

Exercise in elite summer athletes: Challenges for diagnosis

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Background: There is a high prevalence of asthma and exercise-induced bronchoconstriction (EIB) in elite athletes when the diagnosis is based on symptoms and medication use. Objective measurements are now required by some sporting bodies to support a diagnosis of asthma or EIB to justify use of β -agonists. Such measurements could include bronchial provocation with methacholine, with eucapnic voluntary hyperpnea (EVH) of dry air (a surrogate for exercise), or both. **Objective:** The aim of the study was to investigate the relationship between asthma symptoms and responses to methacholine and the EVH challenge in a group of unselected elite summer-sport athletes. The outcome would be to inform practitioners of a suitable objective approach to identifying those with asthma and EIB.

Methods: Fifty elite summer-sport athletes with or without asthma were recruited from sporting teams and sports medicine centers throughout Melbourne, Australia. All subjects completed a respiratory questionnaire and, on separate days, underwent a bronchoprovocation challenge test with methacholine and EVH.

Results: Forty-two subjects reported one or more respiratory symptoms in the past year, 9 had positive methacholine challenge results (mean PD_{20} of $1.69 \pm 2.05 \mu\text{mol}$), and 25 had positive EVH challenge results (mean fall in FEV_1 of $25.4\% \pm 15\%$). Although all subjects with positive methacholine challenge results had positive EVH challenge results, methacholine had a negative predictive value of only 61% and a sensitivity of 36% for identifying those responsive to EVH.

Conclusion: These findings suggest that the pathogenesis of EIB in elite athletes might be different from that of asthma, and as such, neither symptoms nor the methacholine challenge test should be used exclusively for identifying EIB. (*J Allergy Clin Immunol* 2002;110:374-80.)

Key words: Asthma, eucapnic hyperpnea, elite athletes, methacholine challenge

In the 2000 Summer Olympic Games in Sydney, 607 athletes (5.5% of the total) notified the International Olympic Committee—Medical Commission (IOC-MC)

Abbreviations used

BHR: Bronchial hyperresponsiveness

ECH: Eucapnic voluntary hyperpnea

EIB: Exercise-induced bronchoconstriction

IOC-MC: International Olympic Committee—Medical Commission

MVV: Maximum voluntary ventilation

of the use of inhaled β_2 -adrenoceptor agonists (β_2 -agonists) for the treatment of putative asthma.¹ This was a significant increase over the 1996 Atlanta games, when only 383 (3.6% of total) athletes provided notification of use of β_2 -agonists. Although β_2 -agonists administered by means of inhalation in the doses required to prevent exercise-induced bronchoconstriction (EIB) do not enhance exercise performance, the same drugs given systemically do have anabolic effects.² Alternatively, such a high reported prevalence of asthma in elite athletes might reflect a clinical asthma syndrome unique to the elite athlete group. Consequently, the IOC-MC raised concerns over the accuracy of a diagnosis of asthma in elite athletes.¹ For the Winter Olympics in Salt Lake City, objective evidence of asthma or EIB was required to justify the need for and to obtain approval for β_2 -agonist use.

Epidemiologic consensus has been reached on asthma diagnosis, relying on the combination of clinical symptoms, together with evidence of reversible airflow limitation or a positive response to a bronchial provocation test,³⁻⁶ a definition now adopted by many respiratory physicians. The use of symptoms for diagnosis of EIB is often uncertain in elite athletes, particularly when it is associated with supranormal lung function at rest. For this reason, the reliability of standard bronchial provocation challenge tests in relation to asthma symptoms is critical to enable correct asthma diagnosis and treatment in athletes competing at the elite level. Unfortunately, in the elite athlete group, because of extreme cardiovascular fitness, standard laboratory exercise challenge tests are often limited by an inability to achieve the level of ventilation required to induce bronchoconstriction.⁷ Surrogate challenges, such as the eucapnic voluntary hyperpnea (EVH)⁸⁻¹⁰ or osmotic challenges,¹¹⁻¹⁴ have been used, although the correlation of these test results with asthma symptoms in elite athletes is not known.

