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When an athlete can't catch his breath

A patient who's fine during practice but runs out of breath before the game's over may have exercise-induced bronchoconstriction. This practical guide can help.

Practice recommendations

- Don't rely on self-reported symptoms to diagnose exercise-induced bronchoconstriction (EIB) (A).
- Indirect testing is the best way to diagnose EIB in patients who do not have underlying asthma (A).
- Short-acting β 2-agonists should be first-line management in EIB (A).

Strength of recommendation (SOR)

- A Good-quality patient-oriented evidence
B Inconsistent or limited-quality patient-oriented evidence
C Consensus, usual practice, opinion, disease-oriented evidence, case series

Luke, a 16-year-old basketball player, complains that he can't finish a game without running out of breath. He says things are at their worst when the game is close and when it's nearing the end. He doesn't have the problem during practice, or when he is playing other sports. The team physician suggested using an albuterol inhaler half an hour before game time and when he has symptoms, but he gets only minimal relief. Now he has come to you.

His vital signs, lung exam, and cardiac exam are normal. Results of pulmo-

nary function tests with pre- and post-albuterol challenge done a year ago were also normal. Does Luke have exercise-induced bronchoconstriction (EIB)? How can you be sure? And what can you do to help?

Symptoms like Luke's are common among athletes of all abilities. They may add up to EIB, a condition with an estimated prevalence of 6% to 12% in the general population—or they may not.¹ One study showed that only a third of athletes with symptoms or prior diagnosis of EIB had positive objective testing for the condition, and current studies show that reported symptoms are not an accurate guide in athletes like Luke who do not have underlying asthma.^{2,3} To treat him correctly, you will need to nail down the diagnosis with additional tests.^{3,4}

Shortness of breath that's worse than expected

EIB can have many different presentations. The most common symptom is cough associated with exercise.³ Other common signs and symptoms include wheezing, chest tightness, and more severe than expected or worsening shortness of breath. More unusual symptoms

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include a decrease in performance or fatigue out of proportion to workload. Often patients with EIB have other associated medical conditions, such as allergic rhinitis.

Bronchoconstriction usually occurs with maximal or near maximal exertion. Generally, it takes 5 to 8 minutes of exercising at 80% of maximal heart rate to trigger EIB. Classically, the symptoms peak 5 to 10 minutes after exercise begins.⁵

Rule out cardiac problems. If EIB is the correct diagnosis, the physical exam is usually normal. The importance of the physical exam is to evaluate for other diagnoses with similar presentations. Conditions to rule out include cardiac problems, exercise-induced hyperventilation, upper and lower respiratory infections or abnormalities, exercise-induced laryngeal dysfunction, exercise-induced anaphylaxis, and gastroesophageal reflux disease (GERD). The differential diagnosis for EIB is summarized in **TABLE 1**.

Test for asthma. Once you have gone through the differential diagnosis and are comfortable that the symptoms are respiratory, the next step should be pulmonary function tests (PFT), pre- and post-albuterol challenge. Findings of obstruction, such as reduced forced expiratory volume in 1 second (FEV1) or increased lung volume, are consistent with a diagnosis of asthma. In that case, no further workup is needed—unless the patient is unresponsive to asthma treatment. In athletes like Luke who do not have asthma and have a normal non-provocative spirometry, you can move on to either provocative spirometry or empiric treatment.

■ Perform provocative spirometry

Direct spirometry is commonly done with a methacholine challenge. This test is less sensitive than indirect testing for EIB patients who do not have underlying asthma.

TABLE 1

Is it EIB, or something else?

ETIOLOGY	POSSIBLE DIAGNOSES
Pulmonary	Exercise-induced hyperventilation (pseudo-asthma syndrome) Restrictive lung disease Cystic fibrosis Upper and lower respiratory infections Foreign body aspiration
Cardiac	Coronary artery disease Congenital and acquired heart defects Cardiomyopathy Congestive heart failure
Laryngeal	Exercise-induced laryngeal dysfunction Vocal cord dysfunction Laryngeal prolapse Laryngomalacia
Gastroesophageal	Gastroesophageal reflux disease
Allergic	Exercise-induced anaphylaxis
Other	Athlete is out of shape

EIB, exercise-induced bronchoconstriction.
Source: Weiler JM, et al. *J Allergy Clin Immunol*. 2007.⁴

The gold standard for indirect testing is eucapnic voluntary hyperventilation (EVH). Because EVH requires special equipment, however, it may not be an option in your office. The more reasonable choice is exercise challenge testing, which can be done either in your office or in the milieu—the basketball court, for example—where the athlete's symptoms usually occur. In an exercise challenge, you get a baseline spirometry measurement, have the athlete exercise to 80% to 90% of maximal heart rate, and then repeat spirometry at short intervals after exercise ends. If you do an exercise challenge in the office, you can reduce false-negative results by maintaining an ambient temperature between 68° and 77°F (20°-25°C) with a relative humidity of less than 50%.^{6,7}

Or try empiric treatment

Empiric treatment is a reasonable strategy for athletes with EIB symptoms, worth trying both for athletes who have underlying asthma and for those who do not.

