Exercise-Induced Bronchospasm: Diagnosis and Treatment

Case Study and Commentary, Aaron S. Bruns, MD, and Jonathan P. Parsons, MD

CASE STUDY
Initial Presentation

A 23-year-old female college student presents to the student health center complaining of dry cough, wheezing, and chest tightness that occurs frequently with exercise. She is on the varsity soccer team and notes she occasionally has trouble keeping up with the other players. She has no significant medical or family history and is currently taking no medications.

• What is exercise-induced bronchospasm?
• How prevalent is it?

Exercise-induced bronchospasm (EIB) is acute and reversible airway narrowing that occurs during, and also frequently after, exercise. Because the presenting symptoms of EIB are nonspecific, objective evidence of bronchospasm should be documented to confirm a diagnosis. A 10% or greater decrease in the forced expiratory volume in 1 second (FEV₁) from baseline after an adequate exercise challenge is accepted as diagnostic for EIB [1]. Adequate exercise challenges stimulate a significant increase in the ventilatory rate from baseline, which is necessary to trigger EIB in most patients.

EIB occurs commonly in people with and without asthma. In people with a known history of asthma, exercise is one of the most common triggers of bronchospasm and affects 50% to 80% of asthmatics [2]. EIB occurs somewhat less commonly in those with allergic rhinitis or atopic disease but is still found in up to 40% of this cohort [3]. In the general population without asthma or atopy, the prevalence of EIB is approximately 10% [4]. The prevalence of EIB is even higher in elite athletes; reported prevalence rates in this group are as high as 50% [2].

Exercise-induced asthma and exercise-induced bronchospasm are 2 terms that are often used interchangeably.

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to represent the same diagnosis. However, it is important to recognize that the occurrence of bronchospasm during exercise does not mean that a person has chronic asthma. Many people with EIB do not have the typical features of chronic asthma (ie, frequent daytime symptoms, nocturnal symptoms, or impaired lung function). Exercise may be the only stimulus that causes respiratory symptoms in this population. For this reason, the term exercise-induced bronchospasm represents a more appropriate way to term this diagnosis, as it avoids confusing patients with nonasthmatic EIB with patients with chronic asthma, and the term exercise-induced asthma should be reserved for those patients with a clinical diagnosis of asthma.

Why is EIB difficult to recognize?

The prevalence of EIB may actually be underestimated as patients with asthma have been shown to be poor perceivers of symptoms of bronchospasm [5,6]. Athletes often have particularly poor awareness of symptoms suggestive of EIB and are not aware that they may have a physical problem [7,8]. Furthermore, if they do recognize they have a medical problem, many patients, especially athletes, do not want to admit to health care personnel that a problem exists due to fear of social stigma or losing playing time.

Health care providers and coaches also may not consider EIB as a possible explanation for respiratory symptoms occurring during exercise. Athletes with EIB are generally fit and healthy and the presence of a significant medical problem many times is not considered. These patients are commonly considered to be “out of shape” by parents, coaches, or athletic trainers when they are symptomatic, and vague symptoms of chest discomfort, breathlessness, and fatigue are not interpreted as a manifestation of EIB.

What causes EIB?

The exact cause of EIB is not completely understood, but the 2 prevailing theories are the thermal theory [9] and the osmotic theory [10]. The upper airway is responsible for warming air as it enters the lungs. During exercise in cold weather, large volumes of cold air enter the lungs and the capacity of the upper airway to effectively heat the air is overwhelmed. As the cold air reaches the distal airways, vasoconstriction occurs initially. Subsequently, a reactive hyperemia of the lung vasculature occurs presumably in response to the vasoconstriction, which results in increased hydrostatic pressure in the vasculature leading to airway edema and mechanical narrowing of the small airways. The thermal theory may help explain why people with EIB often have more significant symptoms during cold weather.

