

# Evaluation of bronchial responsiveness to exercise in children as an objective measure of asthma in epidemiological surveys

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## Abstract

**Background – Exercise has been proposed as a useful challenge test for the measurement of bronchial responsiveness in community surveys of the prevalence of childhood asthma. This study aimed to develop a standardised exercise challenge in which the sensitivity to detect asthma was increased by inhalation of dry air.**

**Methods – Sixty four children aged 12–13 years who had reported wheeze in the past 12 months and 70 control subjects were invited to participate in an exercise challenge at school. Subjects performed eight minutes of cycle exercise while breathing dry air at a workload calculated to produce a minute ventilation of 60% maximum voluntary ventilation during the final three minutes. A fall in forced expiratory volume in one second ( $FEV_1$ ) of 10% or more from baseline was considered a positive test. Data on recent asthma symptoms, asthma morbidity, and use of medication were collected by parent completed questionnaires in those subjects who reported wheeze in the past 12 months. Repeatability of the exercise test was determined in a further 13 children with known asthma.**

**Results – Fifty five children (88%) who reported wheeze in the previous 12 months and 54 control subjects (77%) were studied. Nine subjects in whom baseline  $FEV_1$  was less than 75% predicted did not perform the exercise test. Technically unsatisfactory tests were obtained in five subjects. Twenty six (57%) subjects who reported wheeze and three controls (6%) had a positive exercise test, giving a sensitivity of 57% (26 of 46) and specificity of 94% (47 of 50). Estimates of the repeatability of the exercise test showed a mean difference in percentage fall in  $FEV_1$  for patients with asthma of 3·08% (95% limits of agreement –7·76% to 13·92%).**

**Conclusions – Despite attempts to maximise the stimulus to bronchoconstriction in this exercise challenge test, its sensitivity and specificity were not improved in comparison with previous epidemiological studies of the prevalence of asthma.**

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The reported prevalence of asthma in children has been increasing worldwide,<sup>1,2</sup> particularly in countries from the southern hemisphere.<sup>3</sup> In

Australia there has been a striking increase of 141% in the prevalence of asthma over 26 years to 1990.<sup>4</sup> This increase may be real or may be due to a greater readiness to diagnose asthma in wheezing children as a result of an increased awareness of the condition.

Epidemiological surveys of the prevalence of asthma in children have traditionally relied upon questionnaires completed by parents to collect information on respiratory symptoms or doctor diagnosed asthma and have lacked an objective measure of abnormal airways function. Such questionnaires lack precision for diagnosing clinically important asthma. Parental responses may be influenced by prior exposure to asthma and by different interpretations of the term "wheeze".<sup>5</sup> Furthermore, the pattern of questionnaire response may vary over time.<sup>6</sup> The prevalence of asthma cannot be measured in terms of abnormalities of lung function since most asthmatic children have normal resting lung function.<sup>7,8</sup>

Objective measures of bronchial responsiveness in field studies of the prevalence of asthma in children have previously used pharmacological challenge with histamine and methacholine. However, the relationship of bronchial hyperresponsiveness to asthma is controversial.<sup>9</sup> While there is a relatively sensitive association between the response to pharmacological challenge and diagnosed asthma, the relationship lacks specificity. Bronchial hyperresponsiveness measured by methacholine challenge is variable over time and correlates poorly with clinical severity of asthma.<sup>10</sup> A study of Australian schoolchildren aged 8–11 years using histamine challenge reported a sensitivity for diagnosed asthma of 53% and specificity of 87%.<sup>11</sup> Other studies from the UK<sup>12,13</sup> and New Zealand<sup>14–16</sup> show that up to 40% of current asthmatics fail to show airways responsiveness to histamine or methacholine and that bronchial hyperresponsiveness is found in 10–15% of asymptomatic children. Bronchial hyperresponsiveness to inhaled methacholine or histamine seems insufficient to discriminate between asthma and non-asthma in population samples.<sup>17</sup>

