Exercise-Induced Bronchoconstriction: Diagnosis and Management

MICHAEL A. KRAFCZYK, MD, *St. Luke's Hospital and Health Network Primary Care Sports Medicine Fellowship Program, Bethlehem, Pennsylvania*
CHAD A. ASPLUND, MD, *Eisenhower Army Medical Center, Fort Gordon, Georgia*

Exercise-induced bronchoconstriction describes the narrowing of the airway that occurs with exercise. More than 10 percent of the general population and up to 90 percent of persons previously diagnosed with asthma have exercise-induced bronchoconstriction. Common symptoms include coughing, wheezing, and chest tightness with exercise; however, many athletes will present with nonspecific symptoms, such as fatigue and impaired performance. Spirometry should be performed initially to evaluate for underlying chronic asthma, although results are often normal. An empiric trial of short-acting beta$_2$ agonists or additional bronchial provocation testing may be necessary to confirm the diagnosis. Nonpharmacologic treatment options include avoiding known triggers, choosing sports with low minute ventilation, warming up before exercising, and wearing a heat exchange mask in cold weather. Short-acting beta$_2$ agonists are recommended first-line agents for pharmacologic treatment, although leukotriene receptor antagonists or inhaled corticosteroids with or without long-acting beta$_2$ agonists may be needed in refractory cases. If symptoms persist despite treatment, alternative diagnoses such as cardiac or other pulmonary etiologies, vocal cord dysfunction, or anxiety should be considered. (*Am Fam Physician.* 2011;84(4):427-434. Copyright © 2011 American Academy of Family Physicians.)

▶ **Patient information:** A handout on exercise-induced wheezing, written by the authors of this article, is provided on page 436.

Exercise-induced bronchoconstriction (EIB) is a common problem in physically active persons. EIB is defined as transient, reversible bronchoconstriction that happens during or after strenuous exercise. It can occur in persons with or without underlying asthma.[1] Bronchoconstriction that is triggered by exercise in persons with underlying asthma is considered exercise-induced asthma. This article discusses the diagnosis and management of EIB in persons without underlying asthma. The National Asthma Education and Prevention Program also provides guidelines for the diagnosis and management of asthma.[2]

Epidemiology and Etiology

EIB is more common in persons who participate in endurance sports and sports that require high minute ventilation. More than 10 percent of the general population and up to 90 percent of persons previously diagnosed with asthma have EIB.[3] The prevalence of EIB in athletes ranges from 11 to 50 percent, although it approaches 90 percent in athletes with asthma.[3] EIB also commonly occurs in cold-weather athletes and has been found to be present in approximately 50 percent of Olympic cross-country skiers.[4]

In persons without asthma, the rapid breathing of cold, dry air over a prolonged period is an ideal setting for EIB. When a person finishes exercising, the airway responds with vasodilation to warm the airway, resulting in water loss and engorgement of the airways. This process causes bronchoconstriction and the release of proinflammatory mediators. Another possible etiology may be environmental irritants, such as chlorine gas in a swimming pool or gases from ice-resurfacing equipment. Persons with EIB and underlying asthma usually experience exacerbation of underlying inflammation and airway hyperactivity caused by any of these mechanisms or by poorly controlled chronic asthma.[5]

Diagnosis

SYMPTOMS

Typical symptoms of EIB include wheezing, shortness of breath, dyspnea, cough, or chest tightness during or after exercise. These symptoms usually occur during strenuous exercise and peak about five to 10 minutes

SORT: KEY RECOMMENDATIONS FOR PRACTICE

Clinical recommendation	*Evidence rating*	*References*	*Comments*
Self-reported symptoms alone should not be used to diagnose EIB.	C	6-8	—
The exercise challenge test can accurately diagnose EIB.	C	9	Varying results because of differences in how the test is performed
Warming up before exercise may reduce the degree of EIB.	B	2, 14	—
Wearing a heat exchange mask over the mouth and nose during cold-weather exercise may reduce symptoms of EIB.	B	2, 16	—
Inhaled short-acting beta$_2$ agonist use before exercise can attenuate symptoms of EIB.	A	2, 14, 21	—
Using inhaled corticosteroids as controller therapy is an effective management strategy for EIB in patients with underlying asthma.	A	2, 14, 25	—
Leukotriene receptor antagonist therapy can effectively manage EIB.	A	14, 26, 29	—

EIB = exercise-induced bronchoconstriction.