FAST TRACK

It typically takes 5 to 8 minutes of exercising at 80% of maximal heart rate to trigger exercise-induced bronchoconstriction.

CONTINUED

Is that drug banned from competition?

Certain medications used in the treatment of asthma and exercise-induced bronchoconstriction (EIB) are considered performance-enhancing drugs and either banned or restricted in athletic competition. The regulatory bodies that make these designations in the United States are the National Collegiate Athletic Association (NCAA) and the International Olympic Committee World Anti-Doping Agency (IOC-WADA). These organizations update their list of banned substances yearly and make the current list available on the Web. You can find the NCAA list at www.pace.edu/emplibary/NCAA%20LIST%20OF%20BANNED%20SUBSTANCESb.doc and the IOC-WADA list at www.wada-ama.org/rtecontent/document/2009_Prohibited_List_ENG_Final_20_Sept_08.pdf.

The IOC-WADA allows competing athletes to use inhaled corticosteroids and β_2 agonists, but requires athletes with asthma to provide documentation that the medication is for therapeutic use. Glucocorticosteroids and oral β_2 agonists remain prohibited by the IOC-WADA, but only oral β_2 agonists are banned by the NCAA. The NCAA warns that student athletes are responsible for knowing which substances are on the banned list and advises them to consult www.drugfreesport.com for more information. To avoid disqualifying a patient from sports participation, check medications you prescribe with the official lists and be sure your EIB patient has the documentation he or she needs to qualify for a therapeutic use exemption.

If the athlete with asthma responds to treatment, the problem is solved. For the athlete who does not have asthma, however, there are some exceptions to this approach—specifically, the elite athlete.

In the elite athlete, you will need to confirm the diagnosis because many of the substances used to treat EIB are restricted by governing bodies such as the International Olympic Committee (IOC) and require provocative testing to obtain a therapeutic use exemption.⁸ There is some debate as to whether nonelite athletes also need bronchoprovocative testing. Some recommendations advise testing all elite and competitive athletes and restricting empiric treatment to recreational athletes.¹ For more information on banned or restricted medications, see “Is that drug

banned from competition?” at left.

If you take the empiric approach and the athlete does not respond to treatment, consider further testing to rule out other, more serious problems. In Luke’s case, where empiric treatment with albuterol has failed, indirect testing would be the next step.

■ **Medicate before exercise: SABAs and LABAs**

Prophylaxis for EIB usually starts with an inhaled short-acting β_2 agonist (SABA) such as albuterol or pirbuterol, taken 15 minutes before starting to exercise.^{9,10} The effectiveness of both short- and long-acting β_2 agonists decreases with frequent use, which may be Luke’s problem. For that reason, patients with mild EIB may choose to use pretreatment medication only for more demanding exercise sessions.¹¹ Advise EIB patients who need daily pretreatment to try adjunctive maintenance therapy (discussed at greater length, below.)

Longer-acting β_2 agonists (LABAs) such as salmeterol or formoterol may be effective for prolonged or all-day exercise, but may lose their prophylactic effect with prolonged use.¹² Furthermore, the US Food and Drug Administration (FDA) has advised against using LABAs alone because of the possibility of severe asthma episodes or death. LABAs should be used only in conjunction with daily maintenance therapy with inhaled corticosteroids. The properties of these and other EIB medications are summarized in

TABLE 2.

■ **Cromolyn, antileukotrienes are options, too**

Mast cell stabilizers (cromolyn) can be used with β_2 agonists as prophylactic therapy. When these agents are used together, they have an additive effect.¹³ The athlete may take them 10 minutes to an hour before exercise. Make sure your patient knows that mast cell stabilizers can-