The exercise challenge is potentially useful in epidemiological studies of asthma in children as a more physiological stimulus to acute airway narrowing. Laboratory studies suggest that some children with clinical asthma constrict in response to an exercise challenge but not to methacholine or histamine and vice versa.<sup>18–22</sup> Furthermore, exercise, but not methacholine challenge, differentiates asthma

Table 1 Severity index for asthma subjects\*

1. Frequency of wheeze
2. Timing of last attack of wheeze
3. Frequency of night cough or wheeze
4. Frequency of early morning wheeze
5. Normal activities limited by cough or wheeze
6. Sporting activities limited by wheeze or breathlessness

\* Maximum score 24, 0–4 for each item.

from other chronic lung diseases in children.<sup>23</sup> Previous laboratory based studies of exercise challenge in asthmatic children have shown a sensitivity of 70–80% and a specificity of 100%,<sup>18 22–24</sup> although selection bias may have influenced these results. Although a standardised exercise test has been developed for laboratory use in children,<sup>25 26</sup> few epidemiological studies have attempted to standardise conditions of workload, minute ventilation, temperature, and humidity of inspired air which all have a significant effect on the degree of bronchoconstriction following exercise.<sup>21 27–31</sup>

The aim of this study was to determine the predictive value of bronchial responsiveness to cycle exercise in 12–13 year old schoolchildren as an objective measure of the prevalence of asthma in a community based cross sectional survey. This paper describes a protocol for exercise challenge where factors known to influence bronchial responsiveness to exercise were standardised as far as possible. Dry air was used to provide standardised inspired air conditions and to improve the sensitivity of the exercise challenge by increasing the stimulus to bronchoconstriction.

## Methods

### SUBJECTS

A population of 12–13 year olds was identified for study. This group was selected for direct comparison with the 1991 asthma prevalence study<sup>4</sup> and was felt to be able to perform an exercise test reliably. Three schools within metropolitan Melbourne with a reasonable representation of the population were sampled. All children in the relevant grade of the selected schools were invited to participate. Schools were given a short questionnaire on respiratory symptoms for distribution to parents which was reissued if the first was not returned. The questionnaire was identical to that used in the Melbourne asthma prevalence study.<sup>4</sup>

All children who were reported to have wheezed in the past 12 months were invited to perform a cycle exercise test at school. In addition, the parents of these children were asked to complete a further postal questionnaire to determine the severity of their child's asthma symptoms. A six item symptom score as shown in table 1 was used to classify the severity of the asthma. Controls, whose parents reported no wheeze in the past 12 months, were randomly selected from the same school and grade as the cases and matched for sex. The control group were also invited to perform a cycle exercise test within school. All cycle exercise challenges were performed within

a four week period from August to September 1992.

Reproducibility of the cycle exercise test was determined in 13 children aged 7–15 years with asthma of varying grades of severity who attended the outpatients department of the Royal Children's Hospital, Melbourne. These children had previously been shown to have reversible airways obstruction as defined by their response to inhaled bronchodilator.

The study was approved by the Royal Children's Hospital ethics in human research committee. Permission to conduct the study was obtained from the principals of the schools involved. Written consent was obtained from the parents of all children.

### PULMONARY FUNCTION TESTING

Subjects were instructed how to perform spirometric tests. Forced expiratory volume in one second ( $FEV_1$ ), forced vital capacity (FVC), and peak expiratory flow rate (PEFR) were measured on three occasions (Flowmate, Jaeger, Germany) immediately before exercise by one investigator (JW). Subjects who obtained repeatable measurements of  $FEV_1$  within 10% which were greater than 75% predicted for height and sex (Polgar and Promhaldt) proceeded to cycle exercise. Those children whose  $FEV_1$  was less than 75% predicted were given a nebulised  $\beta$  agonist (salbutamol 5 mg) and forced expiratory manoeuvres were repeated after 15 minutes to assess responsiveness to the bronchodilator.

