

Pulmonary gas exchange during exercise in young asthmatic patients¹

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ABSTRACT Pulmonary function was examined in 19 young asthmatic patients at rest and during two levels of exercise. Findings at rest included decreased flow rates, increased residual volume, normal minute (\dot{V}_E) and alveolar (\dot{V}_A) ventilation, increased ratio of physiological dead space to tidal volume (VD/VT), increased alveolar-arterial oxygen tension difference (A-a PO₂), and mild arterial hypoxaemia and desaturation. On exercise there was a normal increase in \dot{V}_E and \dot{V}_A , the VD/VT and the A-a PO₂ decreased towards normal, and arterial oxygen tension improved, approaching normal levels. Significant acidosis did not develop.

Pulmonary function patterns in patients with asthma of varying severity have been adequately described (Bates *et al*, 1971). Exercise-induced bronchospasm, in particular, has received much attention (McNeill *et al*, 1966; Rebuck and Read, 1968; Fisher *et al*, 1970; Vassallo *et al*, 1972; Haynes *et al*, 1976). Studies of the physical fitness of asthmatic children and the effect of controlled exercise on their physical and social rehabilitation have been reported (Millman *et al*, 1965; Sly *et al*, 1972), but little information is available on the effects of exercise on ventilation and gas exchange (Beaudry *et al*, 1967; Vavra *et al*, 1969). Thus we were prompted to study ventilation and gas exchange alterations after graded exercise in a group of young asthmatic patients.

Patients and methods

Nineteen (13 male, six female) asthmatic patients were studied. Their ages ranged from 13 to 30 (mean age 19.3 years). All had a family history of asthma or hay fever, and all suffered from moderately severe spasmodic asthma, the average duration of which was 9.1 years (range 1–19). All took bronchodilators, and three took corticosteroids regularly. Informed consent was obtained from all.

All patients were studied in the morning. They had been instructed not to take their medications, except for corticosteroids, on the morning of the study.

Forced vital capacity (FVC) and flow rates were determined using a 9-litre Collins spirometer. The best of three tracings within 10% of one another and

the prediction formulae of Goldman and Becklake (1959) were used. From these data the forced expiratory volume in one second (FEV₁) and the forced expiratory flow over the middle 50% of the vital capacity (FEF_{25–75}) were calculated. Total lung capacity (TLC) was measured in duplicate using a closed-circuit helium dilution method (Bates and Christie, 1950). The average of two determinations that agreed to within 3% was used. Residual volume was obtained by subtracting the best vital capacity from the average TLC. Single breath diffusing capacity for carbon monoxide was determined by the method of Ogilvie *et al* (1957).

An indwelling Riley needle was placed in the brachial artery using 2% lidocaine anaesthesia. The subject then rested for 20–30 minutes. After several washouts, expired gas was collected for three minutes in a Tissot spirometer and simultaneously an arterial blood sample was obtained in the sitting position. The subject then exercised on a cycle ergometer (Siemens-Eléma, Solna 1, Sweden); male subjects exercised at 250 and 500 kilopond-metres a minute (Kpm) and female subjects at 200 and 400 Kpm for five minutes at each level. During the fifth minute expired gas was collected and a simultaneous arterial blood sample over several breaths was obtained. Arterial blood gas was analysed for oxygen (PO₂) and carbon dioxide (PCO₂) tensions and for pH using electrodes manufactured by Radiometer, Copenhagen. Expired gas was analysed using a micro-Schölander apparatus.

From these data minute (\dot{V}_E) and alveolar (\dot{V}_A) ventilation, oxygen consumption ($\dot{V}O_2$), CO₂ production ($\dot{V}CO_2$), and respiratory exchange ratio (R) were calculated using standard formulae (Comroe *et*

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al, 1962). Lung volumes and minute and alveolar ventilation were corrected to BTPS. Oxygen consumption and CO₂ production were corrected to STPD. Alveolar oxygen tension (PAO₂) was obtained from the alveolar air equation, and the alveolar-arterial PO₂ gradient (A-a PO₂) was determined. Physiological dead space (VD) was calculated using the Bohr equation, assuming arterial PCO₂ to be equal to alveolar PCO₂.

