

Evaluating the Athlete with Suspected Exercise-Induced Asthma or Bronchospasm

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Abstract

Exercise-induced asthma (EIA) and exercise-induced bronchospasm (EIB)/bronchoconstriction (EIC) describes two clinical entities by which exercise triggers bronchial hyperresponsiveness. Exercise is a common trigger of bronchospasm in the asthmatic (EIA), as well as athletes without the underlying inflammation associated with asthma (EIC/EIB). Approximately 10% to 20% of the general population have EIA or EIB (1–3). The approach to the diagnosis and subsequent management relies on the clinician's ability to recognize clinical signs and symptoms, then selecting the correct diagnostic test. A baseline spirometry/pulmonary function test is recommended for all athletes to evaluate for underlying asthma. Subsequent direct or indirect bronchial provocation testing is recommended to correctly diagnose EIA or EIB (4). Athletes should not be treated empirically with bronchodilators based on symptoms alone without confirmatory spirometry and provocative testing.

both entities commonly share airway hyperreactivity (AHR), they should be clinically categorized as two distinct entities: testing for and treatment of each may be uniquely different. In athletes who exhibit the appropriate clinical symptomatology, varying methods of confirmatory testing have been used to diagnose EIB. The testing methods which are used will be discussed to include measurement of peak expiratory flow rates, indirect bronchial provocative testing, and direct bronchial provocative testing. Appropriate treatment options can then be initiated to treat exercise-induced symptoms and maximize full performance potential.

Introduction

Exercise-induced asthma (EIA), also known as exercise-induced bronchospasm (EIB), describes a clinical entity by which a transient, reversible increase in airway resistance occurs after or during vigorous exercise. Exercise is a known trigger for those with a history of asthma. However, it is known to affect elite athletes with no established diagnosis of asthma as well (1). It is helpful to clinically distinguish the athlete with symptoms suggestive of increased airway resistance. Exercise-induced asthma historically describes those with a history of asthma who exhibit a bronchospastic response during or after an exercise bout, while those athletes with EIB do not have a history of asthma and experience no symptoms outside of exercise (2). Although

Epidemiology

The earliest published data of bronchial hyperresponsiveness was published in 1989. Young swimmers, those with and those without asthma, were found to have AHR after exertion (3).

In patients with asthma, who do not require inhaled corticosteroid treatment, the prevalence of EIB is 70% to 80%. In comparison, only 50% of those treated with inhaled corticosteroids have a bronchospastic response to vigorous exercise (1).

In the general population, the prevalence of EIA or EIB in adults ranges between 10% and 20% (4–6). In a study of Australian children, the prevalence of EIA was 19.5%; only 60% had a known history of asthma (7). Other conditions, such as allergic rhinitis and atopic dermatitis, have shown an association with EIB. Forty percent of individuals with those conditions were found to have EIB (2).

The prevalence of EIB in elite athletes has been shown in a number of studies to be greater than that in the general population, with data suggesting that the type of sport also may play a significant factor in the development of AHR (3,8). Higher-risk sports include endurance sports which require higher minute ventilation: cycling, track, basketball, or soccer. Cool, dry air also triggers a higher prevalence of EIA/EIB in winter sports such as hockey, ice skating, or skiing (2,3,9). A Finnish study of national track and field athletes found an EIB prevalence of 17% of long distance

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runners, and 8% of speed and power event athletes (10). At the 1998 Winter Olympic Games, the prevalence of EIB in United States athletes was 23% (1). This also suggests that cold, dry environments tend to trigger EIB in those at-risk athletes.

Pathophysiology

Multiple factors play a role in the physiologic mechanism of EIB. Intense exercise leads to an increase in oxygen demand, which in turn leads to increases in tidal volume and respiratory frequency ultimately resulting in a 20-fold increase in minute ventilation (3). Subsequent airway drying occurs as a result of increased minute ventilation during exercise, thereby providing the stimulus for the release of various inflammatory mediators. Inflammatory mediators which may be released include histamine, tryptase, interleukins, and leukotrienes, with a relative decrease in the release of prostaglandin E₂ and thromboxane B₂ that has been seen in induced sputum analysis (11–14). In nonathletes, or those not conditioned, the maximal flow rate with respiration is often not achieved due to early peripheral muscle fatigue (3).

There are two pathophysiological processes that have been postulated for EIA/EIB; the water loss theory and the thermal expenditure theory.

