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# The role of the bronchial provocation challenge tests in the diagnosis of exercise-induced bronchoconstriction in elite swimmers

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## ABSTRACT

**Background** The International Olympic Committee–Medical Commission (IOC-MC) accepts a number of bronchial provocation tests for the diagnosis of exercise-induced bronchoconstriction (EIB) in elite athletes, none of which have been studied in elite swimmers. With the suggestion of a different pathogenesis involved in the development of EIB in swimmers, there is a possibility that the recommended test for EIB in elite athletes, the eucapnic voluntary hyperpnoea (EVH) challenge, may be missing the diagnosis in elite swimmers.

**Objective** The aim of this study was to assess the effectiveness of the EVH challenge, the field swim challenge and the laboratory cycle challenge in the diagnosis of EIB in elite swimmers.

**Design** 33 elite swimmers were evaluated on separate days for the presence of EIB using 3 different bronchial provocation challenge tests: an 8 minute field swim challenge, a 6 minute laboratory EVH challenge, and an 8 minute laboratory cycle challenge.

**Main outcome measurements** Change in forced expiratory volume in 1 second ($FEV_1$) pre and post test protocol. A fall in $FEV_1$ from baseline of $\geqslant$10% post challenge was diagnostic of EIB.

**Results** Only 1 of the 33 subjects (3%) had a positive field swim challenge with a fall in $FEV_1$ of 16% from baseline. 18 of the 33 subjects (55%) had a positive EVH challenge, with a mean fall in $FEV_1$ of 20.4 (SD 11.7)% from baseline. 4 of the subjects (12%) had a positive laboratory cycle challenge, with a mean fall in $FEV_1$ of 14.8 (4.7)% from baseline. Only 1 of the 33 subjects was positive to all 3 challenges.

**Conclusions** These results suggest that the EVH challenge is a highly sensitive challenge for identifying EIB in elite swimmers, in contrast to the laboratory and field-based exercise challenge tests, which significantly underdiagnose the condition. The EVH challenge, a well-established and standardised test for EIB in elite winter and summer land-based athletes, should thus be used for the diagnosis of EIB in elite swimmers, as recommended by the IOC-MC.


Currently the International Olympic Committee-Medical Commission (IOC-MC) requires that all athletes provide objective evidence of exercise-induced bronchoconstriction (EIB) or asthma to obtain approval for the use of inhaled beta 2 agonists.

Recent Olympic data suggests an increasing prevalence of EIB/asthma amongst elite endurance athletes,[1–5] especially swimmers.[1] Such data were obtained using various methodologies. These were commonly based on clinical diagnoses, which have a recognised incidence of EIB/asthma misdiagnosis.[6–8] Infrequently, the diagnosis was confirmed with a bronchial provocation challenge (BPC).

Formalised testing for the confirmation of asthma and EIB was thus introduced by the IOC-MC for the 2002 Winter Olympic Games in Salt Lake City, and for subsequent Summer and Winter Olympic Games. Although both airway reversibility on spirometry and the presence of airway hyperreactivity to a number of BPCs have been accepted by the IOC-MC, the eucapnic voluntary hyperpnoea (EVH) challenge has been recognised as the gold standard challenge for the diagnosis of EIB in elite athletes.[9] This recommendation was based on studies including winter athletes. The EVH challenge has since been shown to be highly sensitive and specific for the diagnosis of EIB in elite summer land-based athletes.[10]

It has been suggested that the high prevalence of EIB in the various endurance athlete subgroups may be due to different triggers of airway hyperreactivity. In winter athletes, this may be a result of airway inflammation secondary to airway exposure of large volumes of cold air.[11] In summer athletes, the trigger is thought to be exposure to large allergen loads.[12] The prevalence of EIB in swimmers is remarkably high; up to 47% in some elite swimming teams.[5] This was initially thought to occur as a consequence of people with asthma being encouraged to swim.[13] However, it is now accepted that the high prevalence of EIB in swimmers is due to injury of the airways as a consequence of repetitive and prolonged exposure to the gases of chlorine and their metabolites, which accumulate at the water/gas interface on the swimming pool surface.[14–16]