The osmotic theory hypothesizes that as athletes inhale large volumes of dry air, there is water loss from the airway surfaces via evaporation. As a result, changes occur in the osmolarity of the epithelial cells lining the airways. It is postulated that dehydration of these epithelial cells triggers the release of inflammatory mediators, including histamine, leukotrienes, and prostanoids, many of which cause bronchospasm [11,12].

Several environmental factors may contribute to the pathogenesis of EIB as well. Exposure to chlorine in swimmers [13], chemicals during ice resurfacing in ice rinks [14], and air pollution [15] have all been linked to increased prevalence rates of EIB.

What information is important to obtain during the history and physical examination?

Common symptoms of EIB include cough, wheezing, dyspnea, fatigue, and chest tightness (Table 1). Exertional chest pain and postexercise cough in athletes is commonly related to EIB. A history of symptoms occurring in specific environments (ie, ice rinks or swimming pools) may also suggest EIB. More subtle indicators may include poor performance for the level of conditioning in competitive athletes or avoidance of physical activity, which is commonly seen in school-aged children.

The timing of onset and resolution of symptoms is important to elicit. Symptoms of EIB usually peak 5 to 10 minutes after exercise and can last for 30 to 60 minutes [16,17]. In most patients with EIB, symptoms will resolve even without treatment after approximately 60 minutes [17]. Symptoms that have a more abrupt onset or resolution may suggest alternative diagnoses such as vocal cord dysfunction.

Specific populations that may be at higher risk for EIB include athletes involved in cold weather sports or sports requiring sustained periods of high ventilatory demand or “high-ventilation sports” (ie, track, soccer) [18,19]. In addition,
individuals with asthma or allergic rhinitis are at a higher risk of EIB [20].

The physical examination at rest in patients with suspected EIB is often normal and is not predictive of whether the patient has EIB. In those with a previous history of asthma, wheezing or a prolonged expiratory time may be elicited during the pulmonary examination. Occasionally, heart murmurs, other signs of cardiac problems, inspiratory stridor, or other abnormal physical findings may be found on examination that lead the clinician to specific diagnoses other than EIB.

Despite the value of a comprehensive history and physical examination of the patient with symptoms suggestive of EIB, the diagnosis of EIB based on self-reported symptoms alone has been shown to be inaccurate. One study found screening history identified subjects with symptoms or a previous diagnosis suggestive of EIB in 40% of the participants, but only 13% of these persons actually had objectively documented EIB [21]. Similarly, another study demonstrated 45% of athletes who complained of respiratory symptoms during exercise were found to be EIB-negative after testing [7]. This study demonstrates that empirically diagnosing and treating symptomatic patients without objectively confirming a diagnosis of EIB may lead to an inaccurate diagnosis over 50% of the time.

Despite the evidence that objective testing is strongly recommended to confirm a diagnosis of EIB, many physicians do not perform objective testing and treat EIB empirically based on history alone. Parsons et al [22] surveyed pulmonologists and family physicians and found that family physicians were significantly more likely than pulmonologists to start a short-acting bronchodilator empirically before exercise when EIB was suspected in a healthy patient (78% versus 47%). Furthermore, pulmonologists were 4 times more likely to order bronchoprovocation testing when compared with family physicians. The study concluded that empiric treatment of EIB may lead to an inaccurate diagnosis and unnecessary morbidity.

In summary, history and physical examination, while important, is usually not enough to confirm diagnosis of EIB. The poor predictive value of the history and physical examination in the evaluation of EIB strongly suggests clinicians should perform objective diagnostic testing when there is a suspicion of EIB.

• What is the differential diagnosis of EIB?

There are several disorders that can mimic EIB (Table 2). Frequent rescue inhaler use or wheezing, dyspnea, and chest tightness that occur at rest or at night may suggest poorly controlled, chronic asthma. Palpitations, skipped beats, dizziness, or syncope may suggest cardiac arrhythmias or cardiomyopathies. Uncontrolled gastroesophageal reflux disease can also present in a similar manner to EIB.