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to http://www.aafp.org/afpsort.xml.

after exercise. Atypical symptoms include fatigue, feeling out of shape, feeling unable to keep up with peers, and abdominal discomfort. Self-reported symptoms have been shown to be poor predictors of EIB because other conditions, such as vocal cord dysfunction, can cause similar symptoms.[6-8] Therefore, symptoms alone should not be used to diagnose EIB.

The physical examination in patients with EIB is often unremarkable. If patients are evaluated when symptomatic, the most common findings are tachypnea and wheezing during end expiration.

TESTING

In patients with possible EIB, spirometry should be performed to rule out underlying asthma[2] *(Figure 1)*. Normal resting spirometry results are common in patients with EIB. If spirometry reveals an obstruction, additional testing before and after albuterol use is recommended. Obstruction with reversibility is indicative of underlying chronic persistent asthma.

If the patient is not an elite athlete, the next step is to prescribe an empiric trial of a short-acting beta$_2$ agonist. Only athletes who participate in high-level competition will need documentation of objective testing to use banned asthma medication. Follow-up, usually after one to two weeks, is necessary to determine whether treatment is successful. If the patient's response to treatment is inadequate, additional testing is warranted.

For elite athletes or for persons with EIB that does not respond to a trial of a short-acting beta$_2$ agonist, bronchial provocation tests can be used to identify provoked decreases in forced expiratory volume in one second (FEV_1). There are two main types of bronchial provocation tests: direct and indirect. Most pulmonary function laboratories can perform direct challenges, such as methacholine challenge.

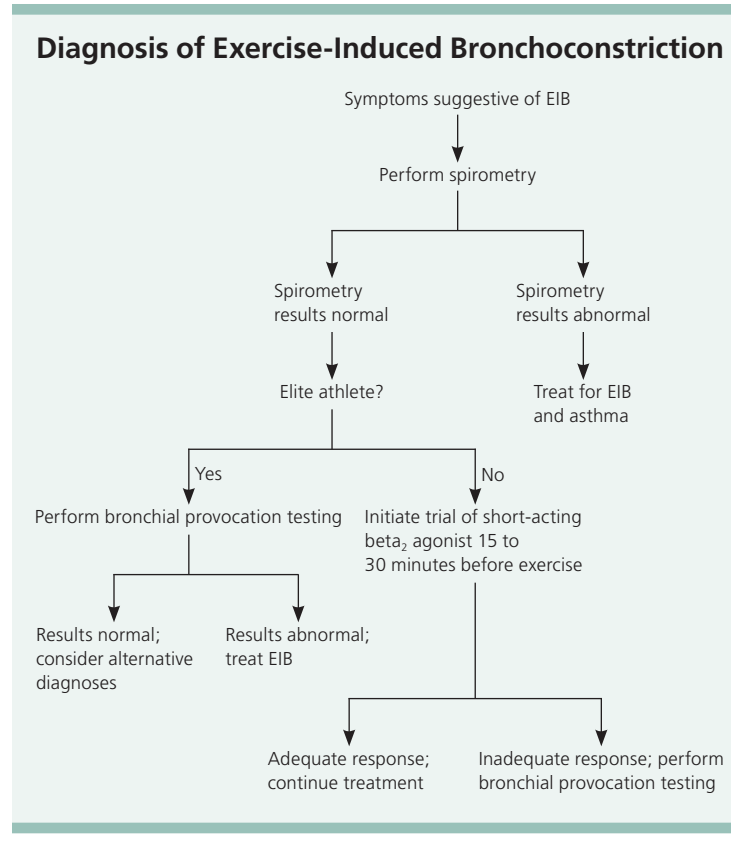

Figure 1. Algorithm for the diagnosis of exercise-induced bronchoconstriction (EIB).