All but one of the diagnostic challenge tests recommended by the IOC-MC fail to account for the exposure of the swimmer's airways to chlorine and its metabolites, and through this omission may result in a significant number of missed diagnoses of EIB in swimmers. The accepted field swim challenge may account for these missed diagnoses. Furthermore, none of the currently recommended challenges have been studied in elite swimmers. The aim of this study is thus to assess the effectiveness of the EVH challenge, the field swim challenge and the laboratory cycle challenge in the diagnosis of EIB in elite swimmers.

## METHODS

Thirty-three volunteer elite swimmers, defined as State Level or above, were recruited from swim clubs throughout Melbourne, Australia, to


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participate in this prospective study. All subjects were aged 14 years and older and were required to have a baseline forced expiratory volume in 1 second ($FEV_1$) greater than 60% predicted for their age, height and gender to exclude any subject with an active exacerbation of asthma. Subjects with a past history of asthma were not excluded from the study. Subjects were excluded if they had had a recent respiratory infection or exacerbation of their asthma. The research protocol was approved by both the University of Melbourne and the Royal Melbourne Hospital Ethics Committees.

Once accepted into the study and having given informed consent, each subject completed a standardised Respiratory Questionnaire adapted from the European Community Respiratory Health Survey.[17]

Each subject was evaluated for the presence of EIB using three different BPCs: a field swim challenge, an EVH challenge and a laboratory cycle challenge. Testing order was random, and consecutive tests were separated by more than 24 h but less than 1 week. All testing occurred in the morning to control for diurnal variation in airway calibre. The subjects were asked to refrain from caffeine and exercise on the days of the testing and withhold their asthma medications for designated times as per Holzer *et al*.[10]

Baseline spirometry was performed prior to each challenge and the best of three values for $FEV_1$ and forced vital capacity (FVC) were recorded and used for subsequent calculations. Spirometry prior to and during the EVH and laboratory cycle challenge was performed on the System 2310 Spirometer, Vmax series (Sensormedics BV) and for the field swim challenge on a portable MicroMedical Superspiro Spirometer (Rochester, Kent, England).

Spirometry was performed at 1, 3, 5, 7 and 10 minutes following the cessation of each of the exercise/hyperpnoea stimuli. At each of these measurement times the better of two values for $FEV_1$ was recorded to be used in subsequent calculations. Following the 10 minute measurement, or earlier if the $FEV_1$ fell greater than 30%, 200 μg of salbutamol was inhaled from a volumatic spacer; further spirometry was performed 10 minutes following this.

The field swim challenge was conducted at the Melbourne Sports and Aquatic Centre, in a chlorine and ozone-filtered indoor 50 m competition pool used for national championships. The challenge required the subject to swim for 8 minutes at the highest intensity sustainable, aiming to maintain a heart rate of >85% $HR_{max}$ ($HR_{max}$ = 220 − age), for the duration of the test. Subjects were fitted with a wireless Polar Heart Rate Monitor (Polar Electro; Oy, Finland) and the average heart rate was taken at the completion of the challenge. Ambient conditions for the indoor pool were 30 (SD 2.7) °C and 82 (4.5)% relative humidity, with a pool temperature of 27 (0.3)°C.

The laboratory EVH challenge was conducted according to the single-stepped protocol of Argyros and coworkers.[18] This challenge required the subject to inhale a dry gas containing 5% carbon dioxide, 21% oxygen and balance nitrogen (BOG Gases, Melbourne, Australia) at room temperature for 6 minutes at a target ventilation of 85% maximum voluntary ventilation (MVV), equivalent to 30 times the resting $FEV_1$. Ambient conditions in the laboratory were 21 (0.8)°C and 60.5 (2.1)% relative humidity.