One disorder than can be particularly difficult to differentiate from EIB is vocal cord dysfunction (VCD) (Figure 1). VCD is characterized by variable, extrathoracic airflow obstruction caused by paradoxical adduction of the vocal cords during respiration. Symptoms of VCD may be similar to symptoms of EIB; however, there are subtle clues to the diagnosis of VCD. Patients with VCD commonly have a very

Table 2. Common Mimics of Exercise-Induced Bronchospasm

<table>
<thead>
<tr>
<th>Disorder</th>
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<tbody>
<tr>
<td>Vocal cord dysfunction</td>
</tr>
<tr>
<td>Gastroesophageal reflux disease</td>
</tr>
<tr>
<td>Cardiac arrhythmias/cardiomyopathies</td>
</tr>
<tr>
<td>Pulmonary vascular disease</td>
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<td>Deconditioning</td>
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EXERCISE-INDUCED BRONCHOSPASM

sudden onset and resolution of symptoms in contrast to patients with EIB. VCD may also present with throat tightness, hoarse voice, or inspiratory stridor on physical examination. Common triggers of VCD include exercise, stress, gastroesophageal reflux disease, postnasal drip, and strong odors or fumes. In a study of 370 elite athletes, 5.1% had inspiratory stridor suggestive of VCD [23]. Of note, 53% of the athletes with VCD had EIB as well, indicating VCD and EIB often occur concomitantly. A suspicion of VCD may be raised if there is flattening of the inspiratory limb of the flow-volume loop during spirometry (Figure 2). The gold standard for confirming VCD is videolaryngostraboscopy, which allows direct visualization of the vocal cords and should be performed to confirm a suspicion of VCD.

• How should the workup of EIB proceed?

If EIB is suspected based on history or physical examination, the next recommended steps are to perform a baseline electrocardiogram (ECG) to rule out any arrhythmia and spirometry before and after bronchodilator therapy. Most often, the ECG will be normal; however, occult conduction system abnormalities and evidence of chamber enlargement can be suggested by ECG. If spirometry reveals an obstructive pattern, a diagnosis of asthma may be considered. However, in many patients with EIB, spirometry will be normal. In this cohort, spirometry is not adequate to diagnose EIB. Adequate exposure to exercise and environmental stress is needed during the evaluation for suspected EIB or false-negative results will likely occur. Therefore, in patients with normal history, physical examination, ECG, and spirometry, bronchoprovocation testing is recommended.

• What bronchoprovocation techniques are used to diagnose EIB?

Methacholine Challenge

Methacholine challenge testing is readily available and is a well-established screening test in asthma. Although it is a valuable test in the diagnosis of asthma, its value in the diagnosis of EIB is limited. The test involves the administration of methacholine, a potent airway agonist that acts directly on the smooth muscle receptors in the airways, at escalated doses following a defined protocol [24]. Spirometry is administered at baseline and is repeated after each dose and then compared with baseline values. A positive test is often defined as a 20% decrease in baseline FEV₁ at a methacholine dose of less than 8 mg/mL [24]. The limitations of methacholine challenge testing are that a positive response does not reliably predict whether EIB is present and a negative response does not exclude the diagnosis of EIB. Hence, despite the fact that it is commonly used in the workup of suspected EIB, its diagnostic value in this setting is questionable.

Exercise Challenge Tests

An exercise challenge can be done in the laboratory or in the field. If performed in the laboratory, usually a treadmill or cycloergometer is utilized [24]. There are multiple protocols for this challenge, but the most widely used is an incremental protocol where the work load is increased to 100% of the predicted maximum voluntary ventilation and then sustained for 4 minutes [24]. If the treadmill is used, a target of 80% to 90% of the maximum heart rate is often used. After the targets have been reached, the exercise is stopped and spirometry is measured at regular intervals for 30 minutes after the challenge. A decrease of 10% in the baseline FEV₁ at any time point postexercise is considered diagnostic for EIB [24]. Field-exercise challenge tests involve the athlete performing the sport in which they participate and then assessing pulmonary function after exercise. Mannix et al [25] studied the prevalence of EIB in elite figure skaters using a field-exercise protocol. In their study, baseline spirometry was obtained prior to testing. The athlete then performed a 3-minute skating warm-up in an ice rink. This was followed by an intense 5-minute skating routine. Spirometry was then repeated at 1, 5, 10, and 15 minutes postexercise. A decrease of 10% in the baseline FEV₁ during any time point postexercise was considered diagnostic of EIB.

