

# Screening for childhood asthma using an exercise test

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## SUMMARY

**Background.** Screening for asthma in children in the community could have advantages at a time when prevalence rates of the condition and associated hospital admission rates are rising.

**Aim.** The aim of this study was to assess the usefulness of a standard exercise test as a marker of asthma or potential asthma in children, and to examine the relationship between asthma and other respiratory tract illnesses.

**Method.** In 1985 a cross-sectional research study was undertaken in 10 primary schools in West Glamorgan; the children were followed up over six years until 1991. The exercise test involved measuring peak expiratory flow rate before and after the children ran as fast as they could for six minutes. A control group of children with a negative exercise test result were compared with those not known to have asthma who had a positive result (fall in peak expiratory flow rate of 15% or greater), using clinical data. Similar clinical comparisons were undertaken between the children known to have asthma and a control group.

**Results.** Of 864 children not known to have asthma, 60 had a positive exercise result. Of 92 children known to have asthma, 33 had a positive test result and seven were unable to finish the test because of bronchospasm, a sensitivity of 43% and a specificity of 93%. Follow up of 55 of the 60 children not known to have asthma but who had an abnormal response to the test showed that 32 had developed clinically recognizable asthma six years later. There was a significantly higher prevalence of atopic and respiratory illnesses (otitis media, hay fever and eczema) in the group of children with bronchial hyperreactivity demonstrated on exercise than in those without bronchial hyperreactivity.

**Conclusion.** This research shows that bronchial hyperreactivity demonstrated by an exercise test can be a marker for childhood asthma. The study has also identified other respiratory tract illnesses which appear to belong to the same spectrum as asthma.

**Keywords:** asthma; screening; ergometric stress testing; exercise; children.

## Introduction

DESPITE various community campaigns about asthma<sup>1,2</sup> and the upsurge in nurse-run asthma clinics there is, as yet, no objective evidence from primary care that there has been any reduction in the previously reported underdiagnosis and undertreatment of childhood asthma.<sup>3</sup> Prevalence rates seem to be increasing<sup>4,5</sup> and hospital admissions for asthma have soared.<sup>6</sup>

The extent to which asthma may be undetected in the community may be hampered by a lack of a precise definition<sup>7</sup> but more importantly by the absence of a simple screening test which would be practical to perform and yet reliable. Questionnaire analysis is the most commonly used screening instrument for asthma in children.<sup>8-11</sup> However, such questionnaires are subjective, involving both parents and children in the recall of previous symptoms. Provocation tests by inhalation of bronchoconstrictor agents have been used in community settings and are objective but are more difficult to perform.<sup>12</sup> The relationship between bronchial hyperreactivity and symptoms is not precise and so far cannot reliably separate asthma sufferers from non-asthma sufferers.<sup>13</sup> Similarly the relationship between positivity to skin prick testing and clinical symptoms of asthma is poor and does not allow skin prick testing to be used as a reliable screening test.<sup>14</sup>

The role of exercise in inducing asthma has been examined extensively<sup>15</sup> and it has been reported that up to 90% of asthmatic children will have an abnormal response to exercise.<sup>16</sup> It has also been shown that the abnormal response is not affected by the clinical state of the child and can be elicited when either well or wheezy.<sup>17,18</sup> These studies have generally been reported on selected groups of asthmatic children attending hospital clinics, often among children with more severe asthma.

Two community studies in the United Kingdom have reported the use of exercise as a screening instrument for asthma.<sup>19,20</sup> The former showed an increase in the bronchial response to exercise when challenged twice over a 15 year period. This was shown not only among current asthmatic patients but also in some subjects with features related to asthma. In the latter study children with a positive exercise test were confirmed as having asthma on examination. Neither of these important studies used concurrent clinical data from primary care.

This present study from general practice set out not only to screen for undiagnosed asthma using a standard exercise tolerance test, but also to examine the relationship between asthma and other upper respiratory tract illnesses using concurrent general practice clinical data. It was also possible to undertake a cohort study over six years of those children who at one point showed an abnormal response to the exercise test but who did not, at that time, have clinically recognized asthma.