The laboratory cycle challenge used the stepped protocol recommended by the American Thoracic Society.[19] The 8 minute challenge was performed on the Ergometrics 800 (Ergoline, Germany) cycle ergometer. A Polar Heart Rate Monitor Watch (Polar Electro; Oy, Finland) was worn by the subject and the average heart rate was recorded at the end of the challenge. Ambient conditions in the lab were 21 (0.8)°C and 60.5 (2.1)% relative humidity.

## STATISTICAL ANALYSIS

Prechallenge values for percent predicted $FEV_1$ were compared with postchallenge values using a paired Student t test. The maximum percent fall in $FEV_1$ from baseline for each challenge test was calculated by subtracting the lowest $FEV_1$ value recorded post challenge from the best baseline value and expressing it as a percentage of the baseline value. A fall in $FEV_1 \geq 10\%$ from baseline was considered positive for EIB.[20] A bronchodilator response of ≥12% rise in $FEV_1$ from baseline was considered positive for asthma.[21] Within-subject comparisons between the EVH and swim challenge tests, between the bike and swim challenge tests, and between the EVH and bike challenge tests were made using paired t tests. Differences between EIB-positive and EIB-negative subjects were examined using independent t tests. A p value $<0.05$ was considered statistically significant for all analyses. All values are presented as mean (SD).

## RESULTS

All 33 subjects (23 male: age 19.3(5.3) years; 10 female: age 15.6 (2.1) years) completed each of the challenges without complication. Baseline spirometry and fall in $FEV_1$ from baseline in response to each of the challenges for the 33 subjects are presented in table 1. Baseline spirometry exceeded the normal predictive values for age, gender and height and correlated well with existing resting values for elite athletes. There was no significant difference in baseline values between those who were EIB-positive or negative, for any challenge.

### Asthma

Thirteen of the 33 subjects (39%) had a previous clinical diagnosis of asthma. Of these, three (23%) were regularly using an inhaled corticosteroid, three (23%) were regularly using an inhaled corticosteroid/long-acting beta agonist combination, one (8%) was using an inhaled mast cell stabiliser prior to exercise, four (44%) were only using an as-required inhaled beta 2 agonist, and two subjects (23%) were not using any asthma medication. One of the 13 (8%) subjects with a previous diagnosis of asthma had a positive field swim challenge, 11 (85%) had a positive EVH challenge and three (23%) had a positive laboratory cycle challenge. Only two (15%) of those previously diagnosed with asthma showed a positive bronchodilator response for asthma. Two subjects (15%) with a previous asthma diagnosis were negative for EIB on all three BPCs and had negative bronchodilator responses. Both of these subjects were using only an as-required inhaled beta 2 agonist.

### Non-asthma subjects

Of the 20 subjects with no previous diagnosis of asthma, seven (35%) had a positive EVH challenge with one (5%) of these also having a positive laboratory cycle challenge test diagnostic of EIB. None of these subjects had a positive field swim challenge. Further, one of these subjects had a positive bronchodilator response for asthma, and negative EVH, swim and cycle tests for EIB.

### Challenge tests

Only one of the 33 subjects (3%) had a positive field swim test with a fall in $FEV_1$ of 16% from baseline compared with 3.0

