L)</th>
<th>FVC (L)</th>
<th>FEV₁/FVC (%)</th>
<th>TLC (L)</th>
<th>FRC (L)</th>
<th>RV (L)</th>
<th>RV/TLC (%)</th>
<th>TI (ml min⁻¹ mmHg⁻¹)</th>
<th>Dm (ml)</th>
<th>Vc (ml)</th>
<th>VA'/VA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S.D.</td>
<td>2.43</td>
<td>3.35</td>
<td>73</td>
<td>5.49</td>
<td>3.36</td>
<td>1.74</td>
<td>32</td>
<td>32.2</td>
<td>48</td>
<td>76</td>
<td>1.03</td>
</tr>
<tr>
<td>T.R.</td>
<td>2.60</td>
<td>4.45</td>
<td>58</td>
<td>8.03</td>
<td>4.14</td>
<td>2.96</td>
<td>37</td>
<td>33.8</td>
<td>53</td>
<td>83</td>
<td>0.94</td>
</tr>
<tr>
<td>A.P.</td>
<td>2.75</td>
<td>4.45</td>
<td>62</td>
<td>6.50</td>
<td>3.89</td>
<td>2.46</td>
<td>38</td>
<td>29.1</td>
<td>45</td>
<td>75</td>
<td>0.95</td>
</tr>
<tr>
<td>D.M.</td>
<td>2.90</td>
<td>4.00</td>
<td>72</td>
<td>6.11</td>
<td>2.90</td>
<td>1.94</td>
<td>32</td>
<td>39.4</td>
<td>59</td>
<td>106</td>
<td>0.92</td>
</tr>
<tr>
<td>Mean</td>
<td>2.67</td>
<td>4.06</td>
<td>66.3</td>
<td>6.53</td>
<td>3.57</td>
<td>2.28</td>
<td>34.8</td>
<td>33.6</td>
<td>51.3</td>
<td>85</td>
<td>0.96</td>
</tr>
<tr>
<td>Group 2</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A.W.</td>
<td>3.45</td>
<td>5.38</td>
<td>64</td>
<td>7.11</td>
<td>4.05</td>
<td>2.15</td>
<td>30</td>
<td>26.9</td>
<td>40</td>
<td>78</td>
<td>0.99</td>
</tr>
<tr>
<td>A.C.</td>
<td>1.23</td>
<td>3.65</td>
<td>34</td>
<td>8.04</td>
<td>5.33</td>
<td>4.05</td>
<td>50</td>
<td>33.6</td>
<td>137</td>
<td>31</td>
<td>0.71</td>
</tr>
<tr>
<td>R.G.</td>
<td>2.05</td>
<td>3.83</td>
<td>54</td>
<td>5.65</td>
<td>4.05</td>
<td>2.06</td>
<td>37</td>
<td>22.1</td>
<td>37</td>
<td>50</td>
<td>0.97</td>
</tr>
<tr>
<td>R.J.</td>
<td>2.03</td>
<td>3.58</td>
<td>57</td>
<td>5.61</td>
<td>4.00</td>
<td>2.00</td>
<td>36</td>
<td>22.6</td>
<td>45</td>
<td>41</td>
<td>0.93</td>
</tr>
<tr>
<td>Mean</td>
<td>2.19</td>
<td>4.11</td>
<td>52.3</td>
<td>6.60</td>
<td>4.36</td>
<td>2.57</td>
<td>38.3</td>
<td>26.3</td>
<td>64.8</td>
<td>50</td>
<td>0.90</td>
</tr>
</tbody>
</table>

FEV₁₀, forced expiratory volume; FVC, forced vital capacity; TLC, total lung capacity; FRC, functional residual capacity; RV, residual volume; TI, transfer factor; Dm, diffusing capacity of alveolar membrane; Vc, volume of blood in alveolar capillaries; VA'/VA, index of distribution of inspired gas. The methods used are described in detail elsewhere (Cotes, 1968).
**Table 3.** Gas exchange at rest and at the highest level of exercise*; the data are for breathing air except where indicated