### EXERCISE TESTING

Subjects were requested to withhold medication before exercise challenge as follows: antihistamines (48 hours), theophylline and sodium cromoglycate (24 hours), aerosol  $\beta$  agonists (6 hours), and inhaled corticosteroids on the morning of the challenge. Children were asked to refrain from physical exercise and to avoid beverages containing caffeine on the day of the test. The technician supervising the cycle exercise test (JW or RR) was blinded to the subject's questionnaire response.

The predicted  $FEV_1$  was used to calculate the indirect maximum voluntary ventilation ( $MVV = \text{predicted } FEV_1 \times 35$ ) and the workload appropriate to achieve 60% of predicted MVV (target ventilation) was calculated.<sup>32</sup> The oxygen consumption required to stimulate the target ventilation and the workload producing this oxygen consumption were determined from data by Godfrey *et al.*<sup>33</sup>

Exercise was performed for eight minutes on a bicycle ergometer (Collins Pedalmate, USA). Subjects breathed by mouth from a cylinder of compressed dry medical air via a demand valve (CIG Medishield, Sydney, Australia) which was attached to the inspiratory port of a two-way non-rebreathing valve (Hans Rudolph, Kansas City, No. 2700). The temperature of the inspired air ranged between 19°C and 22°C. Inspired air passed through a pneumotachograph (Ventilometer Mark 2) and ventilation was recorded throughout exercise. Dur-

**Table 2** Mean (SD) characteristic and performance data from those children who completed the cycle exercise test

Patient group	Number completing exercise	Height (cm)	FEV <sub>1</sub> , %pred (l/min)	Maximum workload/kg (Watts)	Maximum heart rate (bpm)	Inspired V̇ <sub>E</sub> as a % of MVV
Wheeze	46	155.3 (7.7)	90.0 (15.6)	2.52 (0.54)	179 (12)	59.1 (9.1)
Control	50	154.2 (6.2)	97.5 (14.2)**	2.52 (0.50)	176 (15)	57.1 (7.7)

FEV<sub>1</sub> = forced expiratory volume in one second; V̇<sub>E</sub> = expired minute ventilation; MVV = maximum voluntary ventilation.

\*\* p<0.01 versus control.

ing the first three minutes of exercise the workload was increased from 60% to 75% and finally in the fourth minute to 100% of the workload calculated to produce the target ventilation. This workload was then maintained for the final four minutes. Minor adjustments in the workload were made if necessary to achieve the target ventilation in the final three minutes of cycle exercise. Heart rate and oxygen saturation were measured throughout each exercise test (Omeda Biox, BOC, UK).

Measurements of FEV<sub>1</sub> in triplicate were recorded at one, three, five, seven, 10, and 15 minutes following completion of the exercise test by the same investigator (JW). The highest of three values was used in calculations.

#### ASSESSMENT OF REPEATABILITY

Subjects attended the Respiratory Laboratory at the Royal Children's Hospital at the same time of day (within 30 minutes) on two occasions during a seven day period to perform a cycle exercise test as described previously.

#### DATA ANALYSIS

Statistical analysis was carried out using Minitab Version 7.1 (Minitab Inc, 1989). Comparisons of height, pre-exercise pulmonary function, percentage fall in FEV<sub>1</sub>, maximum workload performed, inspired minute ventilation, and maximum heart rate between subjects and controls were performed using the paired Student's *t* test and, where appropriate, using the Mann-Whitney U test. The percentage fall in FEV<sub>1</sub> following exercise challenge was a continuous variable which could be calculated for each subject. The percentage fall in FEV<sub>1</sub> following exercise was expressed as the percentage fall index calculated as follows:

$$(A - B) \times 100/A$$

where A = FEV<sub>1</sub> measured immediately before exercise and B = lowest FEV<sub>1</sub> recorded within 15 minutes of exercise.