To inform practitioners of a suitable test for asthma in elite athletes, our study aimed to investigate the relationship between asthma symptoms and methacholine and EVH challenge tests in a group of elite summer-sport athletes.

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The Victorian Asthma Foundation provided funding for the cost of the equipment and consumables. The Foundation was in no way involved in any stage of the research study. The Alfred Postgraduate Research Trust provided a full-time research scholarship for the main researcher and primary author of this article.

Received for publication May 7, 2002; revised June 16, 2002; accepted for publication June 27, 2002.

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0091-6749/2002 \$35.00 + 0 1/81/127784

doi:10.1067/mai.2002.127784

METHODS

Patients

Fifty elite-level athletes, defined as state level or above in their primary sport, were recruited from sports medicine centers and sporting teams throughout Melbourne, Australia. The subjects were unselected for previous respiratory problems. The subjects were asked to attend the laboratory for challenge on 3 occasions, having refrained from both caffeine and exercise on the day of testing. Those taking pulmonary medications were asked to withhold those medications as follows: short-acting bronchodilators, sodium cromoglycate, nedocromil sodium, or ipratropium bromide for 8 hours; long-acting or sustained released bronchodilators or antihistamines for 48 hours; and leukotriene antagonists for at least 4 days. Inhaled corticosteroids were withheld on the day of the study. All subjects had a baseline FEV₁ of greater than 80% of predicted value.

Approval for the study was gained from the Joint Ethics Committee of the Alfred Hospital and Monash University (protocol no. 95/99), and the procedures were in accordance with the Helsinki Declaration of 1975, as revised in 1983. All subjects provided written informed consent. Each of the subjects attended the Alfred Hospital on 3 occasions separated by greater than 24 hours but less than 1 week.

On visit 1, the subjects completed a respiratory questionnaire based on that of the European Respiratory Society,¹⁵ with additional exercise-related questions. Baseline FEV₁ was measured before the challenge, and the highest value recorded was used in subsequent calculations of changes in FEV₁.

Methacholine challenge tests

All subjects performed a methacholine challenge test according to the protocol described by Yan et al.¹⁶ Briefly, a solution of methacholine chloride USP (ACI Chemicals) was prepared to a concentration of 5% wt/vol in 0.9% saline. Solutions containing 2.5% and 0.625% methacholine chloride were made by diluting the 5% solution through the addition of 0.9% saline. DeVilbiss No. 40 glass handheld nebulizers (Sunrise Medical) were used to deliver the methacholine solution. Initially, the subject received 1 inhalation of the 0.625% methacholine solution, and FEV₁ was measured 60 and 90 seconds later; the highest value was recorded. The dose of methacholine was increased by administering 1 or more inhalations of each concentration of methacholine solution, so that dose increments of methacholine of 0.09, 0.18, 0.4, 0.8, 1.6, 2.6, and 3.8 μ mol were achieved. If the fall in FEV₁ was greater than 20% or the subject reached the maximum dose of 9.47 μ mol (equivalent to 1.9 mg), the challenge was terminated.

Eucapnic hyperpnea challenge test

The protocol used for the EVH challenge was based on that of Argyros and colleagues,^{10,17} involving a single level of ventilation of 85% of maximum voluntary ventilation (MVV; where the MVV is calculated as $35 \times \text{FEV}_{10}$).

The apparatus used for delivering the dry gas was based on that of Smith and Anderson,¹¹ which is a modification of that of Phillips et al.⁸ The subjects inhaled dry gas at room temperature containing 4.9% CO₂, 21% O₂, and balance N₂. The gas mixture passed through a rotameter (250 L; Fisher Rosemount) through a demand valve (Demand Resuscitator; CIG, Medishield) to a target balloon (Meteorological, 320 g; Kaysam Corp). The demand valve could be set to deliver gas at 30 to 150 L/min, and the rotameter permitted the monitoring of gas at up to 200 L/min. The subjects inhaled the gas from the target balloon through a mouthpiece attached to a 2-way nonbreathing valve (Hans Rudolph 2700). The expired gas passed through a household gas meter (model 610; Email Westinghouse Pty Ltd) that measured the volume of air expired so that minute ventilation could be calculated. Before commencing the challenge, the

meteorologic balloon was half filled with the gas, and the subjects were instructed to breathe at a rate in which the balloon was kept at a constant volume. The subjects then breathed at 85% MVV for a total duration of 6 minutes. After cessation of this period of ventilation, FEV₁ was measured at 1, 3, 5, 7, and 10 minutes after the challenge. At each time interval, FEV₁ was measured twice, and the highest value recorded at each measurement was used in calculations. If a fall in FEV₁ of greater than 20% occurred, the challenge was terminated, and a bronchodilator was administered.

