

# Assessment of work performance in asthma for determination of cardiorespiratory fitness and training capacity

CHRISTOPHER J CLARK, LORNA M COCHRANE

*From the Department of Respiratory Medicine, Hairmyres Hospital, Glasgow, and the University of Glasgow*

**ABSTRACT** In view of the lack of objective information on work performance in asthma, a progressive incremental exercise test was carried out in 44 subjects with mild to moderate asthma and 64 normal, healthy subjects matched for habitual activity, to compare cardiorespiratory fitness and to determine the relative contribution of airflow obstruction to exercise limitation. The two groups achieved similar maximum heart rates (mean (SD) 176(12) and 175(10) beats/min). After allowance for confounding factors the asthmatic subjects had a lower maximum oxygen consumption ( $\dot{V}O_2$  max) (by 199 ml min<sup>-1</sup>) than control subjects. Having asthma also accounted for a significant reduction in anaerobic threshold (125 ml min<sup>-1</sup>) and oxygen pulse (0.805 ml/beat). There was no correlation of FEV<sub>1</sub> with  $\dot{V}O_2$  max, anaerobic threshold, or oxygen pulse either before or after bronchodilator. The dyspnoea index ( $\dot{V}E/MVV\%$ ) was increased in the asthmatic subjects at peak exercise, but was less than 60% in all subjects at a workload that produced 75% of the predicted maximum heart rate. Thus the asthmatic subjects had a maximum heart rate similar to that of normal subjects but the low  $\dot{V}O_2$  max, anaerobic threshold, and oxygen pulse suggest suboptimal fitness, which was not directly due to airflow obstruction. All had sufficient ventilatory reserve to allow toleration of training at a work intensity adequate to permit improvements in cardiovascular fitness.

## Introduction

People with asthma have a wide range of disability—from the requirement of competitive athletes for minimal treatment, allowing unrestricted participation in sport, to the steroid dependence of patients with severe and persistent airflow limitation. In between are many patients with moderate airflow limitation who experience frustration in relation to exercise and often lack specific advice about exercise from physicians. An informal survey of our own and our colleagues' practice in this respect confirmed that, beyond advising the use of a beta<sub>2</sub> selective agonist before exercise, encouraging swimming,<sup>1</sup> and warning them to avoid conditions apt to produce exercise induced asthma,<sup>2</sup> a conservative approach is usually adopted: patients are encouraged to use commonsense and remain alert to the development of respiratory complaints—at which point, they are told, exercise should cease. There is a lack of objective information regarding the contribution of airways obstruction to

exercise performance in these patients and consequently difficulty in answering the question "How much exercise can and should be undertaken?"

This study has used progressive incremental exercise testing to determine work performance, the contribution of respiratory factors to exercise limitation, and the likely capacity for endurance training in a group of patients with well controlled asthma of moderate severity.

## Methods

### SUBJECTS

The asthmatic subjects were 44 non-smoking patients (20 male, 24 female) with chronic stable asthma of moderate severity. All subjects required regular prophylactic treatment, had reproducible airways obstruction when treatment was withheld, and had had no recent exacerbation of asthma or admission to hospital. In all cases the provocative concentration of histamine causing a 20% fall in FEV<sub>1</sub> (PC<sub>20</sub>) was less than 8 mg/ml according to the method described by Hargreave *et al*<sup>3</sup> and 39 of the 44 patients fulfilled criteria for exercise induced asthma.<sup>4</sup> The control group consisted of 64 volunteers (28 male, 36 female)

Address for reprint requests: Dr C J Clark, Hairmyres Hospital, Glasgow G75 8RG.

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with no concomitant illness, past history of respiratory disease, or family history of asthma. All had a sedentary lifestyle, not carrying out any form of regular exercise or training.