A value for the percentage fall index of more than 10%, which represents twice the coefficient of variation of the FEV<sub>1</sub> measure, was considered a positive response. Sensitivity and specificity of the exercise challenge were calculated from 2 × 2 tables using a cutoff level of percentage fall index of 10%. To correct for the sampling method the results were weighted to calculate the predictive values for a positive and negative exercise test. The repeatability of duplicate measurements of percentage fall index following cycle exercise challenge in

known asthmatic subjects was analysed according to the method of Bland and Altman.<sup>34</sup>

## Results

### ANALYSIS OF SCREENING QUESTIONNAIRE

Questionnaires were issued to parents of 475 children (233 boys) and were returned by 418 (192 boys), a response rate of 88%. Of these, 64 (15.3%) reported wheeze in the past 12 months. The reported prevalence of wheeze or asthma ever was 35.6% (n=149).

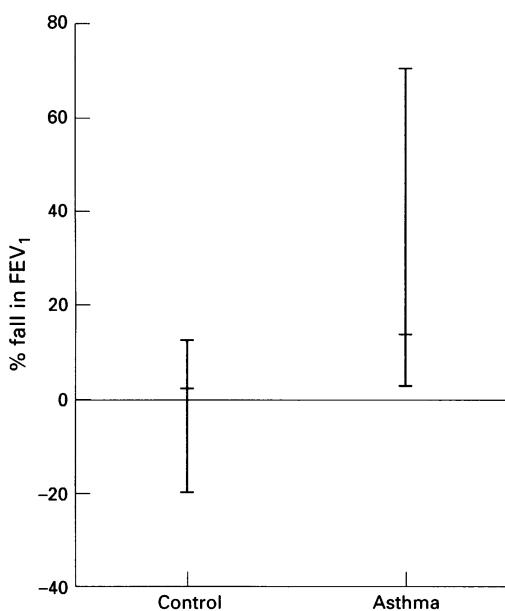
### ANALYSIS OF CYCLE ERGOMETER EXERCISE TEST

All 64 children (36 boys) who were reported to have wheezed in the preceding 12 months and 70 control subjects (38 boys) selected randomly from parents reporting "no" to wheeze or asthma in the past 12 months were invited to participate in a cycle exercise test at school. The participation rate in the exercise challenge was 55 of 64 (88%) for those who were reported to have wheezed in the last 12 months and 54 of 70 (77%) for controls. Of those children declining to participate in the exercise challenge, parental consent was refused in 13 cases (three with wheeze, 10 controls) and nine children were absent from school on the test day (three with wheeze, six controls).

Nine children (six boys) had an initial FEV<sub>1</sub> of less than 75% predicted and were excluded from the exercise test. Bronchodilator responsiveness was not assessed in two subjects. Five of the subjects showed a greater than 10% increase in FEV<sub>1</sub> following bronchodilator. One subject whose parents reported infrequent episodic symptoms of cough and wheeze, and who was receiving a β agonist intermittently, showed a bronchodilator response of 6%, and another child with breathlessness on exertion showed an FEV<sub>1</sub> of 71%, FEV<sub>1</sub>/FVC of 100% with a restrictive pattern, and no response to bronchodilator. Technically unsatisfactory tests were obtained in five children (one with wheeze, four controls). Of these, one child demonstrated poor reproducibility of pretest FEV<sub>1</sub> and did not proceed to cycle exercise. Three children were unable to tolerate the nose clip and only one was unable to complete the required eight minutes of cycle exercise. Data from these five subjects were excluded from further analysis. Complete exercise data were therefore obtained from 46 subjects reporting wheeze in the past 12 months and 50 controls.

Table 2 shows the anthropometric data, pre-test pulmonary function, maximum workload, and inspired minute ventilation, expressed as a percentage of maximum voluntary ventilation (MVV), for those 96 children who satisfactorily completed the cycle exercise challenge. There were no significant differences between subjects and controls in height, maximum workload/kg performed, and inspired minute ventilation expressed as a percentage of MVV. Subjects and controls achieved a mean minute ventilation approaching 60% of MVV and in both groups mean maximum heart rate exceeded 170 bpm. Pretest FEV<sub>1</sub> was significantly lower in children

**Figure 1** Median (range) for maximum fall in forced respiratory volume in one second ( $\text{FEV}_1$ ) as a percentage of baseline value (percentage fall index) following cycle exercise in asthmatic and control subjects.