The water loss theory describes the loss of water through bronchial mucosa as an effect of rapid inhalation during exercise which dries the mucosa and triggers bronchoconstriction through local changes in pH and osmolarity of the periciliary fluid surrounding mucosal membranes. This stimulates epithelial cell and mast cell activation and release of inflammatory mediators (2,13,15). The exact mechanism by which water loss and transient osmotic gradients lead to epithelial and mast cell release of histamine is uncertain (4). This factor is augmented in elite level athletes who might have ventilation rates greater than 280 L·min⁻¹ (3).

The thermal expenditure theory suggests that the respiratory heat loss is itself responsible for cooling of the airway leading to vascular engorgement, hyperemia, and bronchoconstriction once exercise is ceased and the airways rewarm (2,15,16). This concept has been demonstrated through thermal mapping the respiratory tract and monitoring response to increased ventilation. This has been debated by some because animal studies have been devoid of the development of EIB when exposed to cooling and subsequent warming in the absence of hyperpnea. This demonstrates a gap in the thermal expenditure theory that bronchial vasculature is not the primary source of EIB (3,4). Additional evidence published by the *Journal of Allergy and Clinical Immunology* suggests that alterations in airway temperature probably have only a minor effect on the degree of bronchoconstriction (17).

During exercise, flow rates and tidal volumes will increase in both those with and without EIB to a period of approximately 6 to 8 min. After this time, those with EIB will experience a decline in flow rates and tidal volume that is characteristic of airway hypersensitivity (1). The bronchoconstriction response after exercise will last between 30 and 90 min with the lowest flow rates and tidal volumes 5 to 12 min postexercise (4).

Airway function itself can be affected by additional environmental and external stimuli. Due to increased minute

ventilation, the effects of airway irritants, such as allergies, chlorinated compounds in swimming pools, nitrogen oxides, or dry and cold environments, may be more pronounced in the athlete versus the nonathlete population. These effects may be greater and thus easier to provoke airway hyperresponse in established asthma patients (18).

Presentation

The athlete with EIA presents with a variety of clinical symptoms. Such symptoms may include breathlessness, chest congestion or tightness, postexercise cough, fatigue, or wheezing (1,18). Despite this constellation of classic symptoms for EIA/EIB, most elite athletes evaluated with respiratory complaints do not have EIA/EIB (16,19). Atypical symptoms may include stomach cramps, chest pain, nausea, or headache (2). Sometimes, atypical symptoms may persist throughout the day and not during or after exercise, such as recurrent cough or production of phlegm (16).

Respiratory symptoms in athletes are common. However, alone, they are unreliable when attempting to diagnose EIA/EIB (19). Self-reported symptoms are not diagnostic and should never be used alone in the diagnosis of EIA/EIB (4,20). One study of 196 collegiate athletes across eight different sports who were administered a self-reported questionnaire showed 28.6% self-reporting a history of EIB or asthma. Twenty five percent of those athletes who self-reported EIB or asthma were not using a respiratory medication (21). The use of self-reported symptoms to make the diagnosis of EIB is inaccurate and unreliable (22).

The differential diagnosis is broad and includes many masqueraders when considering EIA/EIB. This differential diagnosis includes vocal cord dysfunction, exercise-induced inspiratory stridor, arrhythmia, atrial septal defect, swimming-induced pulmonary edema, pulmonic arteriovenous malformations, exercise induced anaphylaxis, interstitial fibrosis, obstructive or restrictive lung disease, diaphragmatic paralysis, exertional GERD, anxiety, conversion disorder, and overtraining syndrome (4,16,17). Exercise-induced arterial hypoxemia in the highly trained athlete also has been described and is due to gross ventilation and perfusion disparity (23). Errors and misdiagnosis may occur when athletes are diagnosed with airway hyperresponsiveness purely based on history without consideration of a more broad differential diagnosis. For all athletes, it should be of the utmost importance to keep a broad differential as well as performing appropriate confirmatory testing. Describing each of the above diagnosis in more detail is beyond the scope of this publication.

Diagnostic Evaluation

The athlete who coughs, wheezes, or has any of the other symptoms suggestive of EIA/EIB should undergo formal testing to include spirometry followed by a bronchial provocation test.