<table>
<thead>
<tr>
<th>Subject</th>
<th>Ventilation, minute volume (l/min)</th>
<th>Arterial oxygen tension (mmHg)</th>
<th>Arterial carbon dioxide tension (mmHg)</th>
<th>Deadspace/tidal volume ratio (%)</th>
<th>Respiratory exchange ratio</th>
<th>Venous admixture effect (%)</th>
<th>Pulmonary blood shunt (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>GROUP 1</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S.D.</td>
<td>10.0</td>
<td>73.4</td>
<td>65.1</td>
<td>102</td>
<td>106</td>
<td>621</td>
<td>25</td>
</tr>
<tr>
<td>T.R.</td>
<td>10.8</td>
<td>48.0</td>
<td>38.9</td>
<td>88</td>
<td>84</td>
<td>671</td>
<td>29</td>
</tr>
<tr>
<td>D.M.</td>
<td>11.2</td>
<td>45.0</td>
<td>38.6</td>
<td>84</td>
<td>76</td>
<td>601</td>
<td>33</td>
</tr>
<tr>
<td>A.P.</td>
<td>12.0</td>
<td>73.0</td>
<td>60.6</td>
<td>97</td>
<td>79</td>
<td>586</td>
<td>32</td>
</tr>
<tr>
<td>Mean</td>
<td>11.0</td>
<td>59.8</td>
<td>50.8</td>
<td>92.8</td>
<td>86.3</td>
<td>619.8</td>
<td>29</td>
</tr>
</tbody>
</table>

| **GROUP 2** | | | | | | | |
| A.W. | 22.3 | 74.5 | 57.9 | 93 | 98 | 654 | 24 | 30 | 30 | 42 | 38 | 27 | 0.86 | 0.92 | 2:7 | 1:2 |
| R.J. | 9.3 | 36.6 | 35.6 | 87 | 72 | 679 | 39 | 43 | 44 | 35 | 33 | 30 | 0.75 | 0.86 | 2:1 | 4:9 |
| R.G. | 10.6 | 39.7 | 26.6 | 106 | 89 | 664 | 28 | 36 | 51 | 25 | 21 | 28 | 0.75 | 0.96 | 0:8 | 2:5 |
| A.C. | 13.0 | 48.2 | 30.7 | 86 | 67 | 590 | 35 | 44 | 56 | 42 | 44 | 44 | 0.97 | 0.87 | 3:9 | 5:9 |
| Mean | 13.8 | 49.8 | 37.7 | 93.0 | 81.5 | 651.3 | 31:5 | 38:3 | 45:3 | 36:0 | 34:0 | 32:3 | 0:833 | 0:901 | 2:38 | 3:63 |

R, Data obtained at rest; E, data obtained during exercise on air; EO2, data obtained during exercise on oxygen.
* The work levels were for Group 1, 100 W (except for A.P. 120 W) and for Group 2, 80 W.
However, the other data for Group 2, including the relatively large functional residual capacities, are consistent with a mild obstructive type of ventilatory defect. In Group 1 the transfer factor is above average due mainly to a rather large volume of blood in the lung capillaries. But for none of the indices listed is there a significant difference between the two groups of subjects.

Gas exchange at rest and at the highest level of exercise is summarized in Table 3. The tension of carbon dioxide is low or normal in all subjects at rest and normal during exercise. The arterial oxygen tension is also normal at rest; it is somewhat reduced during exercise but not sufficiently to cause a material reduction in the arterial oxygen saturation. On this account the venous admixture and anatomical shunt are at all times normal. The respiratory exchange ratio is normal in both groups but the deadspace as a percentage of tidal volume is somewhat

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**FIG. 1.** Relationship of cardiac output to cardiac frequency in eight subjects breathing air (●) and breathing oxygen (▲).
higher in Group 2, especially during exercise. Possibly on this account the ventilation in relation to the consumption of oxygen is somewhat higher in Group 2, but the difference (5.0 l/min) is not significant. The maximum ventilation is higher in Group 1 due to these subjects achieving a higher level of oxygen uptake; the maximal exercise ventilation as a percentage of the maximum breathing capacity (dyspneic index) is the same for both groups.