#### MEASUREMENTS

Baseline spirometry and flow-volume analysis were performed with a dry rolling seal spirometer (System 5000 IV, Gould Electronics). Progressive incremental exercise was performed until exhaustion on a bicycle ergometer in which the workload was increased by 25 watt increments at one minute intervals while the subject was pedalling at a frequency of 40–60 cycles/min<sup>5</sup> (System 9000 IV, Gould Electronics). Heart rate, respiratory frequency, tidal volumes, minute ventilation ( $\dot{V}_E$ ), and mixed expired concentrations of carbon dioxide and oxygen were measured continuously to allow calculation of oxygen consumption ( $\dot{V}_{O_2}$ ) and carbon dioxide production ( $\dot{V}_{CO_2}$ ). A dyspnoea index<sup>6</sup> was obtained by expressing minute ventilation as a percentage of maximum voluntary ventilation (MVV) (post-bronchodilator  $FEV_1 \times 35$ ). Maximum heart rate was predicted from the formula<sup>5</sup>  $210 - 0.65 \times \text{age (years)}$ . Oxygen pulse was defined as oxygen consumption per heart beat (ml/beat). Anaerobic threshold was determined from the  $\dot{V}_E/\dot{V}_{O_2}$  plot by three independent observers using the method of Wasserman *et al.*<sup>7</sup> Salbutamol (5 mg in 1 ml) was administered to the asthmatic subjects via a Wright mini nebuliser 10 minutes before exercise, which started after repeat dynamic spirometry. Transcutaneous oxygen tension was measured throughout exercise (IL301 Tm Monitor).

#### Analysis

The significance of the difference between control and asthmatic subjects was assessed by Student's *t* test and the magnitude of linear association between pairs of continuous variables with Pearson's coefficient of correlation. Because some of the measurements made during exercise are dependent on several variables including age, sex, weight and height, multiple regression analysis was used to compare the two groups after adjustment for these factors. A *p* value of  $<0.05$  was considered significant.

#### Results

Anthropometric data, baseline lung function values and cardiorespiratory performance data are summarized in the table.

There was no significant difference in mean (SD) heart rate during maximum exercise between the asthmatic (176 (12) beats/min) and the control subjects (175 (10) beats/min). Mean  $\dot{V}_{O_2}$  max and the oxygen pulse were significantly lower in asthmatic than in control subjects for men but not for women. The dyspnoea index (%) was significantly higher in the asthmatic subjects during maximum exercise (61 (19) vs 49 (10);  $p < 0.001$ ) and also at the submaximal workload producing 75% of the predicted maximum heart rate (34 (15) vs 25 (6);  $p < 0.001$ ).

The three "cardiovascular fitness" variables— $\dot{V}_{O_2}$  max, anaerobic threshold, and oxygen pulse—were significantly lower in both men and women with asthma than in control subjects according to multiple regression analysis. Asthma accounted for a mean

Mean (SD) anthropometric data, baseline lung function, and maximal cardiorespiratory performance data for the subjects in the study

	Male		Female	
	Control (n = 28)	Asthma (n = 20)	Control (n = 36)	Asthma (n = 24)
Age (y)	27.5 (5.5)	27.2 (7.6)	33.6 (5.4)	26.2 (7.7)†
Weight (kg)	71.3 (9.4)	72.5 (10.2)	58.0 (6.4)	62.7 (9.4)*
Height (cm)	178.1 (6.2)	176.3 (6.1)	161.4 (5.1)	162.2 (6.9)
FEV <sub>1</sub> (l)	4.54 (0.44)	3.40 (0.77)†	3.19 (0.36)	2.52 (0.75)†
FEV <sub>1</sub> (% pred‡)	105.3 (7.5)	81.1 (17.1)†	110.9 (9.4)	81.0 (21.3)†
Rx FEV <sub>1</sub> (l)		3.72 (0.67)†		2.73 (0.68)†
Rx FEV <sub>1</sub> (% pred‡)		88.9 (14.6)†		88.5 (19.6)†
$\dot{V}_{O_2}$ max (ml kg <sup>-1</sup> min <sup>-1</sup> )	35.2 (6.1)	31.6 (5.1)*	25.3 (2.8)	23.6 (4.9)
Oxygen pulse (ml/beat)	13.9 (2.0)	12.7 (1.5)*	8.4 (1.0)	8.3 (1.3)
Anaerobic threshold (l min <sup>-1</sup> )	1.72 (0.26)	1.59 (0.26)	1.14 (0.03)	1.06 (0.20)
Heart rate, max (% pred‡)	93.2 (4.5)	92.8 (6.7)	92.1 (5.7)	90.5 (5.0)
$\dot{V}_{Emax}$ (l min <sup>-1</sup> )	81.5 (17.2)	77.9 (17.8)	53.3 (11.3)	54.3 (12.8)
DI <sub>max</sub> (%)	51.2 (11.5)	62.6 (21.6)*	48.0 (9.2)	59.7 (17.9)**
DI <sub>75%</sub> (%)	26.5 (5.6)	34.4 (16.1)*	23.8 (5.4)	34.2 (13.3)**
$\dot{V}_{EO_2max}$	33.0 (5.4)	34.3 (5.7)	36.2 (5.5)	37.2 (5.2)