Table 1. Indirect Testing for the Diagnosis of Exercise-Induced Bronchoconstriction

Test	*Description*	*Advantages*	*Disadvantages*
Eucapnic voluntary hyperpnea test	Patient hyperventilates a mixture of cold, dry air Spirometry performed before and after hyperventilation	Sensitive and specific Less laboratory space and equipment needed	Need to control inspired gases and humidity Need to monitor minute ventilation Relatively expensive Not readily available
Field-based exercise challenge	Usually performed in the environment that causes symptoms Spirometry performed before and after exercise	Sensitive and specific for cold-weather athletes Readily available Minimal equipment Inexpensive	Not standardized Unable to control environment
Hypertonic saline test	Patient is given nebulized hypertonic saline Spirometry performed before and after nebulization	Sensitive and specific Less laboratory space and equipment needed	Not as reliable if patient is already being treated with inhaled corticosteroid
Laboratory-based exercise challenge	Usually performed on a treadmill or stationary bike Spirometry performed before and after exercise	Sensitive and specific Standardized	Need to control inspired gases and humidity Need to monitor heart rate and minute ventilation Relatively expensive

Information from reference 9.

Some are also equipped to perform indirect challenges, such as an exercise challenge test, which can accurately diagnose EIB.[9] In addition, indirect challenges can be performed with a handheld spirometer at the location in which the athlete develops symptoms. Direct challenges have a lower sensitivity than indirect challenges[10]; therefore, indirect challenge is the preferred diagnostic test for EIB. Examples of indirect testing are listed in *Table 1*.[9] If bronchial provocation testing results are normal, other diagnoses should be considered *(Table 2*[11]*)*.

Management

EIB can affect many aspects of a patient's life, regardless of the severity of symptoms. The main goal of treatment is to allow patients to exercise safely. Secondary goals should include keeping athletes of all levels active and helping competitive athletes maximize performance. Asthma symptoms in association with exercise have been shown to reduce health-related quality of life scores in adolescents.[12] One report found that among asthma-related deaths during exercise, many athletes had only mild asthma.[13]

NONPHARMACOLOGIC TREATMENT

Several nonpharmacologic options exist for managing EIB. Basic measures include avoiding known triggers (allergen and environmental) and choosing sports with low minute ventilation (short bursts of exercise), such as football, baseball, wrestling, or sprinting. Although nonpharmacologic treatment options can be effective, all athletes with EIB need to have a short-acting beta$_2$ agonist available.

Preexercise Warm-up. There is some evidence that a preexercise interval warm-up may attenuate the bronchoconstriction associated with EIB by inducing a refractory period.[2,14] However, this has not been shown to be helpful in elite cold-weather athletes.[15]

Heat Exchange Mask. Heat exchange masks are designed to limit cold air exposure during exercise in athletes with EIB. They typically can be found in

Table 2. Differential Diagnosis of Exercise-Induced Bronchoconstriction

Anxiety
Cardiac abnormalities (e.g., congestive heart failure, coronary artery disease, dysrhythmias, hypertrophic cardiomyopathy, valvular abnormalities)
Deconditioning
Hyperventilation syndrome
Myopathies
Obesity
Pulmonary arteriovenous malformations
Pulmonary disease (e.g., chronic asthma, chronic obstructive pulmonary disease, cystic fibrosis, interstitial lung disease, pectus excavatum, scoliosis, tracheobronchial malacia)
Vocal cord dysfunction

Information from reference 11.

running stores or online. Using a mask has not been shown to be as effective as pretreatment albuterol in the prevention of bronchoconstriction.[2,16] One of the main limitations of a heat exchange mask is that it may not be practical during competition.

Nutrition. A review of the literature suggests that restricting dietary sodium intake for one to two weeks may reduce bronchoconstriction after exercise in patients with asthma and EIB; however, long-term studies are lacking.[17] Additionally, a small, double-blind crossover study showed that high-dose omega-3 fish oil supplementation for three weeks reduced the use of bronchodilators in the treatment group. The limitations of this study included the small size and no mention of adverse effects from the high dosage of omega-3 fish oil.[18]