**Table 1** Subject baseline spirometry and fall in $FEV_1$ in response to the EVH, swim and cycle challenges

| Subject | $FEV_1$ (litres) (% pred) | FVC (litres/s) (% pred) | $FEV_1$/FVC% | EVH fall in $FEV_1$ (%) | Swim fall in $FEV_1$ (%) | Cycle fall in $FEV_1$ (%) |
|---|---|---|---|---|---|---|
| 1* | 4.70 (96) | 7.36 (125) | 64 | 36 | 7 | 8 |
| 2 | 4.97 (104) | 6.67 (117) | 75 | 33 | 7 | 5 |
| 3 | 3.95 (110) | 5.13 (120) | 71 | 12 | 6 | up 1 |
| 4 | 4.95 (105) | 6.50 (116) | 76 | 10 | 2 | 4 |
| 5 | 3.90 (122) | 4.43 (117) | 88 | 6 | 8 | 8 |
| 6 | 4.67 (98) | 6.13 (104) | 76 | 11 | 1 | up 7 |
| 7* | 2.94 (82) | 4.13 (94) | 71 | 43 | **16** | **15** |
| 8 | 3.78 (118) | 4.40 (116) | 86 | 25 | 5 | 3 |
| 9 | 4.34 (124) | 5.03 (120) | 86 | 2 | up 1 | 3 |
| 10 | 4.71 (98) | 6.11 (105) | 77 | 13 | 3 | 2 |
| 11 | 4.30 (113) | 5.29 (115) | 81 | 12 | 2 | 9 |
| 12 | 3.72 (133) | 4.21 (128) | 88 | 9 | 3 | 3 |
| 13 | 5.57 (119) | 7.04 (126) | 79 | 7 | 3 | 5 |
| 14 | 3.83 (98) | 4.50 (95) | 85 | 6 | 2 | 5 |
| 15 | 4.54 (134) | 4.72 (115) | 96 | 3 | 6 | 2 |
| 16 | 3.54 (126) | 3.78 (115) | 94 | 11 | no change | up 1 |
| 17 | 3.57 (101) | 4.10 (96) | 87 | 5 | 4 | up 1 |
| 18* | 3.53 (101) | 4.36 (109) | 81 | 9 | 1 | up 4 |
| 19 | 3.46 (101) | 4.32 (104) | 80 | 11 | 1 | 4 |
| 20 | 3.34 (120) | 4.23 (129) | 79 | 34 | 6 | **13** |
| 21 | 5.75 (127) | 6.48 (118) | 89 | 9 | 1 | 1 |
| 22 | 6.18 (125) | 7.50 (124) | 82 | 13 | 3 | 4 |
| 23 | 5.17 (115) | 5.79 (109) | 89 | 5 | 1 | 5 |
| 24 | 4.21 (115) | 5.44 (123) | 77 | 12 | 3 | 1 |
| 25 | 4.38 (130) | 4.66 (116) | 94 | 6 | 2 | 3 |
| 26 | 5.57 (119) | 7.40 (130) | 75 | 5 | 3 | up 2 |
| 27 | 5.38 (117) | 6.37 (116) | 84 | 2 | 5 | no change |
| 28 | 4.07 (146) | 4.33 (132) | 94 | 15 | 3 | 3 |
| 29 | 5.44 (126) | 6.58 (129) | 83 | 8 | up 1 | 1 |
| 30 | 5.39 (120) | 6.58 (123) | 82 | 10 | up 1 | 3 |
| 31 | 5.65 (144) | 6.30 (133) | 90 | 5 | 5 | **11** |
| 32 | 3.19 (107) | 3.46 (99) | 92 | 38 | 2 | **21** |
| 33 | 4.00 (92) | 5.50 (107) | 73 | 29 | 6 | 6 |

EIB-positive swimmers identified in bold. pred, predicted.
*Subjects 1, 7 and 18 had a positive bronchodilator response for asthma

(2.4)% in the 32 (97%) who were negative. The swim-positive subject swam at 93% of his predicted $HR_{max}$ and had a postchallenge symptom score of 4/4, whilst the swim-negative subjects swam at 87 (4)% their predicted $HR_{max}$ ($p>0.05$), with mean 2.7/4 symptoms post challenge.