## Method

This study began in 1985 in West Glamorgan in a mainly urban six partner general practice of 10 000 patients. An asthma register compiled by all the partners had shown an asthma prevalence rate in the 0-15 years age group of 8.8%.

Patients were entered on the asthma register where there was recurrent wheezing (other rarer causes having been excluded), variation in peak expiratory flow rate of greater than 15%, or where any two of the six partners had used the term purely on clinical grounds.

## Exercise test

The screening test used was the exercise test.<sup>19</sup> This involved a free running asthma screening test<sup>20</sup> which was performed at the 10 primary schools in the practice area on all children aged 5-11 years registered with the practice. A registered general nurse (M B) together with A J and the research unit secretary, visited

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the schools. Approval for the study was granted by West Glamorgan area health authority ethics committee and the co-operation of the education authority was received.

Any child who had had an upper respiratory tract infection in the last seven days was asked to attend for the test at a later date. Children had their pre-exercise peak expiratory flow rate measured in the gymnasium and those with a value 20% or more below predicted values were excluded. Any child with a physical or mental handicap which made running difficult was invited to participate but the results were excluded from analysis if a pulse rate of 170 beats per minute was not achieved. None of the children was told the date of the exercise test and so children with asthma took their asthma medication as usual.

Each class did the exercise test in the school gymnasium. Tests were carried out in June to avoid exercising in cold air. The classes were each divided into two groups, thus introducing an element of fun and competition. The children were instructed to run as fast as possible for six minutes, receiving encouragement from the study team. After six minutes a check was made to ensure that a pulse rate of 170 beats per minute had been attained for each child. The children then rested for three minutes and their peak expiratory flow rates were remeasured and the change between the pre- and post-exercise measurements calculated, expressed as a percentage change from the pre-exercise measurement. Salbutamol by aerosol or nebulizer was always available but any child who appeared to be having acute bronchospasm was withdrawn from the test, the peak expiratory flow rate recorded and the child closely monitored.

Children with a 15% or greater fall in peak expiratory flow rate were considered to have a positive exercise test result and a note was made of whether they were on the asthma register or not. A check was also made of patients' notes in case a child with asthma had not been entered on the asthma register.

#### *Index and control groups*

Closely matched control pairs of children were identified for the known asthma sufferers so that a comparison of upper respiratory illnesses in both asthmatic and non-asthmatic children could be made. Each control child was identified from the school register as being the child nearest in age to the index child. Each control child was also of the same sex, on the same practice register, and in the same class as the index child.

Those not known to have asthma but with a positive test result became the exercise test index group, and a corresponding control group was chosen from those with a negative test result. Practice records of the control children were checked to ensure that there were no indications of undiagnosed asthma such as frequent cough, nocturnal cough, wheeze or repeated upper respiratory tract illnesses. Therefore the only difference between the index and control groups was their bronchial hyperreactivity.

A questionnaire was sent to the parents of the exercise test index and control groups asking about a personal or family history of atopic characteristics together with any tendency towards coughing or wheezing, and the results were compared. A search was also made of the patients' general practice and hospital notes for references to tonsillectomy, adenoidectomy, insertion of grommets, myringotomy, referral to any outpatient clinic, upper respiratory tract infection, bronchitis, croup, pneumonia, otitis media, whooping cough and any other conditions deemed relevant. Chronic tonsillitis referred to any child currently on a waiting list for tonsillectomy or who had been referred for consideration for surgery.

#### *Follow-up study*

A follow-up questionnaire was sent to the parents of the index and control groups in 1991. Patients' notes were examined and

clinical conditions and receipt of medication was recorded. None of the partners was aware of the exercise test results so that any diagnosis of asthma was made independently of the exercise tests.

#### *Analysis*

Data were analysed using the *SPSS.PC* software package and results presented as frequency distributions. The chi square test was used for the estimation of cross tabulation of variables, and relevant *P* values are given. For the analysis of paired results between index and control groups, a two by two matrix was constructed and a comparison made between the presence of a condition in the index group and its absence in the control group compared with its absence in the index group and its presence in the control group.<sup>21</sup>

#### **Results**

There were 1357 children aged 5–11 years in the practice. Of the 695 boys and 662 girls, 58 boys and 51 girls had current asthma (an asthma attack within the last 12 months), a prevalence of 8.3% among boys and 7.7% among girls. These 109 children were matched with a control group of non-sufferers (four children with asthma not on the asthma register are included in the group of 109 asthma sufferers).