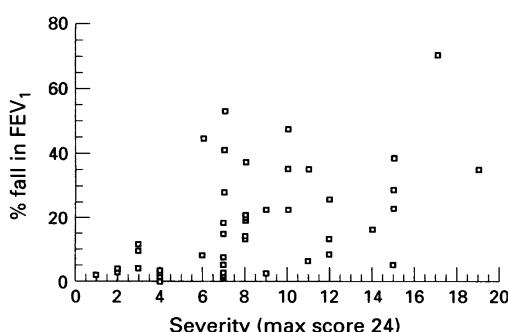


reporting wheeze in the past 12 months than in controls ( $p<0.01$  paired  $t$  test).

The distribution of percentage fall in  $\text{FEV}_1$  following exercise challenge for children with wheeze and control subjects is illustrated in fig 1. The median change in  $\text{FEV}_1$  was 13.6% (range 0-70.5%) for children with wheeze and 2.7% (range 0-12.6%) for control subjects. This difference in percentage fall index was significant ( $p<0.0001$ , Mann-Whitney U test).

Figure 2 shows the relationship between percentage change in  $\text{FEV}_1$  following exercise challenge and the severity index for subjects reporting wheeze in the past 12 months. The two variables were significantly correlated with a Spearman correlation coefficient  $r_s=0.552$  ( $p=0.001$ ).

As shown in table 3, 26 children who reported wheeze had a more than 10% fall in  $\text{FEV}_1$  following cycle exercise. However, for the remaining 20 subjects with wheeze the percentage fall index was less than 10%. Forty seven of the 50 control subjects showed no significant fall in  $\text{FEV}_1$  following exercise challenge. By using wheeze in the past 12 months as the "gold standard" for a diagnosis of asthma, the cycle exercise challenge therefore



**Figure 2** Relationship between the percentage fall index for forced expiratory volume in one second ( $\text{FEV}_1$ ) following cycle exercise and the severity index in subjects reporting wheeze in the past 12 months ( $r_s=0.552$ ,  $p<0.001$ ).

**Table 3** Sensitivity and specificity of the exercise test for (A) patients reporting wheeze in the last 12 months and controls and (B) for those with (symptomatic) and without symptoms suggesting asthma in the last 12 months

Patient groups	Fall in $\text{FEV}_1 > 10\%$	Fall in $\text{FEV}_1 < 10\%$
(A) Wheeze Control	26 3	20 47
(B) Symptomatic No asthma	27 2	11 56

(A) Sensitivity = 57% (26/46), specificity = 94% (47/50).

(B) Sensitivity = 71% (27/38), specificity = 96.5% (56/58).

has a calculated sensitivity of 57% (26 of 46) and a specificity of 94% (47 of 50). The inclusion of those children with an initial  $\text{FEV}_1$  of less than 75% and a bronchodilator response of more than 10% gives a sensitivity of 56% (31 of 55). The positive predictive value of the exercise test as diagnostic for asthma in a population sample was 63% (26 of 41) and the negative value for children with no history of wheeze in the past 12 months was 92% (238 of 258).

The sensitivity and specificity of the exercise challenge may be improved by analysing individual subject responses in more detail as shown in table 3. Three "control" subjects without reported wheeze in the past year showed a fall in  $\text{FEV}_1$  of more than 10% (12.6%, 12.6%, and 10.5%). One child had current night cough and a past history of asthma and a further child reported a history of exercise-induced wheeze within the previous 12 months. If these children are included in the "symptomatic" group rather than the "no asthma" group the specificity of the exercise challenge improves to 96.5% (56 of 58). Similarly, if the relationship between the clinical severity score and percentage change in  $\text{FEV}_1$  is reviewed, 10 subjects had a severity score of 4 or less, of whom all but one had a fall in  $\text{FEV}_1$  of less than 10%. These children, although reporting wheeze in the past 12 months, could be considered to have very mild asthma and only one child in this group was receiving inhaled prophylaxis (sodium cromoglycate), the remainder receiving intermittent bronchodilator or no treatment. If these 10 children form part of the "no asthma" group, the sensitivity of the exercise challenge improves to 71% (27 of 38).