Eighteen of the 33 subjects (55%) had a positive EVH challenge test, with a mean fall in $FEV_1$ of 20.4 (11.7)% from baseline compared with a mean fall of 5.8 (2.3)% in the 15 subjects (45%) who were negative. The EVH-positive subjects demonstrated a mean predicted MVV of 78 (11)% during the challenge, compared with a mean predicted MVV of 75 (9)% in the EVH-negative subjects ($p<0.05$). The EVH-positive subjects had a mean number of 3.5/4 symptoms compared with 2/4 symptoms in those subjects who were EVH-negative ($p<0.01$).

Four of the subjects (12%) had a positive laboratory cycle test, with a mean fall in $FEV_1$ of 14.8 (4.7)% from baseline, compared with 2.4 (3.5)% in the 29 (88%) who were negative. The cycle-positive subjects exercised at 91 (3)% their predicted $HR_{max}$ and had a mean symptom score of 3.5/4, whilst the cycle-negative subjects exercised at 91 (5)% their predicted $HR_{max}$ ($p>0.05$) and had a mean symptom score of 1.5/4.

### Correlation of challenge tests

Only one of the 33 subjects was positive to all three challenges, with a fall in $FEV_1$ from baseline values of 16% for the field swim, 43% for the EVH and 15% for the laboratory cycle challenge. This subject also had a positive bronchodilator response for asthma. This subject reported a mean symptom score of 4/4 following each challenge.

Of the 32 subjects negative to the swim challenge, 17 had a positive EVH and three a positive cycle challenge, with mean falls in $FEV_1$ from baseline of 19.1 (10.6)% and 14.8 (5.8)% respectively.

Two subjects were negative to the swim and positive to both the EVH and cycle challenges, with a mean fall in $FEV_1$ from baseline of 36 (2.8)% for the EVH and 17 (6.2)% for the cycle challenge. One subject positive on the laboratory cycle challenge was negative on the EVH challenge.

## DISCUSSION

The results of this study have shown a significant and substantial discrepancy between the diagnostic results of three BPCs commonly used for the diagnosis of asthma/EIB in elite swimmers. The field swim challenge found that only one of the 33 swimmers (3%) tested had a result consistent with the presence of EIB. In contrast, the EVH challenge identified EIB in 18 of the 33 subjects (55%) tested. These results suggest that either the EVH challenge is overdiagnosing the presence of EIB in swimmers or the field swim challenge is significantly underdiagnosing the condition.

In this study to investigate the diagnostic efficacy of different BPCs for EIB in elite swimmers, we used challenges all considered acceptable by the IOC-MC for objective evidence of EIB. In regards to the EVH challenge, Phillips *et al*[22] demonstrated that the airway response in asthmatics, as measured by changes in $FEV_1$ and specific conductance, to hyperpnoea with 5% $CO_2$ was similar to that provoked in the same asthmatic subjects by exercise at the same ventilation. EVH has been reported to have a high specificity for active asthma, diagnosing 90% of asthma cases when a fall in $FEV_1$ of 10% is taken as abnormal and 100% when a 15% fall is considered abnormal.[23] The symptoms provoked by EVH are very similar to those that occur following exercise. The major advantage in using EVH over exercise is that subjects' ventilation levels are monitored and are able to be sustained at high enough levels to induce bronchoconstriction.[24]

Few studies have been performed comparing the efficacy of the EVH challenge with exercise challenges. Until recently, these had only been performed in winter athletes and concluded, similarly to our results, that the EVH challenge was superior to both the field[25 26] and laboratory[27] exercise challenges in the diagnosis of EIB. A recently published, concurrent study by Pedersen *et al* has suggested that the EVH challenge is a BPC superior to the field swim, laboratory exercise and the methacholine challenge in the diagnosis of EIB in 16 female non-asthmatic elite swimmers.[28] Whilst it showed that the EVH challenge was the superior challenge for EIB diagnosis, it did not show a significant difference over the exercise challenges, perhaps a reflection of its smaller sample size and different exercise challenge protocols.