#### *Asthma sufferers*

Comparison of the clinical conditions among the 109 children known to have asthma and their control group revealed that significantly more children with asthma had had bronchitis than the control group (28 versus three, respectively,  $P < 0.001$ ). They were also more likely to have had an upper respiratory tract infection (38 versus 14, respectively,  $P < 0.001$ ) and to have had acute tonsillitis (21 versus 11, respectively,  $P < 0.05$ ). Croup, otitis media and myringotomy were also more common among asthma sufferers than non-asthma sufferers, but the differences did not reach statistical significance.

#### *Exercise test*

Of the 1357 children, 395 were excluded from the exercise test as they were in schools outside the practice area (private or special need schools). Six other children were excluded: three had severe asthma and their initial peak expiratory flow rate was 20% or more below predicted values, two had cerebral palsy and one child had an injury. Six children remained absent on three consecutive visits to the schools; none of them was on the asthma register. A total of 950 children therefore started the exercise test; 92 (9.7%) were known to have asthma. Thirty four children with asthma had been prescribed either cromoglycate or an inhaled beta-agonist, but none of them had their inhaler at school.

Seven children known to have asthma did not complete the exercise test satisfactorily owing to their fear of bronchospasm. All seven were offered a relief bronchodilator: five declined and two were each given two puffs of salbutamol. Three children with undiagnosed asthma were also given salbutamol (they completed the test). All five treated children became asymptomatic and returned to their classrooms. All 943 children who completed the exercise test had a pulse rate of 170 beats per minute or more.

Of the 85 children known to have asthma and who completed the test, 33 (13 boys and 20 girls) had a positive exercise test result (15% or greater fall in peak expiratory flow rate). Of the 864 children who were not known to have asthma, 60 (35 boys and 25 girls) had a positive test result. These 60 children became the exercise test index group and a control group of 60 children

who had a negative test result were identified.

The 33 children with known asthma had a positive exercise test result and the seven children with asthma who dropped out were deemed to have failed the test. The sensitivity of the test was 43%, the specificity 93% and the positive predictive value 40%.

The results of the peak expiratory flow rate measurements after the exercise test for those with asthma, those without asthma with a negative test result and those without asthma with a positive test result are shown in Figure 1. The seven children with asthma who failed to complete the test but who had a fall in peak expiratory flow rate are included. The results show that the distribution of the index group resembled the distribution of the asthma group more closely than it did the normal group.

### Questionnaire on respiratory symptoms

All questionnaires on atopy and respiratory symptoms sent to the parents of the index and control group were completed and the results are shown in Table 1. A personal history of eczema and maternal history of asthma were significantly more common in the index group although a paternal history of hay fever appeared to be more common in the control group. All symptoms of coughing, wheezing and breathlessness were more common in the index group, most attaining statistical significance. No difference in the family history of asthma among siblings in the index and control groups was found.

Comparison of the clinical conditions recorded in both the general practice and hospital notes for the exercise test index and control group children showed that although bronchitis, upper respiratory tract infection, myringotomy and otitis media were all found to occur more commonly in the index group, only the occurrence of bronchitis attained statistical significance (10 index group children versus three control group children,  $P < 0.05$ ).

### Follow-up study

During longitudinal follow up of the exercise test index and control groups, five index group children (four girls and one boy) had moved from the area. The clinical conditions and prescribed medication among the remaining 55 pairs of children are shown