**Estimation of cardiac output from cardiac frequency**

The relationship of the cardiac output to the cardiac frequency, measured concurrently, was found to be of similar form for all subjects (Fig. 1). However, the positions of the curves varied between subjects. The points obtained when breathing oxygen fell on the same curve as those for air. The residual standard deviation about curves fitted by eye to the exercise data for each subject was 0.28 l/min. On account of this relatively small scatter the curves have been used to predict the cardiac output at the end of each minute throughout exercise. This procedure entailed minimal extrapolation towards the resting values, where the variability was greater, in order to obtain the cardiac outputs at the end of the first minute of exercise. The values for the other five minutes were obtained by interpolation.

**The relation of cardiac output to oxygen uptake**

The results in the eight subjects at rest and during exercise breathing air are shown in Fig. 2. The mean regression for Group 1 was similar to that reported for normal subjects (Reeves et al., 1961). The relationship for Group 2 showed a similar increase in cardiac output per unit increase in oxygen uptake but the total cardiac output was on average lower by 1.5 l/min.

![Fig. 2. Data showing the relationship of cardiac output to oxygen uptake breathing air for Group 1 subjects (○) and Group 2 subjects (●).](image-url)
Table 4. Oxygen uptake and haemodynamic data at rest and at the highest level of exercise*; the data are for breathing air except where indicated

<table>
<thead>
<tr>
<th>Subject</th>
<th>O₂ uptake (l/min)</th>
<th>Cardiac frequency (beats/min)</th>
<th>Stroke volume (ml)</th>
<th>Cardiac output (l/min)</th>
<th>Arterio-venous O₂ content difference (ml%)</th>
<th>Pulmonary Arterial mean pressure (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>R</td>
<td>E</td>
<td>EO₂</td>
<td>R</td>
<td>E</td>
</tr>
<tr>
<td>GROUP 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S.D.</td>
<td>0.36</td>
<td>1.97</td>
<td>90</td>
<td>162</td>
<td>165</td>
<td>62</td>
</tr>
<tr>
<td>T.R.</td>
<td>0.37</td>
<td>1.66</td>
<td>78</td>
<td>141</td>
<td>137</td>
<td>71</td>
</tr>
<tr>
<td>D.M.</td>
<td>0.41</td>
<td>1.98</td>
<td>73</td>
<td>127</td>
<td>116</td>
<td>75</td>
</tr>
<tr>
<td>A.P.</td>
<td>0.36</td>
<td>2.18</td>
<td>66</td>
<td>136</td>
<td>127</td>
<td>64</td>
</tr>
<tr>
<td>Mean</td>
<td>0.375</td>
<td>1.948</td>
<td>76.8</td>
<td>141.5</td>
<td>136.3</td>
<td>68</td>
</tr>
</tbody>
</table>

GROUP 2

| A.W.    | 0.39              | 1.80 | 77 | 148 | 131 | 50 | 87 | 89 | 3.8 | 12.5 | 11.7 | 10.2 | 14.7 | 12 | 26 | 21 |
| R.J.    | 0.33              | 1.41 | 98 | 158 | 164 | 48 | 67 | 68 | 4.7 | 10.6 | 11.1 | 6.9 | 13.8 | 19 | 42 | 29 |
| R.G.    | 0.30              | 1.30 | 84 | 141 | 136 | 41 | 79 | 83 | 3.4 | 11.0 | 11.1 | 8.7 | 11.6 | 15 | 28 | 33 |
| A.C.    | 0.30              | 1.48 | 77 | 124 | 123 | 48 | 79 | 82 | 3.7 | 9.6 | 9.9 | 8.2 | 15.6 | 10 | 33 | 23 |
| Mean    | 0.330             | 1.50 | 84 | 142.8 | 138.5 | 46.8 | 78 | 80.5 | 3.90 | 10.93 | 10.95 | 8.50 | 13.93 | 14.0 | 32.3 | 26.5 |

R, data obtained at rest; E, data obtained during exercise on air; EO₂, data obtained during exercise on oxygen.