The within-patient repeatability of the cycle exercise test in 13 patients with clinical asthma showed the mean difference in percentage fall in  $\text{FEV}_1$  to be 3.08% and the 95% limits of agreement between the two measurements ranged from -7.76% to 13.92%.

## Discussion

Studies of the prevalence of asthma are limited by a lack of an acceptable epidemiological definition. In this study the definition of "true" asthma included those children who reported wheeze in the past 12 months.<sup>4</sup> This definition is currently accepted as the best definition of asthma for epidemiological purposes in the paediatric age group but does have shortcomings. The use of exercise as an appropriate

objective challenge test for asthma in community surveys is attractive as a physiological stimulus to bronchoconstriction which may be more representative of true asthma than a pharmacological challenge. In general, an exercise test is simple to perform and is enjoyed by children who are generally compliant with this type of challenge. The acceptability of standardised exercise challenge used in this study was good. Parental consent was given in 91% and most of the non-attenders (16 of 22) were in the control group of children; 90% (46 of 51) of the 11–12 year old children studied were able to complete the eight minute cycle exercise challenge satisfactorily.

Our standardised exercise challenge was devised from a laboratory based cycle exercise test for clinical asthma<sup>32</sup> adapted for use in children and designed to maximise the stimulus to exercise-induced bronchospasm. Temperature and humidity of inspired air were controlled by the use of cylinder compressed air with a water content of 0 mg H<sub>2</sub>O/l is recommended to stimulate exercise-induced asthma.<sup>34</sup> The inspired ventilation rate was used to quantify the stimulus and standardise the workload. A ventilation rate of 60 l/min which was achieved in both subjects and controls has previously been shown to represent fairly intense exercise for children and sufficient stimulus to provoke exercise-induced bronchospasm.<sup>32</sup> FEV<sub>1</sub> was used to record change in lung function following exercise rather than PEFR as FEV<sub>1</sub> has less within-subject variability than PEFR in population surveys of asthma in children.<sup>35 36</sup> Previous studies using exercise challenge in community studies of asthma prevalence<sup>37–46</sup> have used differing exercise protocols, varying methods of data collection, and have not standardised workload, temperature, and humidity of inspired air. Most studies have used a six minute free running asthma test<sup>37–42 44–46</sup> and in only three studies was intensity of exercise (heart rate) recorded.<sup>39 41 46</sup> Temperature and humidity were recorded in five studies<sup>21 39 41–43</sup> and, although in some<sup>37–39 41 43–46</sup> exercise was performed indoors in an attempt to standardise inspired air conditions, in only one study was a nose clip worn.<sup>21</sup> Three studies recorded a fall in FEV<sub>1</sub> after exercise<sup>21 40 43</sup> rather than PEFR.<sup>37–39 41 42 44–46</sup> Three recent studies have attempted to standardise the exercise challenge for epidemiological studies. Ninan and Russell<sup>31</sup> used a timed cold air-enhanced cycle exercise test with an inspired air temperature maintained between +2°C and –2°C and exercised children at 90% of their age predicted maximum heart rate but minute ventilation was not measured. Backer and coworkers<sup>43</sup> used a timed treadmill exercise test within a climate chamber and speed was adjusted to maintain a heart rate between 160 and 180 bpm. However, humidity was maintained at 50% or 10 mg H<sub>2</sub>O/l which may be insufficient to stimulate exercise-induced asthma in susceptible subjects. These methods of exercise challenge are impractical for field use due to the use of a climate chamber<sup>43</sup> or a heat exchanger.<sup>31</sup> Haby *et al*<sup>21</sup> used timed running exercise and mon-