Table 3. Medications for the Treatment of Exercise-Induced Bronchoconstriction

Medication	*Dosage*	*Onset of action*	*Duration*	*Comments*
Short-acting beta$_2$ agonists				
Albuterol	90 mcg per spray; two puffs 15 minutes before exercise and as needed	Five to seven minutes	Three to six hours	First-line prevention of acute asthma
Levalbuterol (Xopenex HFA)	45 mcg per spray; two puffs 15 minutes before exercise and as needed	Five to 10 minutes	Three to six hours	First-line prevention of acute asthma; similar to albuterol in safety and effectiveness, but more expensive
Pirbuterol (Maxair)	200 mcg per spray; one or two puffs 15 minutes before exercise and as needed	Five minutes	Five hours	First-line prevention of acute asthma; not available as generic; more expensive than albuterol
Long-acting beta$_2$ agonists				
Formoterol (Foradil Aerolizer); combination budesonide/formoterol (Symbicort)	Aerolizer: 12 mcg per capsule; one spray twice per day Metered-dose inhaler: 4.5 mcg per spray; two puffs twice per day	One to three minutes	12 hours	Second-line prevention of chronic asthma in conjunction with inhaled corticosteroid
Salmeterol (Serevent Diskus); combination fluticasone/salmeterol (Advair Diskus or HFA)	Diskus: 50 mcg per blister; one puff twice per day HFA: 21 mcg per puff; two puffs twice per day	30 to 48 minutes	12 hours	Second-line prevention of chronic asthma in conjunction with inhaled corticosteroid
Mast cell stabilizers				
Cromolyn (nebulizer solution)	20 mg per 2 mL; 20 mg taken 10 to 60 minutes before exercise or 20 mg four times per day	Less than one week	Unknown	Second-line prevention of chronic asthma

HFA = hydrofluoroalkane; NA = not available.

**—Estimated retail price based on information obtained at http://www.drugstore.com (accessed April 20, 2011). Generic price listed first; brand price listed in parentheses.*

†—Estimated cost to the pharmacist based on average wholesale prices (rounded to the nearest dollar) in Red Book. *Montvale, N.J.: Medical Economics Data; 2010. Cost to the patient will be higher, depending on prescription filling fee.*

PHARMACOLOGIC TREATMENT

Medication is the mainstay of treatment for persons with EIB *(Table 3*[19,20]*)*. Although pharmacologic treatment has been well studied, more research is needed to differentiate between optimal treatment of persons who have EIB with underlying asthma and those who have EIB without asthma.

Beta$_2$ Agonists. There are two types of inhaled beta$_2$ agonists: short-acting and long-acting. Short-acting beta$_2$ agonists are recommended first-line treatment in the management of EIB, preventively and for acute symptoms.[2,14,21] They should be used 15 minutes before exercise, typically have a peak action of 15 to 60 minutes, and last approximately three hours. There is growing concern about the development of tachyphylaxis with daily use of short-acting beta$_2$ agonists; therefore, they should be used only before more strenuous workouts or before competition.[5] Although long-acting beta$_2$ agonists have been shown to be effective in persons with EIB,[2] the U.S. Food and Drug Administration has recommended that they not be used in persons with asthma unless there is concomitant use of a controller medication, such as inhaled corticosteroids.[22] Concurrent use of inhaled corticosteroids and long-acting beta$_2$ agonists has been shown to be effective and superior to use of inhaled corticosteroids alone in managing EIB.[23]

Mast Cell Stabilizers. Mast cell stabilizers have been shown to be more effective than anticholinergics but less effective than short-acting beta$_2$ agonists for managing EIB.[24] Mast cell stabilizers should be used 15 to 20 minutes before exercise. Metered-dose inhalers have been discontinued because they are difficult to manufacture without chlorofluorocarbon propellants; however, cromolyn is still available as a nebulized solution.

Inhaled Corticosteroids. Inhaled corticosteroids are considered controller medications and are the mainstay of treatment in patients with persistent asthma.[2,14] A meta-analysis showed that use of inhaled corticosteroids for four weeks or more reduced the percentage decrease in FEV_1 after exercise.[25] There is a paucity of studies comparing inhaled corticosteroids with other treatments for EIB.