The rate of ventilation (in liters per minute) achieved during the challenge was calculated by measuring the total volume of gas expired divided by 6. It was then corrected for body temperature and pressure fully saturated by multiplying by the appropriate conversion factor.

Statistics

Data in the whole group are presented as means $\pm$ SD. Comparison between groups of the fall in FEV₁ during EVH was performed by using the Wilcoxon rank sum test because the distribution of this variable was not normal. The methacholine tests were analyzed with ordinal data (positive and negative), and χ^2 comparisons were performed.¹⁸

RESULTS

Subjects

All 50 of the athletes recruited (15 male and 35 female patients; median age, 21 years; age range, 16-42 years) completed the questionnaire and each challenge test. Twenty-seven subjects had a previous diagnosis of asthma made by a clinician. Thirteen of the subjects were using prophylactic medications, of which 5 were taking only inhaled corticosteroids on a twice daily basis, 4 were taking only mast cell stabilizers (sodium cromoglycate or nedocromil sodium) before exercise, and 4 were taking a combination of both. Six subjects used nasal inhaled corticosteroids intermittently, none of whom were using them at the time of testing. The subjects' baseline lung function was as follows: FEV₁, 3.93 ± 0.67 L; forced vital capacity, 4.28 ± 0.78 L, and forced expiratory flow, midexpiratory phase, 4.75 ± 1.18 L/sec. These values represent $103.6\% \pm 10.8\%$, $99\% \pm 13.2\%$, and $104.1\% \pm 22.1\%$ of predicted values, respectively. The predicted values used were those of Quanjer et al.¹⁹

Methacholine challenge

Nine subjects had a positive methacholine challenge result. The mean PD₂₀ of these subjects was 1.69 ± 2.05 μ mol. In the 41 subjects who had negative methacholine challenge results at the maximum dose of 9.47 μ mol, the mean fall in FEV₁ was $5.1\% \pm 4.4\%$. The results of the methacholine challenge in relation to symptoms, previous diagnosis, and medication use are detailed in Tables I and II.

EVH challenge

Twenty-five of the subjects had a positive EVH challenge test result, with a mean fall in FEV₁ in this group of $25.4\% \pm 15\%$, which is in contrast to the $3\% \pm 2\%$ fall in the 25 subjects who had negative results ($P < .001$). The mean ventilation rate achieved by the 50 subjects was 126.8 ± 21.9 L/min, which represented $93.8\% \pm 4.7\%$ of MVV. The results of the EVH challenge in rela-

TABLE I. Relationship between positive questionnaire responses and EVH and methacholine challenge results