Historically, and often, the diagnosis of EIA/EIB had been made solely by subjective history. Unfortunately, this approach is unreliable and often inaccurate (2). The diagnosis should be established by changes in lung function provoked by exercise and not on the report of symptoms alone (4). Also, reductions in peak expiratory flow rate (PEFR) or forced expiratory flow rate (FEF, 25%–75%) also had been

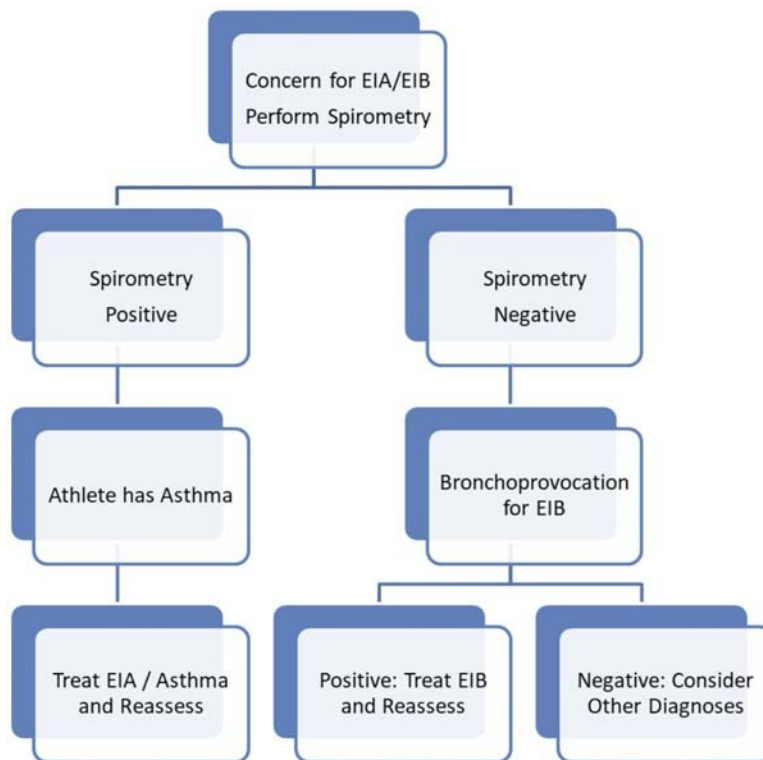


Figure: Approach to the athlete with suspected EIA/EIB.

used to make the diagnosis of EIA/EIB. This is no longer recommended due to lack of reproducibility (1,4).

An initial office spirometry will help rule out underlying asthma in those suspected of having simply bronchoconstriction. If indeed a spirometry test confirms the presence of underlying asthma, then athletes should be appropriately treated based on the severity and frequency of their symptoms. If spirometry is equivocal, then a bronchial provocation test is recommended to evaluate for pure EIC (2,18) (Fig.).

The International Olympic Committee (IOC) consensus regarding the diagnosis of EIA/EIB recommends forced expiratory volume in 1 s (FEV1) determination via spirometry. Since elite level athletes often have a baseline FEV1 above the range of normal compared with the nonathlete, a spirometry test may be equivocal. Thus, spirometry should be repeated with a short-acting bronchodilator challenge to demonstrate reversibility. If this does not yield a reversible airway response (>10% improvement in FEV1 post bronchodilator), then a bronchial provocation test is warranted. If all of the above tests are equivocal or indeterminate, then the clinician should reassess for another plausible diagnosis (18).

There are two types of challenge testing: indirect and direct (18). Indirect testing includes exercise challenge, hyperosmolar aerosols (*e.g.*, mannitol or hyperosmolar saline), and eucapnic voluntary hyperpnea (EVH) (18). These are considered indirect tests because the aforementioned stimuli will indirectly cause airway smooth muscle contraction by the release of inflammatory mediators (16). For exercise challenge and EVH, a 10% decrease in FEV1 suggests EIB. This is in contrast to hypertonic solutions, where a decrease in FEV1 of 15% after administration of mannitol, or 4.5% saline, suggests asthma

either with or without EIB (24). Furthermore, EIB can be characterized as mild, moderate, and severe if the fall in FEV1 is $\geq 10\%$, 25% , and 50% , respectively. Indirect challenge testing is preferred for assessing EIC since it is more sensitive than direct challenge testing with methacholine (4). Exercise challenge testing is an indirect test that uses exercise as a stimulus to provoke symptoms of EIB. This may be performed in a laboratory setting or on a “field” to mimic the athlete’s competitive or training environment. Although on field testing may more closely mimic actual competition and is shown to be more sensitive in the diagnosis of EIA/EIB, it is difficult to standardize environmental factors and perform appropriate monitoring of vital parameters with exertion (23,25).

In the laboratory setting, treadmill, or free running is commonly used for 6 to 8 min at high intensity with an exercise load sufficient to raise the heart rate to 80% to 90% of the calculated maximum in a temperature- and humidity-controlled environment. Certain target ventilatory rates rather than heart rates also have been used in the clinical setting. FEV1 can be measured at regular intervals of 5, 10, 15, and 30 min after exercise, although monitoring may be more frequent depending on the clinical scenario (4). The change in FEV1 is expressed as a percentage of the pre-exercise FEV1 ($\text{PreFEV1-PostFEV1/PreFEV1}$), with a drop >10% being diagnostic for EIB as per the American Thoracic Society and European society guidelines (26). With environment standardization and adequate exercise load, good reproducibility maintaining sensitivity and specificity has been shown (27).