* The work levels were for Group 1, 100 W (except for A.P. 120 W) and for Group 2, 80 W.
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(P<0·05). The significance of this difference was not reduced when cardiac output was expressed per m² of body surface.

Of the components of cardiac output (Table 4) the cardiac frequency in relation to consumption of oxygen was invariably higher in Group 2, whilst the cardiac stroke volume, with the exception of data for one subject during exercise at 40 W was invariably lower. The maximal stroke volume in both groups was attained at an oxygen uptake of about 1·0 l/min and did not vary thereafter by more than 11 ml in any one subject.

Pulmonary arterial mean pressure

In the Group 1 subjects the pulmonary arterial mean pressures at cardiac output of up to 14 l/min were similar to those reported for normal subjects of mean age 30 years by Damato, Galante & Smith (1966); the mean pressure in the subject A.P. who attained a cardiac output of 17 l/min was also similar to the average reported by these authors for subjects who completed exercise at their highest work level. In the Group 2 subjects at rest breathing both

![Graph](image)

Fig. 3. Data showing the relationship of pulmonary arterial mean pressure to cardiac output breathing air for Group 1 subjects (○) and Group 2 subjects (●).

air and oxygen the mean pressures were also normal and almost exactly the same as in Group 1; however, the cardiac outputs were on average lower. In relation to cardiac output the pressures at rest and on exercise were systematically higher in Group 2 (Fig. 3). In addition, the relationships of the mean pressure to flow were more nearly linear and in three of the subjects had lost the plateau or inflection which is a feature of the normal curve (Fig. 4). The subject A.W. in
whom the inflection persisted also had the lowest pressures of the four bronchitics and the best overall lung function.

In all the subjects studied the pressures during the first period of exercise at 40 W could be represented on the same curve as for rest; breathing air this was also true for the subsequent period of exercise in the subjects without bronchitis (Fig. 5) and the bronchitic subject A.W. (Fig. 6) in whom the physiological disturbance was relatively mild. However, in the remaining three bronchitic subjects the mean pressure/flow curves during the second period of exercise breathing air were displaced to the right so that the subjects achieved a greater cardiac output without much increase in pressure. The change, compared with the previous air period, was most marked in subject R.G. in whom the second period of exercise breathing air followed the period of breathing oxygen and did not precede it as in the other subjects.

On breathing oxygen instead of air the mean pressure/flow curve was displaced downwards in all the subjects so that a given cardiac output was associated with a lower mean pulmonary arterial pressure than during the preceding exercise breathing air. The displacement was visibly greater in the subjects with bronchitis than in those without (Fig. 6 cf. Fig. 5); the mean displacements calculated from the pressures which corresponded to the middle of the range of

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**Pulmonary pressure|flow curves**

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FIG. 5. Relationship of pulmonary arterial mean pressure to cardiac output for Group 1 subjects breathing air (●) and breathing oxygen (▲).

FIG. 6. Relationship of pulmonary arterial mean pressure to cardiac output for Group 2 subjects breathing air (●) and breathing oxygen (▲).
**Pulmonary pressure/flow curves**

![Graph showing pulmonary pressure and flow curves](image)

**Fig. 7.** Data showing the relationship of the respiratory variation in pulmonary arterial systolic pressure to ventilation minute volume for Group 1 subjects (○) and Group 2 subjects (●). The data are for breathing air and breathing oxygen but do not include those observations where only a mean (i.e. damped) pressure was obtained.