Reported symptom	Positive EVH result (mean % fall in FEV ₁ ± SD)	Negative EVH result (mean % fall in FEV ₁ ± SD)	Positive methacholine result (mean PD ₂₀ in μmol ± SD)	Negative methacholine result (PD ₂₀ >9.47 μmol; mean % fall in FEV ₁ ± SD)
Have you had wheezing or whistling in your chest at any time in the last 12 months? (n = 28)	18 (26.7 ± 15.5)	10 (3.6 ± 1.5)	7 (2.46 ± 2.01)	21 (6.6 ± 4.8)
Have you been at all breathless when the wheezing was present? (n = 19)	13 (26.6 ± 16.9)	6 (4.2 ± 1.6)	6 (2.20 ± 2.00)	13 (7.6 ± 5.1)
Have you had wheezing-whistling when you have not had a cold? (n = 21)	15 (28.4 ± 15.8)	6 (4.1 ± 1.7)	6 (2.20 ± 2.07)	15 (7.3 ± 4.9)
Have you woken with a feeling of chest tightness at any time in the past 12 months? (n = 13)	11 (32.2 ± 16.1)	2 (2.6 ± 2.7)	6 (2.20 ± 2.07)	7 (6.4 ± 4.4)
Have you had an attack of shortness of breath in the last 12 months? (n = 32)	21 (27.6 ± 15.3)	11 (3.8 ± 2.6)	8 (2.27 ± 2.11)	24 (6.9 ± 4.6)
Have you been woken by an attack of shortness of breath at any time during the last 12 months? (n = 5)	3 (39.3 ± 19.2)	2 (4.2 ± 1)	2 (3.54 ± 3.72)	3 (5.3 ± 3.2)
Have you had an attack of shortness of breath that began after strenuous exercise in the last 12 months? (n = 31)	21 (27.6 ± 15.3)	10 (4.2 ± 2.4)	8 (2.27 ± 2.11)	23 (7.2 ± 4.5)
Do you get a cough after strenuous activity? (n = 28)	19 (25.6 ± 14.9)	9 (4 ± 2.3)	6 (2.43 ± 2.40)	22 (6.8 ± 4.1)
Are you ever woken with a cough? (n = 20)	11 (23.1 ± 13.8)	9 (3.1 ± 1.7)	2	18 (5.2 ± 4.9)
Have you ever had asthma? Was this confirmed by a doctor? (n = 27)	18 (29.6 ± 15.6)	9 (4 ± 2.6)	8 (2.27 ± 2.11)	19 (6.1 ± 5.0)
How many asthma attacks have you had in the last 12 months?				
0 (n = 27)	8 (14.6 ± 2.7)	19 (2.3 ± 1.7)	1 (3.99 ± 0)	26 (4.3 ± 3.9)
1-20 (n = 12)	9 (20.1 ± 12.3)	3 (4 ± 2.1)	1 (1.58 ± 0)	11 (6.1 ± 5.7)
>20 (n = 11)	8 (42.1 ± 9.7)	3 (6.1 ± 2.6)	7 (2.37 ± 2.26)	4 (4.9 ± 2.3)
Preventative medications				
Corticosteroid only (n = 5)	3 (28.9 ± 20.4)	2 (5.4 ± 1)	1 (0.91 ± 0)	4 (4.8 ± 2.9)
Mast cell stabilizer only (n = 4)	1 (10.6 ± 0)	3 (4.2 ± 3.6)	0	4 (6.3 ± 2.1)
Both (n = 4)	3 (18.9 ± 22.1)	1 (4.6 ± 0)	1 (6.17 ± 0)	3 (3.2 ± 1.1)
Current reliever (n = 21)	15 (27.9 ± 16.3)	6 (5.1 ± 2.4)	5 (2.33 ± 2.29)	16 (6.1 ± 4.8)
Nasal allergies and hay fever (n = 30)	19, 63% (5.8 ± 2.7)	11, 37% (3.2 ± 2.3)	8, 27% (2.43 ± 2.15)	22, 73% (5.2 ± 4.5)

tion to symptoms, previous diagnosis, and medication use are detailed in Tables I and II.

Comparison between methacholine and EVH challenge results

All 9 subjects with a positive methacholine challenge test result also had a positive EVH challenge test result. For the 16 subjects who had a negative methacholine challenge test result and a positive EVH challenge test result, the mean maximum fall in FEV₁ was 17.8% ± 19.5% after the EVH challenge and 7.6% ± 4.9% after the methacholine challenge. The positive predictive value of the methacholine challenge test for detecting hyperpnea-induced bronchoconstriction was 100%, and the negative predictive value was 61%, with a sensitivity of 36% and a specificity of 100%. The κ coefficient correlating the 2 challenges was 0.36, indicating a low level of agreement.

Association between asthma symptoms and challenge testing

Of the 42 subjects reporting one or more symptoms, 25 had a positive EVH challenge result, with a mean fall in FEV₁ of 25.4% ± 14.9%, which was in contrast to the

3.2% ± 2.2% fall in the remaining 17 subjects. Only 9 of 42 subjects reporting symptoms had a positive methacholine challenge test result. The 8 subjects not reporting symptoms had negative results on both challenge tests.