Figure 2. Flow-volume loops showing a normal flow-volume loop (A) and variable extrathoracic airway obstruction which can be suggestive of vocal cord dysfunction (B).
study found a significant prevalence of EIB in this cohort but concluded that field-exercise tests are less sensitive than other bronchoprovocation techniques and allow for little standardization of protocol.

**Eucapnic Voluntary Hyperventilation Challenge**

Eucapnic voluntary hyperventilation (EVH) involves hyperventilation of a gas mixture of 5% carbon dioxide and 21% oxygen at a target ventilation rate of 85% of the patient’s maximum voluntary ventilation. The patient continues to hyperventilate for 6 minutes and FEV₁ is measured at specified intervals up to 20 minutes after the test and are compared with baseline [26]. The criteria for a positive EVH test can be variable. Most consider an EVH test positive if there is a 10% decrease in FEV₁ from baseline at any time-point post-hyperventilation [27]. EVH is portable, relatively inexpensive, and there are protocols [27] that allow standardization between laboratories.

- **Which test is best?**

Although there are several bronchoprovocation tests available to diagnose EIB, not all are equally valuable or accurate. Pharmacologic challenge tests, such as the methacholine challenge test, have been shown to have a lower sensitivity than EVH for detecting EIB in athletes [28]. In addition, they do not simulate exercise. Holzer et al [28] showed that of 42 elite athletes with symptoms suggestive of EIB, EVH detected 25 (60%), while methacholine challenge only detected 9 (21%). EVH has also been shown to be more sensitive in some studies for detecting EIB than field or lab-based testing [29,30]. EVH is considered by many to be the best bronchoprovocation technique available given its sensitivity, specificity, portability, and standardization of protocol. In addition, the International Olympic Committee endorses EVH challenge as the preferred test to document EIB in Olympians [31]. However, the value of EVH is limited by its lack of availability to many health care providers. If EVH is unavailable, we recommend exercise testing with particular attention being paid to ensuring the patient achieves adequate ventilation rates, which can be challenging in highly trained athletes.

An algorithm to help guide the workup of an individual suspected of having EIB is shown in Figure 3. As with most disorders, a complete history and physical examination is the starting point. If the history, examination, and spirometry are all normal, one should proceed next with bronchoprovocation testing. The choice of which bronchoprovocation test to use depends on a multitude of factors including cost and availability. If the physical examination, spirometry, and bronchoprovocation testing are all normal in a patient with suspected EIB, alternative diagnoses should be considered.

**Patient Workup**

A complete history is taken and is suggestive of EIB. A full physical examination is essentially normal, and spirometry is obtained. Spirometry reveals an forced vital capacity of 102% of predicted, an FEV₁ of 97% of predicted, a normal FEV₁/forced vital capacity ratio, and normal flow-volume loops. An EVH test is performed and a 13% drop in FEV₁ compared with baseline is documented at 10 minutes post-EVH testing, confirming a diagnosis of EIB.

- **What treatments are available for EIB?**

Many different treatments, both pharmacologic and non-pharmacologic, are available for EIB. Most pharmacologic treatments are similar to those used in patients with chronic asthma but have not been validated specifically in nonasthmatic patients with EIB.

**Pharmacologic Treatments**

Short-acting β-agonists such as albuterol are the first-line therapy for EIB [32]. Two puffs of a short-acting bronchodilator taken 15 to 30 minutes prior to exercise will provide prophylaxis against EIB symptoms within 15 to 60 minutes in 80% of patients and can last for up to 3 hours [32]. As long as albuterol is used prophylactically on an intermittent basis, tachyphylaxis generally is not a concern. Tachyphylaxis refers to a decreasing therapeutic response to medication over time secondary to repeated use. However, it is important to stress that repeated albuterol use as a rescue medication can lead to tachyphylaxis [32].