![Graph showing pulmonary arterial mean pressure vs arterial oxygen tension](image)

**Fig. 8.** Data showing the relationship of pulmonary arterial mean pressure to arterial oxygen tension breathing air for Group 1 subjects (○) and Group 2 subjects (●).
the cardiac outputs during exercise breathing oxygen were respectively 3.3 and 8.6 mmHg. The slopes of the relationships were on average unchanged.

The respiratory variation in pulmonary arterial pressure, both systolic and diastolic, was related to ventilation in a roughly linear fashion which was the same for the subjects with and without bronchitis (Fig. 7). The slope of the relationship was such that an increase in the pressure-swing of 1 cm H$_2$O was on average associated with an increase in the tidal volume of about 0.1 litre.

Fig. 8 shows the relationship between pulmonary arterial mean pressure and the arterial oxygen tension during exercise. The pulmonary arterial mean pressure in Group 2 tends to exceed that in Group 1 at all levels of oxygen tension. No correlation was found between pulmonary arterial mean pressure and the degree of venous admixture.

DISCUSSION

The subjects for study were coalminers with well-developed simple pneumoconiosis and early changes of progressive massive fibrosis. In Group 1 subjects who had no respiratory symptoms the forced expiratory volume, whilst on average lower than in most series for non-miners, is fairly typical of coalminers (Ashford et al., 1968). The physiological deadspace during exercise is increased in one subject (A.P.) and the arterial oxygen tension during exercise is reduced in two (S.D. and D.M.); the remaining indices of pulmonary and cardiovascular function are definitely normal. In Group 2 the subjects have minimal evidence of obstruction to the larger airways; no measurements were made of static and dynamic lung compliance to provide evidence for obstruction to the smaller airways (cf Macklem & Mead, 1967). The ventilatory and gas transfer characteristics of the lungs are relatively well maintained. The physiological deadspace as a percentage of tidal volume is increased in three of the four subjects but the presence of a normal venous admixture excludes a material degree of ventilation perfusion inequality. Thus, the condition of the Group 2 subjects conforms to simple chronic bronchitis in the terminology of the M.R.C. Bronchitis Committee (1965) whose criteria do not include the condition of the pulmonary vascular bed. The radiological abnormality of pneumoconiosis in these subjects is slightly greater than in Group 1 but the differences are small in relation to the absolute radiological involvement. Thus, it is unlikely to be the cause of the differences in pulmonary vascular function between the groups. Since the function is normal in Group 1, the abnormality in Group 2 is probably due to bronchitis alone; Kremer et al. (1967) came to a similar conclusion. However, on the present evidence, some interaction between bronchitis and pneumoconiosis cannot be excluded.

The pulmonary pressure/flow curves obtained in Group 1 closely resemble those described in normal subjects (Damato et al., 1966). The relatively flat middle portion of the curve is consistent with the pulmonary vascular bed expanding to accommodate the increase in cardiac output which occurs during exercise, both by passive dilatation of resistance vessels and recruitment of vessels in which the effective outflow pressure initially exceeds the pulmonary arterial pressure (cf West, 1965). The final increase in slope presumably occurs when the limits of dilatation and recruitment are reached. The steeper, more linear curves obtained in Group 2 indicate that the distensibility of the pulmonary vascular bed is reduced even at this early stage of chronic bronchitis when clinical impairment is still slight. This may arise from compensatory vasoconstriction in poorly ventilated regions of the lung and serve to reduce
Pulmonary pressure/flow curves

hypoxaemia at the expense of an increase in the work done by the right ventricle. Harris (1968) has pointed out that airway obstruction may contribute to pulmonary hypertension directly by increasing the respiratory fluctuations in the intra-thoracic pressure. However, this mechanism can be excluded in the present instance since both the airway obstruction is mild and the relationship of the respiratory pressure swing to the ventilation minute volume for Group 2 is the same as for Group 1.