Leukotriene Receptor Antagonists. Leukotriene receptor antagonists have been shown to have a persistent benefit against EIB.[14,26] Montelukast (Singulair) has an onset of action within two hours and continued EIB preventive benefit up to 24 hours after a single oral dose.[27] Compared with salmeterol (Serevent), montelukast is equally effective at preventing EIB at two hours and at eight and one-half hours, but montelukast is more effective at 24 hours.[21] Short-acting beta$_2$ agonists have been shown to be more effective than montelukast in the prevention of EIB.[28] Use of montelukast has not been shown to cause tachyphylaxis.[29]

Other Agents. Ipratropium (Atrovent) is an anticholinergic that provides some protection against EIB but is not as effective as short-acting beta$_2$ agonists or leukotriene receptor antagonists.[14] Inhaled heparin[30] and furosemide[31] (Lasix) have been shown to be effective for

	*Cost of generic (brand)**
	90 mcg per actuation, 17-g inhaler: $29 to $58 (NA)†
	Box of 24 1.25 mg per 3 mL vials: NA ($123) 0.63 mg per 3 mL vials: NA ($136) 0.31 mg per 3 mL vials: NA ($121)
	200 mcg per actuation, 14-g inhaler: NA ($146)
	Aerosol: 60 12-mcg capsules: NA ($176) Inhaler 80/4.5 mcg per actuation aerosol, 10.2-g inhaler: NA ($196) 160/4.5 mcg per actuation aerosol, 10.2-g inhaler: NA ($230)
	Serevent Diskus (60 doses) 50 mcg per dose powder inhaler: NA ($178) Advair Diskus (60 doses) 100/50 mcg per dose aerosol: NA ($186) 250/50 mcg per dose aerosol: NA ($216) 500/50 mcg per dose aerosol: NA ($286) Advair HFA 45/21 mcg per actuation aerosol, 12-g inhaler: NA ($198) 115/21 mcg per actuation aerosol, 12-g inhaler: NA ($231) 230/21 mcg per actuation aerosol, 12-g inhaler: NA ($296)
	120 vials: 20 mg per 2 mL: $190 (NA)

continued

Table 3. Medications for the Treatment of Exercise-Induced Bronchoconstriction *(continued)*

Medication	*Dosage*	*Onset of action*	*Duration*	*Comments*
Inhaled corticosteroids				
Beclomethasone (QVAR)	40 or 80 mcg per spray; one to four puffs twice per day	One week	Variable	Second-line prevention of chronic asthma
Budesonide (Pulmicort Flexhaler)	90 or 180 mcg per spray; two puffs twice per day	One week	Variable	Second-line prevention of chronic asthma
Ciclesonide (Alvesco)	80 or 160 mcg per spray; one or two puffs twice per day	One week	Variable	Second-line prevention of chronic asthma
Flunisolide	250 mcg per spray; one or two puffs twice per day	One week	Variable	Second-line prevention of chronic asthma
Fluticasone (Flovent Diskus or HFA)	Diskus: 50, 100, or 250 mcg per blister; one or two puffs twice per day HFA: 44, 110, or 220 mcg per spray; two puffs twice per day	One week	Variable	Second-line prevention of chronic asthma
Mometasone (Asmanex)	110 or 220 mcg per spray; one or two puffs, divided, once or twice per day	One week	Variable	Second-line prevention of chronic asthma
Leukotriene receptor antagonists				
Montelukast (Singulair)	Six to 14 years of age: 5 mg per day or two hours before exercise 15 years and older: 10 mg per day or two hours before exercise	Two hours	24 hours	Second-line prevention of chronic asthma and allergic rhinitis
Zafirlukast (Accolate)	Five to 11 years of age: 10 mg twice per day, one hour before or two hours after meal 12 years and older: 20 mg twice per day, one hour before or two hours after meal	Unknown	12 hours	Second-line prevention of chronic asthma
Zileuton, extended-release (Zyflo CR)	Older than 12 years: 1,200 mg twice per day	Two hours	12 hours	Second-line prevention of chronic asthma
Anticholinergics				
Ipratropium (Atrovent HFA)	17 mcg per spray: two to four puffs, 15 to 30 minutes before exercise and as needed	15 minutes	Two to four hours	Third-line prevention of acute asthma

HFA = hydrofluoroalkane; NA = not available.