The data were analysed for differences between exercise levels using *t* tests (Snedecor and Cochran, 1967).

Results

Table 1 shows the resting lung volumes, flow rates, and diffusing capacity in the subjects. The vital capacity was within normal limits. The flow rates were moderately decreased, and there was hyperinflation. The diffusing capacity was normal.

Table 1 Resting pulmonary function in asthmatics (means ± SD)

Test	
Forced vital capacity (l)	3.85 ± 0.98
% predicted	103.5 ± 18.3
Forced expiratory volume in 1 s (l)	2.32 ± 0.87
FEV ₁ /FVC %	59.2 ± 12.4
Forced expiratory flow, 25–75% vital capacity (l s ⁻¹)	1.54 ± 1.0
Total lung capacity (l)	5.96 ± 1.32
% predicted	127.7 ± 13.5
Residual volume (l)	2.12 ± 0.96
RV/TLC %	35.5 ± 12.0
Transfer factor per M ² BSA (ml min ⁻¹ mmHg ⁻¹ M ⁻²)	21.1 ± 3.7

The results of ventilation, gas exchange, and arterial blood gas determinations at rest and on exercise are shown in table 2. The minute and alveolar ventilation and the $\dot{V}O_2$ and $\dot{V}CO_2$ were comparable to predicted normal values (Jones *et al*, 1975). There was mild arterial hypoxaemia at rest which improved significantly ($P < 0.01$) with mild exercise to nearly normal levels. The PAO₂ on the other hand was normal at rest and on exercise. Thus the A-a PO₂, abnormally wide at rest, decreased on exercise but remained significantly abnormal (Hesser and Matell, 1965). The PCO₂ was at the lower limit of normal and did not change with exercise. The pH was normal at rest, decreased significantly with exercise, but remained within physiologically normal limits. The ratio of physiological dead space to tidal volume (VD/VT) was increased at rest but decreased to normal levels during exercise (Jones *et al*, 1966).

In an attempt to determine whether the severity of airways obstruction at rest influenced the response to exercise, we compared the exercise values of the patients arbitrarily divided into a group of eight with

Table 2 Ventilation and gas exchange values at rest and two levels of exercise (E₁ and E₂) in asthmatic patients. Exercise 1: 200–250 Kpm; Exercise 2: 400–500 Kpm. Means ± Standard Deviation

Test	At rest	Exercise level 1 (P, E ₀ -E ₁)	Exercise level 2 (P E ₁ -E ₂)
\dot{V}_E (l/min)	8.41 ± 1.76	22.71 ± 4.76 (P < 0.001)	36.81 ± 6.19 (P < 0.001)
\dot{V}_A (l/min)	5.20 ± 0.80	17.26 ± 0.47 (P < 0.001)	30.01 ± 0.67 (P < 0.001)
$\dot{V}CO_2$ (l/min)	0.203 ± 0.029	0.682 ± 0.117 (P < 0.001)	1.169 ± 0.192 (P < 0.001)
$\dot{V}O_2$ (l/min)	0.269 ± 0.045	0.820 ± 0.130 (P < 0.001)	1.286 ± 0.204 (P < 0.001)
R	0.76 ± 0.07	0.84 ± 0.08 (P < 0.01)	0.91 ± 0.09 (P < 0.05)
VD (l/min)	0.182 ± 0.048	0.259 ± 0.070 (P < 0.001)	0.260 ± 0.112 N.S.
VT (l/min)	0.486 ± 0.178	1.036 ± 0.242 (P < 0.001)	1.376 ± 0.314 (P < 0.001)
VD/VT × 100%	39.5 ± 12.0	25.7 ± 7.1 (P < 0.001)	19.4 ± 8.1 (P < 0.05)
PAO ₂ mmHg	106.1 ± 6.9	108.5 ± 7.2 NS	112.0 ± 6.8* NS
Pao ₂ mmHg	72.7 ± 6.8	81.6 ± 8.6 (P < 0.01)	82.9 ± 7.7 NS
Paco ₂ mmHg	34.0 ± 4.1	35.0 ± 4.7 NS	34.3 ± 5.6 NS
pH	7.43 ± 0.04	7.40 ± 0.04 (P < 0.05)	7.37 ± 0.04 (P < 0.05)
Sao ₂ %	94.1 ± 1.8	95.6 ± 1.5 (P < 0.02)	95.8 ± 1.8 NS
A-a PO ₂ torr	32.6 ± 9.5	27.1 ± 7.4 (P < 0.02)	28.6 ± 6.6 NS
Respiratory frequency	17.9 ± 5.2	22.9 ± 5.6 (P < 0.02)	28.1 ± 7.5 (P < 0.05)
$\dot{V}_E/\dot{V}O_2$	31.6 ± 4.4	28.0 ± 5.2 (P < 0.05)	29.1 ± 5.3 NS