In the patient who has persistent EIB despite proper prophylaxis with albuterol, inhaled corticosteroids are considered first-line treatment [32]. Petersen et al [33] showed that the use of inhaled beclomethasone decreases the change in FEV₁ during exercise in pediatric athletes. This effect was achieved at a very low dose (50 μg daily), thereby minimizing the likelihood of systemic effects. In addition, Thio et al [34] showed that a single high dose of fluticasone also had a protective effect against EIB. It is critical to stress to the patient that these inhaled medications must be used on a daily basis and are maintenance medications and not rescue medications. Also, the prescribed regimen of medication will differ based on the type of inhaled steroid prescribed.

Leukotriene inhibitors such as montelukast and zafirlukast are used commonly in asthmatics and are effective in treating EIB. Several studies have shown that leukotriene modifiers exhibit a bronchoprotective effect in patients with...
Exercise-induced bronchospasm (EIB) [35–37]. Additionally, many patients, especially children, prefer the convenience of once-daily dosing with some leukotriene modifiers in contrast to multiple daily doses of inhaled controller medications.

For those who are in need of additional long-term protection, long-acting β-agonists are also effective [38]. In comparison studies, formoterol has been shown to have a quicker onset of action than salmeterol (12 min versus 31 min), but both were equally effective at 4 hours [39,40]. It is important to stress that these are long-acting medications and should not be used more than twice daily and are not recommended as monotherapy in patients with chronic asthma [41].

Mast cell stabilizers such as cromolyn or nedocromil are additional pharmacologic options. These can be administered prophylactically, usually 2 to 4 puffs 15 to 20 minutes prior to exercise. A meta-analysis of mast cell stabilizers demonstrated that these medications provide a significant protective effect against EIB with few adverse effects [42]. However, the study also found that on average, short-acting β-agonists resulted in more effective attenuation of EIB than mast cell stabilizers.

Despite the numerous effective treatment options, EIB still occurs commonly during recreational sports, athletic practices, and competitive sporting events. Acute, sideline management of EIB requires athletic trainers and coaches to be prepared to intervene if an athlete experiences an acute episode of EIB. All athletic trainers should have pulmonary

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**Figure 3.** Evaluation and management of exercise-induced bronchospasm. (Adapted with permission from Parsons JP, Mastromarade JG. Exercise-induced bronchoconstriction in athletes. Chest 2005;128:3966–74.)
function measuring devices (e.g., peak flow meters) at all athletic events including practices [43]. In addition, a rescue inhaler should be available during all games and practices. Spacers are recommended to be used with the rescue inhalers, and nebulizers should be readily available for emergencies in which inhalers do not work. Any athlete presenting with symptoms of respiratory distress should be removed from competition and receive immediate evaluation by a physician. It is recommended that any athlete with a peak expiratory flow lower than 80% of baseline be removed from activity until their peak flow returns to at least 80% of their baseline [44].

Nonpharmacologic Treatments

Since cold air and allergens can increase EIB symptoms, avoidance of these conditions can help improve performance. Wearing a facemask in cold weather can aid in warming and humidifying cold, dry air and may help reduce symptoms [45].

Many patients with EIB find that a period of precompetition warm-up reduces the symptoms of EIB that occur during competitive activity. This “refractory period” occurs in some patients with EIB and these athletes can be refractory to significant episodes of EIB if competition occurs within 2 hours of a vigorous exercise warm-up [46,47]. The refractory period is thought to potentially occur secondary to release of epinephrine and norepinephrine, which act locally in the lung as bronchodilators [46]. It is also hypothesized that the initial bout of bronchospasm depletes necessary inflammatory mediators for subsequent episodes of bronchospasm and that specific prostaglandins released during an initial episode of EIB may exert a protective effect against subsequent EIB [48]. While some can capitalize on the refractory period, it does not occur in all individuals with EIB, and it has not been consistently demonstrated to occur in nonasthmatics with EIB [49].