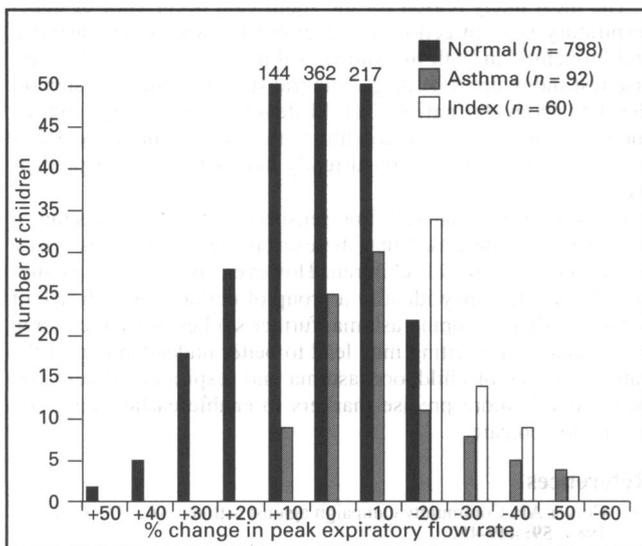


Figure 1. Percentage change in peak expiratory flow rate measurements after exercise test for those with asthma (asthma group), those without asthma with a negative test result (normal) and those without asthma with a positive test result (index).

Table 1. Results of questionnaire on atopy and respiratory symptoms among exercise test index and control group children.

	No. of children	
	Index group (n = 60)	Control group (n = 60)
Personal history of:		
Eczema	5	0*
Hay fever	11	8
Maternal history of:		
Asthma	5	1*
Eczema	3	7
Hay fever	8	6
Paternal history of:		
Asthma	3	4
Eczema	1	4
Hay fever	0	6*
Personal history of coughing:		
When running	15	5**
At night	10	3*
With a cold	10	3*
Without a cold	16	6*
When laughing	8	6
When emotionally upset	10	7
In contact with dog, cat	10	8
Personal history of:		
Occasional wheeze	15	9*
Feeling out of breath	10	4*
Refraining from sport	6	2

n = number of children in group. Chi square: \* $P < 0.05$ , \*\* $P < 0.01$ .

in Table 2. Of the 32 children in the index group who developed asthma between 1985 and 1991, a pattern of prescribing for asthma was reflected both on an acute and repeated prescribing basis on the practice computer. Hay fever, eczema, otitis media and family history of atopy were all found to occur significantly more commonly in the index group, according to the patients' notes and the questionnaire. There was a non-significant trend for upper respiratory tract infection/bronchitis, cough and wheeze in this group. Eight children in the control group developed asthma over the six year period, six of whom had siblings with asthma.

### Discussion

Performing exercise tests on children in schools proved to be a feasible, practical and safe procedure. The low sensitivity of the test (43%) was considered acceptable because of the ease and practicality of screening in schools compared with the higher sensitivity but impracticality of laboratory tests.

As the observed prevalence rate of asthma in the study practice was lower than that generally reported in most United Kingdom studies<sup>22</sup> it seems likely that some children may have had undiagnosed asthma. There are several reasons why 52 of the children known to have asthma had a negative exercise test result. For example, these children could have been taking medication. However, the 34 children who had been prescribed asthma medication did not have their inhalers at school. The children may have had inter-current asthma, although evidence suggests that even then, bronchoconstriction with exercise would tend to occur even when a person was asymptomatic.<sup>17,23</sup> It is possible that the exercise test itself was suboptimal but all the children had a pulse rate after the exercise test of 170 beats per minute or more. It is possible that bronchoconstriction may have occurred after the three-minute interval when peak expiratory flow rates were

**Table 2.** Clinical conditions and receipt of medication among exercise test index and control group children between 1985 and 1991.

	No. of children	
	Index group (n = 55)	Control group (n = 55)
<i>Clinical condition</i>		
Asthma	32	8***
Hay fever	16	4**
Otitis media	16	5*
Upper respiratory tract infection/bronchitis	15	7
Eczema	10	3*
Cough		
At night	7	2
Other	8	4
Wheeze	7	3
Family history of atopy	5	0*
Tonsillitis	4	6
Non-specific abdominal pain	4	5
Headaches	3	2
Croup	1	1
ENT operations	1	4
Whooping cough	1	3
<i>Medication for asthma</i>		
For acute condition	25	4***
Repeat prescription	9	2*

n = number of children in group. ENT = ear, nose and throat. Chi square test: \*P<0.05, \*\*P<0.01, \*\*\*P<0.01.

recorded although no clinically obvious bronchoconstrictor events were noticed by the study team. The results from this study and those of a Sheffield study<sup>20</sup> are at variance with comments by Balfour-Lynn and colleagues,<sup>24</sup> that exercise induced asthma is a sensitive indicator of clinical asthma. However, they looked at a hospital sample of 33 severely asthmatic cases.