**—Estimated retail price based on information obtained at http://www.drugstore.com (accessed April 20, 2011). Generic price listed first; brand price listed in parentheses.*

†—Estimated cost to the pharmacist based on average wholesale prices (rounded to the nearest dollar) in Red Book. *Montvale, N.J.: Medical Economics Data; 2010. Cost to the patient will be higher, depending on prescription filling fee.*

Information from references 19 and 20.

*Cost of generic (brand)**
40 mcg per actuation, 8.7-g inhaler: NA ($110)†
80 mcg per actuation, 8.7-g inhaler: NA ($132)†
90 mcg per actuation aerosol inhaler: NA ($122)
180 mcg per actuation aerosol inhaler: NA ($160)
80 mcg per actuation aerosol, 6.1-g inhaler: NA ($166)
160 mcg per actuation aerosol, 6.1-g inhaler: NA ($167)
250 mcg per actuation aerosol, 7-g inhaler: NA ($98)
Diskus (60 doses)
50 mcg per blister aerosol inhaler: NA ($115)
100 mcg per blister aerosol inhaler: NA ($116)
250 mcg per blister aerosol inhaler: NA ($155)
HFA
44 mcg per actuation aerosol, 10.6-g inhaler: NA ($120)
110 mcg per actuation aerosol, 12-g inhaler: NA ($153)
220 mcg per actuation aerosol, 12-g inhaler: NA ($247)
60 metered doses
220 mcg per inhalation aerosol, 0.24-g inhaler: NA ($168)
30 5-mg tablets: NA ($157)
30 10-mg tablets: NA ($152)
60 10-mg tablets: NA ($90)
60 20-mg tablets: NA ($90)
120 600-mg tablets: NA ($610)
17 mcg per actuation aerosol, 12.9-g inhaler: NA ($172)

Table 4. NCAA and USOC Restricted Medications

Medication class	*NCAA*	*USOC*
Anticholinergics	Not prohibited	Not prohibited
Inhaled $beta_2$ agonists	Permitted only by prescription	Salmeterol (Serevent) and albuterol: athletes must declare use All other inhaled $beta_2$ agonists: therapeutic use exemption is needed
Inhaled corticosteroids	Not prohibited	Declaration of use required in competition
Leukotriene receptor antagonists	Not prohibited	Not prohibited
Mast cell stabilizers	Not prohibited	Not prohibited

NCAA = National Collegiate Athletic Association; USOC = United States Olympic Committee.

Information from references 32 and 33.

treating EIB, but only small sample sizes have been used in studies.

A Practical Approach to the Patient

Chronic, persistent asthma should be treated according to the National Asthma Education and Prevention Program guidelines.[2] In athletes with confirmed EIB, a reasonable approach is to start with a short-acting $beta_2$ agonist before exercise *(Figure 1)*. If regular dosing of a short-acting $beta_2$ agonist is needed, or if EIB is not controlled with short-acting $beta_2$ agonists, a second-line agent (e.g., leukotriene receptor antagonist, mast cell stabilizer, inhaled corticosteroid with or without a long-acting $beta_2$ agonist) can be added. Inhaled corticosteroids and leukotriene receptor antagonists are the preferred agents in persons with underlying asthma. Leukotriene receptor antagonists are preferred in persons with allergic rhinitis. When prescribing medications to high-level athletes (e.g., those who participate in the National Collegiate Athletic Association or the Olympics), physicians should be aware of which medicines require a waiver *(Table 4[32,33])*. Patients should be reassessed periodically; if a satisfactory response is not achieved, the diagnosis of EIB should be reconsidered.

The opinions and assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the U.S. Army Medical Department or the U.S. Army at large.

This sports medicine article was written in collaboration with the American Medical Society for Sports Medicine (http://www.amssm.org).

Data Sources: A search was performed using the Agency for Healthcare Research and Quality, Cochrane Database of Systematic Reviews, the U.S. Preventive Services Task Force, UpToDate, and the National Guideline Clearinghouse. Search date: May 3, 2010. A PubMed search was performed

on May 7 and May 17, 2010. For each source, the following keywords were used: exercise-induced asthma, exercise-induced bronchoconstriction, exercise-induced bronchospasm, exercise-induced, and asthma.