TABLE 2

EIB medications

MEDICATION	INDICATION	DOSE	CAUTIONS	COMMENT
Short-acting β_2 agonists (SABAs)				
Albuterol, pirbuterol	Pre-exercise prophylaxis, acute treatment	2 puffs pre-exercise or 2 puffs every 4-6 h as needed	May cause tachycardia, hypokalemia. Tachyphylaxis can develop with frequent use.	First-line treatment
Mast cell stabilizers				
Cromolyn	Pre-exercise treatment	2 puffs 30-45 min before exercise	None	Best combined with SABA. Tell patients not to use for rescue.
Inhaled corticosteroids				
Flunisolide, fluticasone, budesonide, triamcinolone, beclomethasone, mometasone	Daily maintenance	Variable	Can cause oral candidiasis, hoarseness.	Tell patients this is not a rescue inhaler.
Leukotriene inhibitors				
Zafirlukast	Daily maintenance	20 mg PO, bid	None	Variable response. Works well with inhaled corticosteroids. Low side-effect profile.
Montelukast	Daily maintenance, pre-exercise prophylaxis	10 mg PO daily or up to 2 h pre-exercise	None	Variable response. Works well with inhaled corticosteroids. Low side-effect profile.
Zileuton	Daily maintenance	1200 mg PO, bid	Risk of elevated liver function tests.	Variable response. Low side-effect profile.
Combinations				
Inhaled fluticasone and salmeterol	Daily maintenance	Variable doses (100/50, 250/50, 500/50 mcg/spray); 1 puff bid	Can cause oral candidiasis, hoarseness, tachycardia, hypokalemia. Tachyphylaxis can develop with frequent use.	Tell patients this is not a rescue inhaler.
Inhaled budesonide and formoterol	Daily maintenance	Variable doses (80/4.5, 160/4.5 mcg/spray); 1 puff bid	Can cause oral candidiasis, hoarseness, tachycardia, hypokalemia. Tachyphylaxis can develop with frequent use.	Tell patients this is not a rescue inhaler.

EIB, exercise-induced bronchoconstriction.

Adapted from the National Asthma Education and Prevention Program. Expert Panel Report 3: Guidelines for the diagnosis and management of asthma.⁹

not be used as a rescue inhaler or bronchodilator.

Inhaled corticosteroids (flunisolide, fluticasone, others) may be needed for athletes with poorly controlled chronic asthma; they can also be used as adjunct preventive treatment for athletes who have EIB with no underlying chronic asthma.¹⁴⁻¹⁶ Often, inhaled corticosteroids are used as combination therapy with a LABA or an antileukotriene agent

(montelukast, zafirlukast; see below). Recent research shows that montelukast in combination with inhaled corticosteroids is more efficacious than LABA with inhaled corticosteroids.^{14,17}

Antileukotriene agents can be especially helpful for EIB in patients with mild, stable asthma.¹⁸ Patients who do respond to antileukotriene agents usually respond very favorably. Antileukotrienes offer a reasonable alternative to inhaled corti-

FAST TRACK

LABAs should be used only in conjunction with daily maintenance therapy with inhaled corticosteroids.

costeroids and LABAs. They have a low side-effect profile and should be considered as daily prophylaxis.^{19,20} The effects of montelukast are evident as early as 2 hours after administration, and bronchoprotective effects can last as long as 24 hours.^{21,22} For that reason, montelukast is especially useful in children whose exercise patterns are not always predictable.

Be prepared for acute exacerbations. Prophylactic medication does not always prevent acute exacerbations. When that happens, your EIB patient will need to use a β_2 agonist as rescue therapy. Make sure your patient knows that none of the other medications are effective bronchodilators in acute exacerbations.

Remember, too, that EIB cannot be effectively treated if the athlete has poorly controlled chronic asthma. Underlying causes of asthma exacerbations like allergies or respiratory infections must be addressed and stabilized first, following guidelines of the National Asthma Education and Prevention Program (NAEPP).⁹ You can access the guidelines at www.nhlbi.nih.gov/guidelines/asthma/asthgdln.htm.

These tips can help the athlete

Encourage athletes with EIB to keep up their exercise routines, because cardiovascular fitness has a beneficial effect on this condition. Fit individuals breathe more slowly, which reduces the likelihood of exacerbations. Of note, though: Certain sports are easier on patients with EIB. Patients may want to keep this in mind when deciding which team they want to go out for. Specifically, indoor sports, where air temperature, humidity, and exposure to allergens are controlled, and sports like baseball, sprinting, or football, which require less prolonged aerobic endurance, are good options.

Tell athletes whose sports require cold, dry conditions—ice skating, or skiing, for instance—to try breathing through a scarf or mask to keep inspired air warm and less irritating.

And tell all athletes with EIB to warm

up properly before they start to compete.²³ That means a 15-minute warm-up at moderate exertion, followed by a 15- to 30-minute rest period. The rest period is the time to take their medication.

When therapy fails

When an EIB patient fails to respond despite multiple drug therapy, it's time to reconsider other diagnoses, such as vocal cord dysfunction and severe GERD, which may mimic symptoms of EIB.

On the horizon. Other therapies for possible treatment of EIB are being studied. These include omega-3 fatty acid dietary supplementation and inhaled enoxaparin.^{24,25} Data are currently insufficient to recommend use of these agents in clinical practice.

As for Luke, indirect testing via exercise challenge was positive for EIB. Adjunctive therapy with montelukast was added to his albuterol inhaler, and the combination has worked well for him. He's still playing basketball, and enjoying it. ■

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