

Exercise-induced bronchospasm: symptoms are not enough

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“Exercise is one of the most common triggers of bronchospasm in patients with chronic asthma and occurs in more than 40% of asthmatic individuals.”

Exercise-induced bronchospasm (EIB) describes airway narrowing that occurs with exercise. Exercise is one of the most common triggers of bronchospasm in patients with chronic asthma and occurs in more than 40% of asthmatic individuals [1]. EIB also occurs in an estimated 10–15% of the general population without asthma and is more prevalent in various cohorts of athletes [2,3]. Clinical presentations of EIB can range from mild impairment of exercise performance to severe bronchospasm and respiratory failure. Most authorities consider a drop from baseline of 10% or more in the forced expiratory volume in 1 s (FEV₁) after an appropriate airway challenge to be diagnostic of EIB.

Despite the fact that EIB is prevalent, there still remain significant diagnostic challenges in its work-up. Probably the most significant barrier to accurately diagnosing EIB is attributing exercise-induced respiratory complaints to EIB without any confirmatory objective testing at all. EIB typically presents with very nonspecific symptoms (i.e., shortness of breath or chest tightness). The lack of specificity and sensitivity of symptoms makes the diagnosis of EIB based on clinical history alone extremely inaccurate, resulting in inaccurate diagnoses in many cases [4,5]. One study showed that only 35% of participants who had symptoms suggestive of EIB actually had objectively documented EIB after pulmonary function testing [4]. Similarly, another study demonstrated that 45% of athletes who complained of respiratory symptoms during exercise

were found to be EIB negative after testing [5]. Although the poor predictive value of symptoms for the diagnosis of EIB has been well documented, evidence still suggests that the majority of health-care providers rely on symptoms alone to diagnose EIB, which probably results in large numbers of inaccurate diagnoses of EIB [6]. These data highlight the critical need for confirmatory, objective bronchoprovocation testing to diagnose EIB [4,5,7]. There is, however, no single definitive, gold-standard bronchoprovocation test for diagnosing EIB, which may be part of the explanation of why many patients are diagnosed with EIB without any confirmatory testing at all.

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Pharmacological challenge tests rely on the administration of agents such as histamine and methacholine to act directly on the airway smooth muscle receptors to induce bronchoconstriction. Methacholine challenge testing is readily available in most places and is a well-established screening test for asthma. Although it is a valuable test for the diagnosis of asthma, its value in diagnosing EIB is limited. These particular challenges assess for nonspecific airway hyper-responsiveness, are not specific for EIB and do not simulate exercise. Hence,

a positive test does not specifically confirm EIB. Conversely, pharmacologic tests, specifically methacholine challenge tests, have been shown to have low sensitivity for documenting EIB, particularly in athletes [8]. In one study comparing eucapnic voluntary hyperventilation (EVH) testing with methacholine challenge testing, the methacholine challenge test only detected nine out of 25 athletes to have a positive EVH challenge test. By contrast, all athletes with a positive methacholine challenge test also had a positive EVH challenge test [8]. Hence, in this study, methacholine had a negative predictive value of only 61% and a sensitivity of 36% for identifying those responsive to EVH. Based on its limitations in the evaluation of EIB, pharmacologic tests such as methacholine and histamine are suboptimal choices for the diagnosis of EIB [9].

Exercise testing, either laboratory based (i.e., treadmill, cycle or ergometer) or field based (i.e., performing the sport/activity in which the patient participates and then assessing pulmonary function after exercise), is a very commonly used method to diagnose EIB. Exercise tests involve a measurement of baseline spirometry and then repeated spirometric measurements after the chosen exercise stimulus. These tests have a high specificity for EIB but a relatively lower sensitivity. One of the most important reasons why exercise testing can lack the sensitivity for detecting EIB is the failure of the exercise stimulus to be intense enough to increase the ventilatory load to the necessary level in order to trigger EIB. This is particularly true in field-based exercise tests, where the workload and environmental conditions of the test are very difficult to control and measure. It is important to document in exercise testing that the heart rate reaches at least 80–90% of predicted maximum, which typically translates to 40–60% of the maximum voluntary ventilation (MVV) [10] and enough of a ventilatory burden to trigger EIB in the majority of affected individuals. It is also critical that spirometry is measured for up to 20 min after the exercise stimulus, as EIB often occurs several minutes after an exercise session is concluded. Simply assessing a postexercise spirometry at one time point shortly after the test is complete may result in many false negatives.

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Eucapnic voluntary hyperventilation testing involves hyperventilation of a gas mixture of 5% carbon dioxide and 21% oxygen at a target ventilation rate of 85% of the patient's MVV. The patient continues to hyperventilate for 6 min and FEV₁ measurements occur at specified intervals up to 20 min after the test and are compared with baseline [11]. EVH has a relatively high sensitivity to identify EIB and a high negative-predictive value [12]. The International Olympic Committee Medical Commission has specified EVH as the preferred test for EIB when athletes seek waivers allowing them to use restricted asthma medications during competition [9]. EVH has been shown to be an effective research tool and has also been studied extensively in cohorts

of athletes [4,10,13,14]. The major limitations of EVH are that it requires specialized equipment and is not widely available in community settings, and that the premixed gas mixture can be expensive.

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Mannitol inhalation is an example of an osmotic challenge test for documenting EIB. As a diagnostic tool, mannitol inhalation compares well with EVH and exercise testing [15,16]. It is available as a convenient and standardized test kit with prefilled dry powder capsules and single-use dry powder inhaler devices, which are portable [12]. This is a significant advantage over other bronchoprovocation techniques that require expensive equipment that is not portable. The ability to take a reliable tool for the diagnosis of EIB to the athletic field could potentially allow the screening of many athletes for EIB in one setting. Mannitol is not currently approved for use in the USA; however, it is used in Europe and Australia.

The question that many clinicians are faced with is what test is best for documenting EIB. There have been many studies that have compared different bronchoprovocation techniques but at this point, there is no gold-standard test. The choice of which specific bronchoprovocation test an individual clinician uses depends on a multitude of factors, including cost and availability. Exercise testing, with specific attention to the intensity of the exercise stimulus, and EVH testing, if available, are both modalities that clinicians can use for documenting EIB. Methacholine inhalation challenge testing remains an important tool in the diagnosis of asthma, but is less useful in the diagnosis of EIB. Mannitol may eventually emerge as the most useful test given its portability, but it is not yet available in the USA.

In conclusion, it is worth re-emphasizing that the diagnostic accuracy of symptoms alone is often less accurate than flipping a coin in terms of diagnosing EIB. Along the same lines, spirometry at rest without any assessment of postexercise lung function has extremely limited value in the diagnosis of EIB. We are still in search of the best test for documenting EIB, but diagnosing EIB without any testing at all should be avoided. Making an accurate diagnosis of EIB can be rewarding, as it often is easily treated, which can translate into improved health, athletic performance and, potentially, quality of life.

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