The positive and negative predictive values for each symptom in relation to the EVH and methacholine challenges are detailed in Table III. The questions with the greatest positive predictive value for EVH challenge were wheeze without a cold, night waking with chest tightness, and exercise-associated dyspnea.

DISCUSSION

This study contained a significant proportion of athletes competing at an international level, thus placing it in an international context. The results of this study in elite summer-sport athletes showed that respiratory symptoms are not highly sensitive for predicting bronchoconstriction to dry air hyperpnea or methacholine. In this group of elite summer-sport athletes, the EVH challenge test determined a prevalence of bronchial hyperresponsiveness (BHR) of 50%, comprising 60% of those who reported asthma symptoms. By contrast, the metha-

TABLE II. Relationship between negative questionnaire responses and the EVH and methacholine challenge results

Negative response to symptom	Positive EVH result (mean % fall in FEV ₁ ± SD)	Negative EVH result (mean % fall in FEV ₁ ± SD)	Positive methacholine result (mean PD ₂₀ in μmol ± SD)	Negative methacholine result (PD ₂₀ >9.47 μmol; mean % fall in FEV ₁ ± SD)
Have you had wheezing or whistling in your chest at any time in the last 12 months? (n = 22)	7 (21.7 ± 13.9)	15 (2.5 ± 2.5)	2 (2.49 ± 3.09)	20 (3.4 ± 3.2)
Have you been at all breathless when the wheezing was present? (n = 31)	12 (24 ± 13)	19 (2.5 ± 2.3)	3 (2.99 ± 2.35)	28 (3.9 ± 3.5)
Have you had wheezing-whistling when you have not had a cold? (n = 29)	10 (20.7 ± 12.9)	19 (2.6 ± 2.2)	3 (2.99 ± 2.35)	26 (3.7 ± 3.5)
Have you woken with a feeling of chest tightness at any time in the past 12 months? (n = 37)	14 (20 ± 12)	23 (3.0 ± 2.2)	3 (2.99 ± 2.35)	26 (4.8 ± 4.4)
Have you had an attack of shortness of breath in the last 12 months? (n = 18)	4 (13.7 ± 2.4)	14 (2.3 ± 1.6)	1 (3.99 ± 0)	17 (2.4 ± 2.1)
Have you been woken by an attack of shortness of breath at any time during the last 12 months? (n = 45)	22 (23.5 ± 13.7)	23 (2.8 ± 2.3)	7 (2.16 ± 1.68)	38 (5.0 ± 4.5)
Have you had an attack of shortness of breath that began after strenuous exercise in the last 12 months? (n = 19)	4 (13.7 ± 12.4)	15 (2.1 ± 1.6)	1 (3.99 ± 0)	18 (2.3 ± 2.1)
Do you get a cough after strenuous activity? (n = 22)	6 (24.7 ± 16.5)	16 (2.3 ± 1.7)	3 (2.54 ± 1.55)	19 (3.1 ± 4.0)
Are you ever woken with a cough? (n = 30)	14 (27.1 ± 16.1)	16 (2.8 ± 2.5)	7 (2.06 ± 1.74)	23 (4.9 ± 4.1)
Have you ever had asthma? Was this confirmed by a doctor? (n = 23)	7 (14.4 ± 3.1)	16 (2.3 ± 1.7)	1 (3.99 ± 0)	22 (4.1 ± 3.7)
Preventative medications (n = 37)	18 (24.8 ± 13.4)	19 (2.3 ± 1.7)	7 (2.16 ± 1.68)	30 (4.8 ± 4.1)
Current reliever (n = 29)	10 (21.6 ± 12.4)	19 (2.3 ± 1.7)	4 (2.64 ± 2.04)	25 (4.4 ± 4.1)
Nasal allergies and hay fever (n = 20)	6 (17.7 ± 10.8)	14 (2.7 ± 2.2)	1 (2.72 ± 0)	19 (4.3 ± 0)

choline challenge test revealed a prevalence of BHR of 18%, with all of these patients reporting symptoms. This finding suggests that EVH is a more sensitive test for the diagnosis of BHR in elite athletes than either asthma symptoms or the methacholine challenge. This study is the first to compare the methacholine and EVH challenge tests with asthma symptoms in the elite summer athlete population, and as such, our findings provide evidence for diagnostic guidelines for asthma in elite athletes. Furthermore, our data support the use of different criteria for the diagnosis of asthma or EIB in the elite athlete group compared with in the remainder of the population, raising important questions as to the likely pathogenesis of BHR in elite athletes.