Dietary factors may also play a role in treatment of EIB. Patients with high dietary salt intake may have fewer symptoms when they reduce their salt intake [50]. In addition, fish oil supplementation and omega-3 fatty acids may be beneficial in reducing airway hyperreactivity in EIB [51,52].

• What are the potential complications of EIB?

The goals of treating patients with EIB are to optimize their pulmonary function prior to starting any athletic competition and to attempt to prevent significant episodes of respiratory distress from occurring during exercise. Unfortunately, bronchospasm often goes unrecognized and the consequences can be significant, especially in patients who have chronic asthma. Becker et al [53] identified 61 deaths secondary to asthma over a 7-year period occurring in close association with a sporting event or physical activity. Of these deaths, 81% occurred in subjects who were younger than 21 years and 57% occurred in subjects who were considered elite or competitive. Strikingly, almost 10% of deaths occurred in subjects with no known history of asthma. Similarly, Amital et al [54] found that asthma was the single greatest risk factor for unexplained death in a review of Israeli military recruit data over a 30-year period. Whether similar risks exist for nonasthmatic patients with EIB has not been clearly shown. Results from these reviews suggest that all individuals involved in organized sports or physical activity should be specifically trained in the recognition and treatment of bronchospasm that occurs during exercise.

CONCLUSION

The goals of treating a patient with EIB are to optimize their pulmonary function prior to starting any athletic competition and to attempt to prevent significant episodes of EIB from occurring during exercise. In our experience, both pharmacologic and nonpharmacologic approaches are essential to achieve these goals. We recommend starting athletes that have clinical evidence of EIB on short-acting bronchodilators before exercise and instructing them on the importance of adequate warm-up and avoidance of known triggers. If symptoms persist, especially in athletes with asthma, we recommend adding inhaled corticosteroids as maintenance therapy. It is also essential that coaches and athletic trainers be prepared to manage an athlete with an acute episode of EIB at all practices and competitive events.

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EXERCISE-INDUCED BRONCHOSPASM

CASE-BASED REVIEW


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CME EVALUATION: Exercise-Induced Bronchospasm: Diagnosis and Treatment

DIRECTIONS: Each of the questions below is followed by several possible answers. Select the ONE lettered answer that is BEST in each case and circle the corresponding letter on the answer sheet.

1. What is first-line treatment for objectively documented exercise-induced bronchospasm?
   A. Inhaled corticosteroids
   B. Leukotriene modifiers
   C. Short-acting bronchodilators before exercise
   D. Rest

2. Symptoms that may be suggestive of exercise-induced bronchospasm include
   A. Poor performance for level of conditioning or training
   B. Avoidance of physical activity
   C. Symptoms in specific environments
   D. All of the above

3. Which of the following statements concerning exercise-induced bronchospasm is FALSE?
   A. Exercise-induced bronchospasm is accurately diagnosed based on subjective history
   B. Vocal cord dysfunction and exercise-induced bronchospasm can occur concomitantly in the same patient
   C. Exercise-induced bronchospasm is commonly misinterpreted as a normal manifestation of exercise
   D. Athletes often do not want to admit they are having respiratory problems to their coaches and athletic trainers

4. Common mimics of exercise-induced bronchospasm include
   A. Gastroesophageal reflux disease
   B. Vocal cord dysfunction
   C. Cardiac disorders
   D. All of the above

5. Which of the following statements concerning exercise-induced bronchospasm is FALSE?
   A. Symptoms of exercise-induced bronchospasm usually peak 5 to 10 minutes after exercise and can last for 30 to 60 minutes
   B. Brisk warm-up before competitive events is recommended for patients with exercise-induced bronchospasm
   C. Individuals with asthma or allergic rhinitis are at a higher risk for exercise-induced bronchospasm
   D. Bronchoprovocation testing is not an essential facet of the workup for exercise-induced bronchospasm
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