*Difference in alveolar PO₂ between rest and the second level of exercise is significant at the 2% level.

Conversion of mmHg to SI units: 1 kPa = 7.5 torr. Symbols as in text.

an FEV₁ less than 2 l and a group of 11 with an FEV₁ greater than 2 l. The patients with the lower FEV₁ had a greater respiratory frequency, a lower tidal volume, and a wider A-a PO₂ at the higher exercise level (table 3). The patients with a lower FEV₁ also had a lower PO₂ at rest and at both exercise levels.

Discussion

Most previous studies of asthmatic patients during exercise have dealt with the effect of exercise on flow rates and lung compliance. Itkin and Nacman (1966) studied 39 young asthmatics and showed that brief (1–2 min) exercise increased the FEV₁ whereas longer (8–12 min) exercise often decreased it, sometimes during the exercise period but usually after its completion. Jones *et al* (1963) also showed that asthmatics had increased flow rates during exercise with a postexercise reduction. Bevegård *et al* (1976) showed that severe asthmatics had increased minute ventilation during exercise; however, maximal oxygen consumption and aerobic muscle power were normal.

Table 3 Ventilation and gas exchange data correlated with resting airways obstruction

	At rest		Exercise level 1		Exercise level 2	
	<2L	>2L	<2L	>2L	<2L	>2L
FEV ₁	8	11	8	11	8	11
No	68.6 ± 7.8	75.7 ± 4.0	77.0 ± 8.6	84.9 ± 7.3	78.6 ± 9.5	86.1 ± 4.3
PaO ₂	P < 0.05		P < 0.05		P ≈ 0.05*	
VT	463 ± 69	503 ± 230	928 ± 216	1114 ± 238	1189 ± 195	1513 ± 320
VD/VT	37.9 ± 7.8	40.7 ± 14.6	29.9 ± 8.6	22.6 ± 3.9	20.3 ± 8.0	18.7 ± 8.6
Respiratory frequency	17.8 ± 2.4	18.0 ± 6.7	25.3 ± 3.6	21.2 ± 6.4	32.4 ± 8.2	24.9 ± 5.2
A-a Po ₂	36.4 ± 8.5	29.9 ± 9.7	29.4 ± 8.6	25.4 ± 6.3	32.6 ± 6.7	25.7 ± 5.1
	NS		NS		P < 0.05	

Symbols and abbreviations as in text.

Data were analysed in the same manner for \dot{V}_E , VD, PCO₂, pH, Vo₂, VCO₂ and no significant correlation with degree of airways obstruction was found.

*Value very slightly over P = 0.05.

1 kPa = 7.5 torr.