Criticisms of this study might relate to the recruitment method, in which the sample might not be representative of the entire population of elite athletes, because those with breathing difficulties or a prior diagnosis of asthma might be more likely to have volunteered. Despite this, a number of individuals with and without prior asthma symptoms or diagnosis were recruited, permitting comparison of challenge and symptom data. The methods used are well established and reflect extensive past experience. The response to each of the challenges in the 9 athletes using regular inhaled corticosteroids might have been diminished, even though these medications were withheld for 24 hours. A number of studies have shown

that the regular use of inhaled corticosteroids might cause a person with asthma or EIB to have negative results to such challenges.^{20,21} In our study 6 of the 9 individuals taking inhaled corticosteroids had a positive EVH challenge test result, suggesting that therapy had not rendered these individuals completely nonreactive. By contrast, only 2 of these 9 subjects had a positive methacholine challenge test result, both of whom also had a positive EVH challenge test result.

It remains a subject of debate as to the appropriate bronchial provocation test for identifying EIB in a laboratory environment.^{7,10,22,23} The EVH challenge, a bronchial provocation challenge involving the hyperventilation of a dry gas containing 4.9% CO₂, is a well-characterized and standardized challenge test for EIB^{8-10,17} and is a potent challenge for provoking bronchoconstriction in patients with clinically recognized asthma responsive to exercise.^{13,24} The simplicity of the equipment and the protocol permits easier standardization between laboratories and between repeated tests.¹⁷ A number of authors have suggested that the EVH challenge test has both a high sensitivity and specificity for EIB, with the sensitivity paradoxically being higher than that of an exercise challenge performed either in the laboratory or in the field.^{24,25} A study by Mannix et al²⁴ involving figure skaters found that the EVH challenge identified the presence of BHR better than a field exercise challenge. Similarly, in our study we

TABLE III. Sensitivity, specificity, and positive and negative predictive values for EIB of questions on the questionnaire determined by using the EVH challenge as the gold standard

Question-symptom	EVH positive predictive value* (%)	EVH negative predictive value† (%)	Methacholine positive predictive value (%)	Methacholine negative predictive value (%)
Have you had wheezing or whistling in your chest at any time in the last 12 months?	64	68	25	90.9
Have you been at all breathless when the wheezing was present?	68	61	32	90.3
Have you had wheezing-whistling when you have not had a cold?	71	66	29	89.7
Have you woken with a feeling of chest tightness at any time in the past 12 months?	85	62	46	91.9
Have you had an attack of shortness of breath that began during the day when you were at rest at any time during the last 12 months?	66	78	25	94.4
Have you been woken by an attack of shortness of breath at any time in the last 12 months?	60	51	40	94.7
Have you had an attack of shortness of breath that came on after strenuous exercise in the last 12 months?	68	79	31	84.4
Have you been woken by an attack of coughing at any time in the last 12 months?	55	53	10	76.7
Do you get a cough after strenuous activity?	68	73	21	86.4
Have you ever had asthma? Was this confirmed by a doctor?	67	70	30	95.7
How many asthma attacks have you had in the last 12 months?	74	70	34.8	96.3
1-20	75		8	
>20	72.7		63.6	

*Positive predictive value = true-positive results/total number of patients with positive test results.

†Negative predictive value = true-negative results/total number of patients with negative test results.

found that the EVH challenge had a much higher sensitivity for BHR in elite athletes than the methacholine challenge. Such findings highlight the differences in the underlying mechanism of each challenge test, an important consideration when assessing patients for EIB.