Although field exercise challenges are known to be highly specific for EIB, the sensitivity of these in the detection of EIB is only moderate.[24 29 30] Unlike the EVH challenge, a number of variables may unknowingly influence the results of the exercise challenges. Although the subjects' average $HR_{max}$ exceeded 85% for both the exercise challenges, we were unable to monitor their ventilation rates. Rundell *et al* suggested that the exercise challenge should be performed at race pace, or greater than 95% $HR_{max}$, to achieve and maintain ventilations high enough to induce bronchoconstriction.[31] The Pedersen study, whilst not directly monitoring ventilation or heart rates, attempted to address this by asking subjects to exercise at the highest intensity possible until exhaustion, reflecting a higher prevalence of positive field swim and laboratory treadmill challenges for EIB.

For the field swim challenge, difficulties in standardising the environmental conditions at the pool surface may have affected the respiratory response to the swim challenge and thus the results. Although the poolside ambient air conditions and pool temperature were measured on each occasion, factors such as the concentration of ozone, chlorine and its metabolite gases on the pool surface, pool chlorine and ozone concentrations and poolside ventilation were not measured.

In both the laboratory-based challenges, despite standardisation of the environmental conditions, the athletes were not exposed to the potential environmental triggers that are in the pool environment. This may have potentially reduced the sensitivity of these challenges for EIB in swimmers. However, the results of this study, in particular the high prevalence of positive EVH challenges, suggest that the airway hyperresponsiveness that develops in response to repetitive exposure to chlorine is non-specific and, once developed, does not rely on exposure to chlorine to occur.

Furthermore, the sensitivity of the laboratory cycle challenge may have been artificially reduced for two reasons. First, a number of subjects were limited by leg fatigue from the unaccustomed exercise rather than ventilatory restriction. During the EVH challenge, there was no such limitation. Second, and perhaps more importantly, the air inhaled during the laboratory cycle challenge was the ambient room air, which had an average relative humidity of 60%, greater than the recommended 50% stated in the exercise guidelines.[19] To overcome this, the subjects should have inspired dry air during the challenge.

Perhaps the major limitation of this study relates to the humidity of the air inhaled during each of the challenges. The hypercapnic dry gas mixture used for the EVH challenge test has a low enough water content to promote EIB, whereas the air inhaled during the field swim challenge was of such high water content that it was protective against EIB.[32] The relative falls in $FEV_1$ following each of these challenges, as well as the postchallenge EIB symptom scores, reflects this.

In conclusion, the results of this study display the wide discrepancy that occurs between the different BPCs in the diagnosis of EIB in swimmers. Importantly, it demonstrates that exposure to chlorine or its metabolite gases is not required to induce the airway hyperresponsiveness at the time of the challenge. Our study shows that the EVH challenge is highly sensitive at identifying EIB in elite swimmers, whilst the exercise challenge tests may significantly underdiagnose the condition. As the EVH challenge test is a well-established and standardised test for EIB in elite winter and summer land-based athletes, it supports the recommendations of the IOC-MC that the EVH challenge test should be used for the diagnosis of EIB in all elite athletes, including swimmers. However, where the EVH challenge test is not available, a laboratory exercise challenge where the subject exercises until exhaustion whilst breathing dry air should be considered for identifying EIB in elite swimmers.

### What is already known on this topic

EIB and asthma are common conditions in elite swimmers. The cause is thought to be the repeated exposure to ozone, chlorine and their metabolites which accumulate at the pool/air interface. These conditions are commonly diagnosed and confirmed with a number of objective bronchial provocation tests.

### What this study adds

This study shows a wide discrepancy between a number of bronchial provocation tests accepted by the IOC-MC as objective evidence of EIB in elite swimmers. It further shows that exposure to chlorine or its metabolite gases is not required to induce EIB at the time of the challenge. It shows that the EVH challenge test is highly sensitive at identifying EIB in elite swimmers.

**Competing interests** None.

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