In this group the ratio of the tidal volume to the vital capacity was greater than 50%; blood lactate was also increased in relation to $\dot{V}O_2$. These authors commented on the normal circulatory and respiratory function in severe asthmatics and on their good response to exercise. Vavra *et al* (1969) divided 32 young asthmatics into three groups on the basis of frequency of symptoms and pulmonary function abnormalities. The subjects were then exercised on three consecutive days at progressive weight-related levels. Their results, which are presented only in graphic form, showed increased minute ventilation, increased ventilatory equivalent for oxygen ($\dot{V}_E/\dot{V}O_2$), and pronounced lactic acidosis in the group with the severest disease. Inspection of their figures shows no change in arterial saturation with exercise; this, in view of the lowered pH, suggests that the Po₂ did in fact rise (Bohr effect). These authors concluded that ventilation did not limit oxygen transport but that a circulatory limitation to oxygen transport existed, which they attributed to poor general conditioning.

In a careful study of pulmonary response to exercise in asthma, Haynes *et al* (1976) showed that $\dot{V}O_2$, $\dot{V}CO_2$, and \dot{V}_E did not differ significantly from normal, but the \dot{V}_E was achieved at a higher frequency and lower tidal volume in the asthmatics. The asthmatics had a lower end-tidal PCO₂ and a higher $\dot{V}_E/\dot{V}O_2$. These patients exercised at a heavier work load than ours, and this may explain their increased $\dot{V}_E/\dot{V}O_2$. Beaudry *et al* (1967) studied 12 asthmatic children in remission at rest and during exercise on a cycle ergometer. They observed that the mean FEV and the physiological dead space did not change after exercise, but that the VD/VT decreased. They also showed a significant metabolic acidosis and a rise in the respiratory exchange ratio in four of their asthmatics without an accompanying rise in PCO₂. These workers used arterialised capillary blood and did not report Po₂ values.

In our patients the average pH remained within normal physiological limits on exercise, but six out of 19 had a pH below 7.35 during the higher exercise level. Similarly, although the average PCO₂ was low normal at rest and did not change with exercise, four patients had a PCO₂ below 30 torr (4 kPa) during the higher exercise level, and one had a PCO₂ of 45 torr (6 kPa). Estimation of base deficit from the Sigaard-Andersen nomogram showed evidence of metabolic acidosis (base deficit -5) in nine of the 19 subjects. Unfortunately blood lactate levels were not determined.

Our most interesting observation is the increase in Po₂ to low normal levels that occurred in the asthmatics during even mild exercise. This is in contrast to the usual relative constancy of arterial Po₂ during exercise in the normal subjects and is similar to, though greater than, the increase reported by Jones (1966) in chronic bronchitis. Jones explained his findings by postulating improved ventilation in areas of the lungs that had a low ventilation/blood flow (\dot{V}/\dot{Q}) ratio at rest, presumably a result of opening up of narrowed small airways. This would be consistent with the improved flow rates observed during exercise in the studies quoted earlier (Irnell and Swartling, 1966; Itkin and Nacman, 1966) and may reflect the increased tidal volume and the associated increase in end-inspiratory transpulmonary pressure.

Another likely explanation for the improved Po₂ stems from the observation that the apices of the lungs are better perfused during exercise (West, 1963). Since airway closure is more likely to occur at the base of the lung because of the gradient of transpulmonary pressure down the pleural surface, at any level of bronchoconstriction the small airways are more likely to be open in the apices than at the bases. Thus the increase in apical blood flow during exercise will improve (that is, decrease) the \dot{V}/\dot{Q} ratio in the upper zones and thus possibly decrease the proportion of

blood going to low \dot{V}/\dot{Q} areas at the bases. The effect of either or both of these possibilities would be a decrease in the A-a P_{O_2} , which we have observed, and which is similar to that observed by Whipp and Wasserman (1969) in normal subjects at comparable work levels.

In conclusion we have shown that a group of moderately severe young asthmatic patients tolerated moderate exercise well, with improvement in arterial oxygenation and relatively normal pulmonary gas exchange.

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