The Authors

MICHAEL A. KRAFCZYK, MD, FAAFP, is the associate program director of the Primary Care Sports Medicine Fellowship Program and a faculty member in the Family Medicine Residency Program at St. Luke's Hospital and Health Network in Bethlehem, Pa.

CHAD A. ASPLUND, MD, FACSM, is a staff family physician and a primary care sports medicine physician at Eisenhower Army Medical Center in Fort Gordon, Ga.

Address correspondence to Michael A. Krafczyk, MD, St. Luke's Hospital, 153 Brodhead Rd., Bethlehem, PA 18017 (e-mail: mkrafczyk@gmail.com). Reprints are not available from the authors.

Author disclosure: No relevant financial affiliations to disclose.

REFERENCES

1. Randolph C. An update on exercise-induced bronchoconstriction with and without asthma. *Curr Allergy Asthma Rep.* 2009;9(6):433-438.
2. Managing asthma long term—special situations. In: National Heart, Lung, and Blood Institute, National Asthma Education and Prevention Program. Expert panel report 3: guidelines for the diagnosis and management of asthma. NIH publication no. 07-4051. Bethesda, Md.: National Heart, Lung, and Blood Institute; 2007:363-372. http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.pdf. Accessed May 3, 2010.
3. Parsons JP, Mastronarde JG. Exercise-induced bronchoconstriction in athletes. *Chest.* 2005;128(6):3966-3974.
4. Wilber RL, Rundell KW, Szmedra L, Jenkinson DM, Im J, Drake SD. Incidence of exercise-induced bronchospasm in Olympic winter sport athletes. *Med Sci Sports Exerc.* 2000;32(4):732-737.
5. Weiler JM, Bonini S, Coifman R, et al.; Ad Hoc Committee of Sports Medicine Committee of American Academy of Allergy, Asthma & Immunology. American Academy of Allergy, Asthma & Immunology Work Group report: exercise-induced asthma. *J Allergy Clin Immunol.* 2007;119(6):1349-1358.
6. Parsons JP, Kaeding C, Phillips G, Jarjoura D, Wadley G, Mastronarde JG. Prevalence of exercise-induced bronchospasm in a cohort of varsity college athletes. *Med Sci Sports Exerc.* 2007;39(9):1487-1492.
7. De Baets F, Bodart E, Dramaix-Wilmet M, et al. Exercise-induced respiratory symptoms are poor predictors of bronchoconstriction. *Pediatr Pulmonol.* 2005;39(4):301-305.
8. Rundell KW, Im J, Mayers LB, Wilber RL, Szmedra L, Schmitz HR. Self-reported symptoms and exercise-induced asthma in the elite athlete. *Med Sci Sports Exerc.* 2001;33(2):208-213.
9. Rundell KW, Slee JB. Exercise and other indirect challenges to demonstrate asthma or exercise-induced bronchoconstriction in athletes. *J Allergy Clin Immunol.* 2008;122(2):238-246.
10. Holzer K, Anderson SD, Douglass J. Exercise in elite summer athletes: Challenges for diagnosis. *J Allergy Clin Immunol.* 2002;110(3):374-380.
11. Weiss P, Rundell KW. Imitators of exercise-induced bronchoconstriction. *Allergy Asthma Clin Immunol.* 2009;5(1):7.
12. Hallstrand TS, Curtis JR, Aitken ML, Sullivan SD. Quality of life in adolescents with mild asthma. *Pediatr Pulmonol.* 2003;36(6):536-543.
13. Becker JM, Rogers J, Rossini G, et al. Asthma deaths during sports: report of a 7-year experience. *J Allergy Clin Immunol.* 2004;113(2):264-267.
14. Dryden DM, Spooner CH, Stickland MK, et al. Exercise-induced bronchoconstriction and asthma. Evidence Reports/Technology Assessments, no. 189. AHRQ publication no. 10-E001. Rockville, Md.: Agency for Healthcare Research and Quality; January 2010.
15. Rundell KW, Wilber RL, Szmedra L, Jenkinson DM, Mayers LB, Im J. Exercise-induced asthma screening of elite athletes: field versus laboratory exercise challenge. *Med Sci Sports Exerc.* 2000;32(2):309-316.