Eucapnic voluntary hyperpnea is another indirect test that is helpful but less available for most clinicians. This test requires the athlete to ventilate 22 to 30 times per minute

for 6 min while breathing dry, cold air containing 5% carbon dioxide. The examiner is able to vary the length of time, ventilation level, and temperature to mimic the appropriate sport (18). EVH is considered the gold standard test; however, its availability for most sports medicine professionals in a community setting is limited (2). Currently, it is the recommendation of the IOC to use EVH as the bronchial challenge test of choice for diagnosing AHR (16). EVH also is the indirect bronchial provocation test of choice for EIB in the athlete without a history of asthma per the American Thoracic Society guidelines (4). The EVH test should not be administered if an athlete has a baseline FEV1 < 70% predicted and used with caution with an FEV1 between 70% and 80% predicted. These patients have an increased risk of a precipitous drop in FEV1 during testing (17).

Hyperosmolar aerosols administration is an indirect testing technique used to provoke evaporative water loss in the airways. Hyperosmolar (4.5%) saline can be inhaled via a nebulizer, and mannitol powder may be delivered via a dry powder inhaler. A drop in FEV1 > 15% after either hyperosmolar saline or mannitol is suggestive of bronchoconstriction (18,28). Inhalation of adenosine monophosphate (AMP) also has been used (16). Although FDA approved, mannitol dry powder for bronchial provocation tests is currently not available in the United States (17). Both mannitol and EVH testing have similar sensitivities (16).

Direct challenge testing involves the administration of an agent, such as methacholine or histamine, to directly provoke airway smooth muscle to stimulate bronchoconstriction. In a methacholine challenge test, a nebulizer acts to deliver methacholine in increasing concentrations, requiring multiple complete inhalations, and then testing postinhalation FEV1 measurements after each dose. The concentration of methacholine by which a fall in FEV1 by 20% is measured as the prechallenge value (PC₂₀) with concentration and cumulative dosing cutoffs suggestive of airway hyperresponsiveness varied based on whether the athlete is currently being treated with inhaled corticosteroids. In a steroid naive athlete, a cutoff value of <4 mg·mL⁻¹ is generally accepted as suggestive of EIA/EIB with a methacholine challenge test (4,28). In athletes who have taken inhaled corticosteroids for at least 3 months, a PC₂₀ < 16 mg·mL⁻¹ would be suggestive (16). Direct challenge testing can be useful as a screening test for chronic asthma, but it has not been shown to be useful as a test to diagnose EIC (4).

Conclusions

Athletes will commonly present to a medical provider's office with complaints of cough or wheezing during or shortly after exercise. They may complain of shortness of breath and/or having difficulty keeping up with their peers during practice or competition. Although more serious cardiopulmonary conditions must always be kept in the differential diagnosis, EIA/EIB has a high prevalence in the general and athletic population.

Baseline spirometry with and without a short-acting bronchodilator to assess airway reactivity should be performed on all athletes as the first diagnostic test. If underlying asthma is revealed, whether intermittent or persistent, treatment of the underlying asthma should be initiated or modified. If the asthma with its underlying inflammation

is optimally controlled, then the EIA (exercise trigger) is likely to substantially improve or resolve. Controlling the underlying inflammation therefore is critical to help improve EIA airway reactivity. If spirometry does not reveal underlying asthma or if an athlete with asthma continues to have what appears to be an exercise trigger despite inflammatory control, then proceeding to provocation testing is recommended. Although EVH testing is the gold standard, it is recognized that this testing modality is not always readily available for most practicing clinicians. If EVH testing is available, then it is in fact the preferred test to diagnose EIA/EIB. If EVH is not available, and an "on field sport-specific" exercise challenge testing is logistically possible, then this would be the provocation test of choice. If "on field sport-specific" exercise challenge testing is not possible, then the next best option would be a pulmonary laboratory-based, but sport-specific (running, cycling, rowing), challenge test. Unfortunately, the laboratory-based test cannot simulate all athletic exposures, such as ice skating, skiing, or other outdoor sports where humidity, air temperature, allergens, and air pollutants may contribute to airway reactivity in an athlete. If despite testing the diagnosis remains elusive, then other diagnoses must be considered and appropriate specialists consultation is highly recommended.

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