There could be several reasons why 33 children with asthma had a positive exercise test result. With adequate asthma control it is not unreasonable to expect any child with mild or moderate asthma to be able to complete a six minute running test. However, these children may not have been taking prescribed medication or may indeed not have been offered advice on pre-exercise medication. Alternatively, their treatment may have been suboptimal, lacking any prophylactic medication such as cromoglycate.

Sixty children not known to have asthma had a positive exercise test and there are several possible explanations to account for these potential false positives. Some of these children were obviously undiagnosed asthma sufferers who should have been detected and diagnosed earlier. As children had been asked before the exercise test whether they had had a recent upper respiratory tract infection this is an unlikely explanation. It is known that siblings of known asthma sufferers, who may themselves be asymptomatic can have a positive exercise test result.<sup>25</sup> However, no difference in the family history of asthma among siblings in the index and control groups was found.

The false positive rate found in the Sheffield study (60%),<sup>20</sup> from a combination of the false positive rate for the peak expiratory flow rate at five minutes after exercise (42%) and 18% at 10 minutes, is the same as the 60% false positive rate found in the present study's three minute post-exercise measurement.

Examination of peak expiratory flow rates showed that there was a general trend towards a decrease in peak expiratory flow rate after exercise. The exercise test index group showed a trend

towards a decrease and they resembled the asthma group more closely than the normal group. This skew in distribution is similar to that shown by Burr and colleagues, among children who were not known to be asthmatic but had wheezed at some time previously.<sup>19</sup>

A personal history of cough was more common among the index than the control group, which is in keeping with other studies which have shown cough to be a predominant symptom of asthma, particularly in children.<sup>26-28</sup> It is also in keeping with our previous finding that it is the person who coughs frequently rather than the person who wheezes occasionally who is most likely to be missed when making a diagnosis of asthma.<sup>29</sup> Wheeze, shortness of breath and refraining from sport were more common in the index group.

Further data on related upper respiratory tract conditions in the exercise test index group again showed bronchitis and upper respiratory tract infection to be common, as they were among those with asthma. In other words, the children with a positive exercise test result tended to have respiratory conditions more like the asthma group than the controls.

During the longitudinal follow-up period from 1985 to 1991, 32 of the 55 children with a positive exercise test result were noted to have a clinical diagnosis of asthma recorded in the notes. A number of the 55 children had had upper respiratory tract infection/bronchitis, otitis media, cough, wheeze and eczema. The sensitivity of the test when the 32 who had developed asthma over the follow-up period is taken into account changes to 58%, the specificity to 97% and the predictive value to 72%. The results may therefore reflect the effectiveness, or indeed ineffectiveness, of the quality of medical management and of life of asthma sufferers and do not necessarily indicate the poor discriminatory power of the exercise test. This is further evidenced by the fear of bronchospasm in the seven children who did not complete the test. Even in a practice motivated to provide good asthma care, evidence was found of suboptimal control.

Eight children in the control group had developed asthma over the follow-up period, six of whom had siblings with asthma. There was no other indicator of asthma or potential asthma on further examination of the notes and questionnaires. An advantage of an exercise test over questionnaires is that in a questionnaire feelings of pessimism or stigma may introduce recall bias.<sup>30</sup>

The most likely reason for the significant occurrence of upper respiratory tract infection in the group known to have asthma, and bronchitis in both the known asthmatic group and the exercise test index group is diagnostic transfer. The findings support the data from the national child development study<sup>31</sup> which showed similar groups of conditions that were found to be either predictive of asthma or concurrently associated but not predictive.

In view of the relatively low sensitivity of exercise testing, it cannot be recommended that the exercise test be used as a routine clinical test for all children. However, as the findings suggest that the test may identify a group of children at high risk of subsequently developing asthma, further studies of such children in a primary care setting may lead to better understanding of the natural history of childhood asthma and respiratory illness and may identify more precise markers to enable earlier diagnosis and improved care.

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## HORMONE REPLACEMENT THERAPY

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## HORMONE REPLACEMENT THERAPY

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