16. Beuther DA, Martin RJ. Efficacy of a heat exchanger mask in cold exercise-induced asthma. *Chest.* 2006;129(5):1188-1193.
17. Mickleborough TD. Salt intake, asthma, and exercise-induced bronchoconstriction: a review. *Phys Sportsmed.* 2010;38(1):118-131.
18. Mickleborough TD, Lindley MR, Ionescu AA, Fly AD. Protective effect of fish oil supplementation on exercise-induced bronchoconstriction in asthma. *Chest.* 2006;129(1):39-49.
19. *Physicians' Desk Reference.* 64th ed. Montvale, N.J.: Physicians' Desk Reference, Inc.; 2010.
20. Sinha T, David AK. Recognition and management of exercise-induced bronchospasm. *Am Fam Physician.* 2003;67(4):769-774.
21. Medications. In: National Heart, Lung, and Blood Institute, National Asthma Education and Prevention Program. Expert panel report 3: guidelines for the diagnosis and management of asthma. NIH publication no. 07-4051. Bethesda, Md.: National Heart, Lung, and Blood Institute; 2007:213-276. http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.pdf. Accessed May 3, 2010.
22. U.S. Food and Drug Administration. FDA announces new safety controls for long-acting beta agonists, medications used to treat asthma. February 18, 2010. http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm200931.htm. Accessed May 3, 2010.
23. Pearlman D, Qaqundah P, Matz J, Yancey SW, Stempel DA, Ortega HG. Fluticasone propionate/salmeterol and exercise-induced asthma in children with persistent asthma. *Pediatr Pulmonol.* 2009;44(5):429-435.
24. Spooner CH, Spooner GR, Rowe BH. Mast-cell stabilising agents to prevent exercise-induced bronchoconstriction. *Cochrane Database Syst Rev.* 2003;(4):CD002307.
25. Koh MS, Tee A, Lasserson TJ, Irving LB. Inhaled corticosteroids compared to placebo for prevention of exercise induced bronchoconstriction. *Cochrane Database Syst Rev.* 2007;(3):CD002739.
26. Coreno A, et al. Comparative effects of long-acting beta$_2$-agonists, leukotriene receptor antagonists, and a 5-lipoxygenase inhibitor on exercise-induced asthma. *J Allergy Clin Immunol.* 2000;106(3):500-506.
27. Philip G, Pearlman DS, Villarán C, et al. Single-dose montelukast or salmeterol as protection against exercise-induced bronchoconstriction. *Chest.* 2007;132(3):875-883.
28. Raissy HH, Harkins M, Kelly F, Kelly HW. Pretreatment with albuterol versus montelukast for exercise-induced bronchospasm in children. *Pharmacotherapy.* 2008;28(3):287-294.
29. Edelman JM, Turpin JA, Bronsky EA, et al. Oral montelukast compared with inhaled salmeterol to prevent exercise-induced bronchoconstriction. A randomized, double-blind trial. Exercise Study Group. *Ann Intern Med.* 2000;132(2):97-104.
30. Ahmed T, Gonzalez BJ, Danta I. Prevention of exercise-induced bronchoconstriction by inhaled low-molecular-weight heparin. *Am J Respir Crit Care Med.* 1999;160(2):576-581.
31. Melo RE, Solé D, Naspitz CK. Comparative efficacy of inhaled furosemide and disodium cromoglycate in the treatment of exercise-induced asthma in children. *J Allergy Clin Immunol.* 1997;99(2):204-209.
32. National Collegiate Athletic Association. NCAA banned drug list. http://www.ncaa.org/wps/wcm/connect/public/NCAA/Student-Athlete+Experience/NCAA+banned+drugs+list. Accessed May 3, 2010.
33. World Anti-Doping Agency. The World Anti-Doping Code: The 2010 Prohibited List: International Standard. http://www.wada-ama.org/Documents/World_Anti-Doping_Program/WADP-Prohibited-list/WADA_Prohibited_List_2010_EN.pdf. Accessed May 3, 2010.