Although historically the clinical diagnosis of EIB has largely relied on the presence of respiratory symptoms, the actual relationship between symptoms and EIB in elite summer-sport athletes has not been clearly defined. Our study suggests that the presence of symptoms might indicate a diagnosis of EIB but can not be used as the sole means of diagnosis. Although most athletes with a positive EVH challenge result reported symptoms, the positive predictive values for EIB of individual symptoms was only in the range of 60% to 70%. Other studies investigating the association between symptoms and the presence of EIB, as detected with a bronchial provocation test, have supported this. Rundell et al²⁶ found that only 61% of athletes with a positive field exercise challenge result reported symptoms, whereas 45% of those with a negative challenge result also reported symptoms. Similarly, in our study 17 individuals reported symptoms but had negative EVH challenge results. Moreover, some athletes who are clearly symptomatic after exercise, who

exhibit performance decrements in cold conditions, or both demonstrate normal postexercise spirometry. In a study performed on intercollegiate athletes referred for pulmonary function tests on the basis of a medical history consistent with EIB, only 46% had a positive laboratory exercise challenge test result.²⁷ This is important because a large number of athletes might be given medications for asthma inappropriately if the diagnosis of EIB is made solely on the basis of symptoms.

Twenty-one subjects in this study used β_2 -agonists; however, only 15 (71%) of these subjects had BHR, as diagnosed on the basis of the EVH challenge result. This suggests that approximately one third of athletes using β_2 -agonists might be using these medications unnecessarily. This is important given the IOC's recent concern over the increased reported use of β_2 -agonists at the Sydney 2000 Summer Olympic Games. Pharmacologic challenge tests have frequently been used in the diagnosis of EIB. These challenge tests assess nonspecific BHR, and therefore a positive challenge test result does not necessarily indicate a diagnosis of EIB,⁹ nor does a negative challenge result exclude the diagnosis,²⁸ particularly when investigating a random population with nonspecific respiratory symptoms.

In this group of athletes, however, the methacholine challenge test had a low sensitivity (36%) for identifying those responsive to dry air hyperpnea. This might have been due to mediators more potent than methacholine, such as the cysteinyl leukotrienes, being more important in the pathogenesis of EIB. The cysteinyl leukotrienes are potent bronchoconstricting agents such that one thousandth of the concentration is required to induce the same degree of airway narrowing as either methacholine or histamine.²⁹⁻³¹ Leukotrienes also stimulate mucus production and produce airway mucosa edema by increasing permeability of postcapillary venules.³² This lower sensitivity of methacholine to detect a positive response to EVH is consistent with studies in children comparing histamine and exercise challenge tests.^{28,33}

EIB is a common condition, both in the general population and particularly in elite athletes,^{34,35} in whom it is likely to have significant implications on performance. To date, there has not been a uniform consensus as to accepted diagnostic criteria for this condition, with the diagnosis revolving around symptoms and, if in doubt, a methacholine or exercise challenge test result. Our study suggests that symptoms, although useful, have only a moderate sensitivity for identifying EIB and thus should not be used as the sole diagnostic criteria. The methacholine challenge test had a low sensitivity for identifying BHR to dry air, a surrogate for exercise, and as such should not be used as an alternative challenge for EIB. Overall, EVH identified more athletes with symptoms than did methacholine, and the magnitude of the fall in FEV₁ was consistent with a diagnosis of EIB.

Given that the accepted diagnosis of asthma in the general population is a combination of symptoms plus a positive bronchoprovocation challenge test result, some might argue that a diagnosis of EIB should be based on the presence of exercise-related symptoms in conjunction with a positive challenge result with dry air. However, a number of athletes with EIB might be unaware of their symptoms, given that dyspnea is a corollary of intense exercise. These athletes often believe they are being limited by fitness or have reached their maximum possible ventilation. Consequently, in the elite athlete group a different criteria should probably apply. Our results indicate that EVH challenge is an appropriate challenge for elite athletes. High rates of ventilation are more easily achievable than with ergometers in the laboratory and can be shown to elicit bronchoconstriction in athletes with negative pharmacologic challenge results, who might otherwise have been missed. We conclude that this test ought to be widely available to enable accurate diagnosis and treatment in elite athletes of asthma-related symptoms. The task now is the education of medical practitioners in the use and interpretation of these tests in the international sporting arena.

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