Table 4 Summary data on sensitivity and specificity of exercise challenge from previous epidemiological studies

Reference	Sensitivity	Specificity
Burr (1974) <sup>37</sup>	70	92
Tsanakas (1988) <sup>39</sup>	50	97
Terblanche (1990) <sup>40</sup>	31	97
Barry (1990) <sup>41</sup>	47	—
Bransford (1991) <sup>41</sup>	43	95
Backer (1992) <sup>43</sup>	54	87
Ninan (1993) <sup>31</sup>	22	96
Williams (1993) <sup>45</sup>	33	97
Jones (1994) <sup>46</sup>	43	93
Haby (1994) <sup>21</sup>	27	94
West (current study)	57	94

itored heart rate continuously during exercise in order to modify exercise intensity. All children studied wore a nose clip during exercise. Oxygen consumption was estimated from data on distances run by each child. Although the relative humidity was less than 10 mg H<sub>2</sub>O/l for all tests, a wide range of water content (6·4–9·7 mg H<sub>2</sub>O/l) and temperature (11–16°C) of inspired air was documented.

Despite our attempts to maximise the stimulus to bronchoconstriction in the exercise challenge, the sensitivity and specificity of the test was not improved in comparison with previous epidemiological studies which have measured bronchial responsiveness to exercise. Table 4 summarises the data on sensitivity and specificity of exercise challenge from previous epidemiological studies. Most previous studies have quoted sensitivity of the test for those children with doctor diagnosed asthma and children with respiratory symptoms within the past 12 months, and the poor sensitivity of 57% in our study may be a reflection of the questionnaire. If the children are reclassified into a "symptomatic" group and a "no asthma" group as outlined in the results, the sensitivity of this exercise challenge improves to 71%. In the study by Haby *et al*<sup>21</sup> the sensitivity of the exercise test for the diagnosis of asthma in children with wheeze in the past 12 months was 27%, and for subjects with respiratory symptoms including asthma in the study by Backer and Ulrick the sensitivity was 54%.<sup>43</sup> Ninan and Russell<sup>31</sup> were only able to demonstrate a sensitivity of 22% for cold air-enhanced exercise in producing bronchoconstriction in doctor diagnosed asthmatic subjects.

The intrapatient reproducibility of the standardised cycle exercise test is disappointing despite exercise being performed at the same time of day while breathing the same inspired air condition at the same rate of ventilation. The measurements were performed on a different hospital based population of asthmatic subjects with a wider age range than in the community group and therefore should be interpreted with caution. Previous studies have reported a coefficient of variation for the percentage fall index in FEV<sub>1</sub> of 19–25% when an interval of more than two hours and less than 28 days elapses between tests.<sup>25 26</sup>

The exercise challenge, like questionnaires and pharmacological challenges, has shortcomings in epidemiological studies of the prevalence of asthma in children. Exercise is only

one provoking stimulus for asthma, a condition which is known to have many triggers which induce bronchospasm, and further long term studies are needed to clarify the role of the exercise challenge in the diagnosis of asthma in epidemiological studies. The study lacks a pharmacological challenge for comparison but we feel there would be ethical difficulties in using a challenge such as histamine or methacholine which has previously been shown to have poor sensitivity and specificity.<sup>18-21-24</sup> However, pharmacological challenge does allow the determination of a dose response curve which may provide more sensitive information about the severity of the underlying bronchial responsiveness.

In summary, despite attempts to maximise the stimulus to bronchoconstriction in a community based cycle exercise challenge test, this study shows that such a sophisticated exercise challenge offers little advantage over a simple six minute free run in epidemiological studies of the prevalence of asthma. However, standardisation of minute ventilation and the water content of inspired air does allow objective comparisons of bronchial responsiveness in epidemiological studies of the prevalence of asthma in children between different populations worldwide and also within communities over time.

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