\* $p < 0.05$ , \*\* $p < 0.01$ , † $p < 0.001$  (Student's *t* test). ‡See Knudson *et al.*<sup>21</sup>  
 Rx FEV<sub>1</sub>—FEV<sub>1</sub> after 5 mg salbutamol (asthmatic subjects only);  $\dot{V}_{O_2max}$ —maximum oxygen consumption;  $\dot{V}_{Emax}$ —maximum minute ventilation;  $\dot{V}_{EO_2max}$ —ventilatory equivalent for oxygen at maximal exercise ( $\dot{V}_E/\dot{V}_{O_2}$ ); DI<sub>75%</sub>—dyspnoea index at a work rate producing 75% predicted maximum heart rate (see under "Methods" for details of definitions).

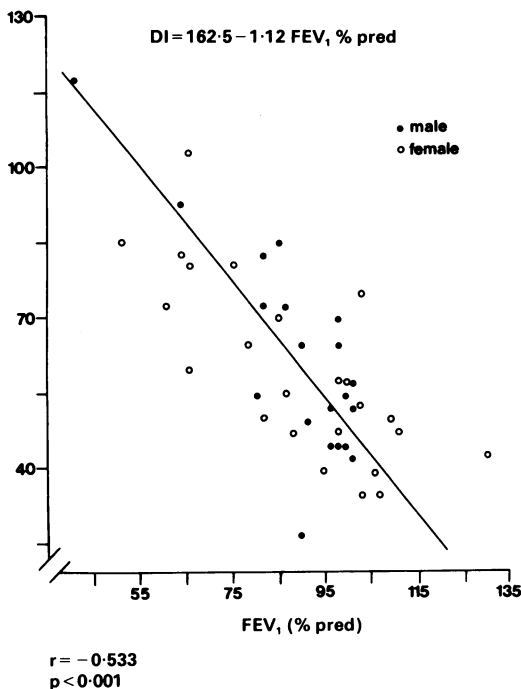
Dyspnoea  
index  
( $\dot{V}_E/\dot{V}_{MVV}$ )

Fig 1 Relation between dyspnoea index ( $\dot{V}_E/\dot{V}_{MVV}\%$ ) at maximum exercise and FEV<sub>1</sub> % predicted in the 44 asthmatic subjects.

reduction in  $\dot{V}O_2$  max of 199 ml min<sup>-1</sup> ( $p < 0.001$ ). The relation between  $\dot{V}O_2$  and the diagnosis of asthma is described in the equation

$$\dot{V}O_2 \text{ max (ml min}^{-1}\text{)} = 1906.3 + 13.33 \text{ wt (kg)} - 723.8 \text{ SEX} - 14.19 \text{ age (y)} - 199.23 \text{ ASTHMA}$$

(SEE 27.03,  $r = 0.88$ ),

where ASTHMA = 1 for asthmatic and 0 for control subjects and SEX = 1 for females and 0 for males.

The anaerobic threshold was 125 ml min<sup>-1</sup> lower ( $p < 0.001$ ) and oxygen pulse 0.805 ml/beat lower ( $p < 0.001$ ) in the asthmatic than in the non-asthmatic subjects.