In subjects with pulmonary hypertension a reduction in pulmonary arterial pressure on repetition of exercise has been observed by Widimsky, Berglund & Malmberg (1963); we have observed a reduction during breathing oxygen (Cotes et al. 1963) and this is also the experience of others (e.g. Horsfield, Segal & Bishop, 1968). Both observations have been attributed to a reduction in the resistance to flow of the pulmonary arterial tree; however, in this event it should be accompanied by a reduction in slope of the mean pressure/flow curve. Instead our data suggest that the curve is displaced downwards and to the right without material change in its slope.

This change is consistent with a reduction in the effective outflow pressure distal to the resistance vessels. The pattern resembles that described by Banister & Torrance (1960), De Bono & Caro (1963) and Permutt & Riley (1963) for models of the pulmonary circulation which include, in series with the resistance component and the outflow system, a collapsible segment described as a sluice or waterfall, where closure occurs when the sum of the applied pressures exceeds the intraluminal pressure.

The displacement of the pressure/flow curves may arise from a reduction in pressure or tension in the air-containing structures of the lung, the interstitial tissue, the vessel walls, or the left atrium if this determines the effective outflow pressure. Of these, the interstitial tissue may be excluded since the subjects were not in heart failure and had no transfer defect or other physiological evidence of interstitial oedema. A change in left atrial pressure is also unlikely to have been responsible for the displacement in either group of subjects. In Group 1 the pulmonary arterial pressure and hence probably the left atrial pressure were normal throughout. In Group 2 a change in left atrial pressure cannot be excluded (cf. Lockhart et al., 1969); however, in three of the four subjects breathing air a displacement of the curves was observed on repetition of the exercise despite a rise in cardiac output which, if it had affected the left atrial pressure would have caused an increase and not a reduction.

Systematic changes in intra-thoracic pressure may have occurred during oxygen breathing as a result of reductions in either ventilation minute volume or airway resistance. The latter has been reported in patients with chronic airway obstruction by Astin & Penman (1967) but may be excluded in the present subjects since the relationship of the respiratory pressure fluctuation to the minute volume was the same breathing oxygen as it was breathing air. The reduction in ventilation during breathing oxygen was not positively correlated with the reduction in pulmonary arterial pressure and in Group 2 during repetition of the exercise breathing air a comparable reduction in pressure occurred in association with an increase in ventilation in three of the four subjects. These findings appear to be incompatible with respiratory changes in alveolar or extra-alveolar pressure being the cause of the reduction in pulmonary arterial pressure which we have observed. But such changes may be a contributory factor when airway obstruction is more marked. The remaining explanation for the downward displacement of the pressure/flow curves is a reduction in critical closing pressure of blood vessels at the site of the ‘vascular waterfall’ (Lopez-Muniz et al., 1968). The site is likely to be
distal to the resistance vessels since the displacement of the pressure/flow curves is not apparently associated with a change in slope. However, whether the vessels are alveolar or extra-alveolar and how it is that they appear to respond both to breathing oxygen and, in the case of Group 2 subjects, to repetition of the exercise breathing air remain subjects for speculation.

These observations suggest a need for further study of the pulmonary circulation using pressure/flow curves. The results are also of practical importance for the management of patients with bronchitis. First in relation to early progressive massive fibrosis, the data provide evidence that the pulmonary circulation is not impaired except when there is superimposed bronchitis. Second, a reduction in the ability of the pulmonary vascular bed to accommodate an increase in blood flow during exercise may occur early in the natural history of bronchitis. Thus, it is misleading to describe as 'mild bronchitis' the condition of a patient whose only symptoms are chronic cough and sputum. Third, there is already good evidence for the load on the right ventricle during exercise being reduced by inhalation of oxygen. Our results suggest that, in relation to a task of a few minutes duration breathing air, the load may also be reduced by the subject dividing the exercise with a rest period.

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