Within the asthmatic group there was no linear correlation between FEV<sub>1</sub> before or after bronchodilator and the "cardiovascular fitness" variables  $\dot{V}O_2$  max, anaerobic threshold, or oxygen pulse, whether FEV<sub>1</sub> was expressed in absolute terms or as percentages of predicted values. Once age, weight and sex had been taken into account, there was no separate contribution from FEV<sub>1</sub> to these variables. A relatively poor correlation was found between post-bronchodilator FEV<sub>1</sub> and dyspnoea index at peak exercise ( $r = -0.53$ ,  $p < 0.001$ ; fig 1). There was no fall

in transcutaneous oxygen tension from baseline during exercise in any asthmatic subject.

## Discussion

The progressive incremental exercise test used in this study provides anaerobic threshold and oxygen pulse as "cardiovascular fitness" variables<sup>8,9</sup> in addition to  $\dot{V}O_2$  max, which is currently recognised as the best overall determinant of cardiorespiratory performance.<sup>9</sup> Simultaneous measurement of minute ventilation also allows an analysis of the interrelation of the ventilatory response to exercise with the cardiovascular response.

Contrary to the expectation of the asthmatic subjects that their condition would not permit exercise of high intensity, they achieved a maximum heart rate with progressive incremental exercise similar to that of control subjects. We might therefore expect a similar degree of fitness because our subjects were matched for lifestyle and asthma was apparently not a limiting factor. The three measures of "cardiovascular fitness," however— $\dot{V}O_2$  max, anaerobic threshold, and oxygen pulse—were all significantly lower in the asthmatic subjects. If we assume that the FEV<sub>1</sub> before bronchodilator administration represents the severity of airflow obstruction, then the lack of correlation with these measures of fitness in the asthmatic subjects suggests that factors other than the severity of asthma are responsible for their lack of fitness. The fitness measures also failed to show a correlation with post-salbutamol FEV<sub>1</sub>, which may better represent average daily lung function. In this study nebulised salbutamol was given to the asthmatic subjects but not to the control subjects and we cannot therefore exclude an effect of the drug on our findings. Beta<sub>2</sub> selective agonists given intravenously and orally produce several metabolic changes, including an increase in glucose, insulin, lactate, and pyruvate.<sup>10,11</sup> These changes were not, however, seen in a study using nebulised salbutamol.<sup>12</sup> Furthermore, Ingemann-Hansen *et al.*,<sup>13</sup> using an exercise protocol similar to ours in asthmatic subjects, found no effect of 5 mg nebulised salbutamol (by comparison with nebulised saline) on maximal oxygen consumption or oxygen pulse at peak exercise. There was also no significant difference in the metabolic response to exercise, including plasma pH and bicarbonate concentrations. We conclude that the administration of nebulised salbutamol is unlikely to explain our results and that the reduction in oxygen pulse is likely to be due to lack of fitness, particularly as this measure agrees with the other "cardiovascular fitness" measures.

The reason for the poorer level of fitness in the asthmatic subjects is a matter for speculation. The subjects were young adults and possibly in early

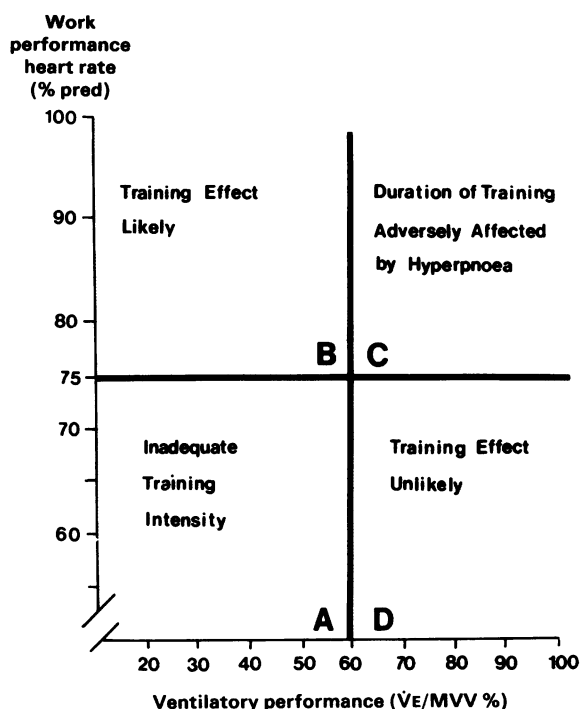


Fig 2 Interrelation between exercise intensity and the resulting ventilatory response in determining training effect in an individual with asthma. The heart rate, expressed as percentage of predicted maximum, represents the intensity of work undertaken. The minute ventilation ( $\dot{V}_E$ ) produced by that level of exercise is expressed as a percentage of maximum voluntary ventilation (MVV). The thick horizontal line represents the work intensity below which a training effect is unlikely. The thick vertical line represents the  $\dot{V}_E$ /MVV above which exercise is unlikely to be tolerated for long enough to achieve a training effect (see ref 18).

adolescence their asthma had been much worse, so that they were less able to carry out exercise and hence developed a sedentary lifestyle. Alternatively, they may have a more fundamental and continuing aversion to exercise as a result of longstanding asthma,<sup>14,15</sup> perhaps compounded by the lack of advice from physicians and school physical education teachers.<sup>16</sup> Even for the normal, healthy individual exercise will improve aerobic fitness only if certain criteria for its intensity, frequency, and duration are consistently fulfilled over several months. The recommended guidelines<sup>17</sup> suggest a workload that produces about 75% of the predicted maximum heart rate for 20 minutes at least three times a week. In those with asthma the underlying obstruction may limit exercise tolerance if there is inadequate ventilatory reserve. It is not clear how individuals should determine the extent of their ventilatory reserve and how the recommended

guidelines should be adapted to their own circumstances. These uncertainties may deter even well-motivated individuals from taking exercise. High levels of minute ventilation close to the MVV can only be tolerated for a short time because of breathlessness. This principle is used routinely in progressive incremental exercise testing, where the relationship  $\dot{V}_E$ /MVV during maximal exercise is used to identify "respiratory limitation."<sup>18</sup> The potential contribution of reduced ventilatory reserve to intolerance of the submaximal exercise necessary for endurance training was shown in a study that measured the endurance time for various levels of minute ventilation in relation to the MVV by using voluntary isocapnic hyperventilation.<sup>18</sup> As minute ventilation fell to 60% of MVV, endurance time rose to about 15 minutes. At this point in the relationship the "asymptote," the tangent to the curve of minute ventilation versus endurance time, "extended to infinity." Lower levels of ventilation were comfortable and could be sustained continuously. The importance for endurance training in the person with asthma is that for a given frequency and intensity of exercise the ventilatory reserve will determine the duration of exercise and therefore the potential for achieving a training effect. This is illustrated schematically in figure 2. Sector A represents the case where exercise intensity (max heart rate <75% predicted) is inadequate for achieving a training effect. Patients who choose this pattern of performance, because they misinterpret the perceived severity of more strenuous exertion as being due to their underlying condition, will fail to improve fitness despite adequate ventilatory reserve, regardless of the duration of exercise sessions. Sector B represents the case where the patients choose an adequate exercise intensity and have enough ventilatory reserve (low  $\dot{V}_E$ /MVV%) to allow the necessary duration of exercise to achieve a training effect. This was the pattern seen in our study group, as the dyspnoea index was below 60% in all the asthmatic subjects at a submaximal workload that produced 75% of the predicted maximum heart rate. In sector C the duration of exercise at high workloads is impaired by inadequate ventilatory reserve. In sector D inadequate ventilatory reserve at low workloads makes even mild exercise difficult and precludes a training effect.

As asthmatic patients relying solely on subjective response may be unable to determine the appropriate level of exercise and as resting lung function will not predict exercise ventilation accurately, we conclude that there may be a need for objective exercise testing as the basis for training. A modified incremental exercise test using the principles outlined in this paper with emphasis on measurements of heart rate and minute ventilation may have practical application in allowing individual exercise prescription for asthmatic



tion for asthmatic individuals with a wide spectrum of disability. There is an increasing public awareness of the long term benefits of active participation in sport and exercise,<sup>19</sup> including a reduction in the risk of accelerated atherosclerosis,<sup>20</sup> and there is likely to be an increasing obligation to provide advice and information to those with asthma, who have aspirations to a healthy lifestyle much as normal people do.

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