# Improving Screening and Diagnosis of Exercise-Induced Bronchoconstriction: A Call to Action

John M. Weiler, MD, MBA<sup>a</sup>, Teal S. Hallstrand, MD, MPH<sup>b</sup>, Jonathan P. Parsons, MD, MSc<sup>c</sup>, Christopher Randolph, MD<sup>d</sup>, William S. Silvers, MD<sup>a</sup>, William W. Storms, MD<sup>f</sup>, and Amy Bronstone, PhD<sup>g</sup> Iowa City, Iowa; Seattle, Wash; Columbus, Ohio; New Haven, Conn; Englewood and Colorado Springs, Colo; and Moss Beach, Calif

This article summarizes the findings of an expert panel of nationally recognized allergists and pulmonologists who met to discuss how to improve detection and diagnosis of exerciseinduced bronchoconstriction (EIB), a transient airway narrowing that occurs during and most often after exercise in people with and without underlying asthma. EIB is both commonly underdiagnosed and overdiagnosed. EIB underdiagnosis may result in habitual avoidance of sports and physical activity, chronic deconditioning, weight gain, poor asthma control, low self-esteem, and reduced quality of life. Routine use of a reliable and valid self-administered EIB screening questionnaire by professionals best positioned to screen large numbers of people could substantially improve the

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detection of EIB. The authors conducted a systematic review of the literature that evaluated the accuracy of EIB screening questionnaires that might be adopted for widespread EIB screening in the general population. Results of this review indicated that no existing EIB screening questionnaire had adequate sensitivity and specificity for this purpose. The authors present a call to action to develop a new EIB screening questionnaire, and discuss the rigorous qualitative and quantitative research necessary to develop and validate such an instrument, including key methodological pitfalls that must be avoided. © 2014 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2014;2:275-80)

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Exercise-induced bronchoconstriction (EIB) is a common clinical problem in persons with asthma and also occurs in some people who lack other features of asthma. Despite evidence-based clinical practice guidelines for the diagnosis and management of EIB,<sup>1,2</sup> physicians frequently underdiagnose and overdiagnose EIB, which suggests that many physicians are not adhering to these recommendations. Physicians' poor performance in diagnosing EIB may be due to a number of issues, including a lack of awareness of the prevalence and burden of this condition, the absence of an effective screening questionnaire to help detect EIB, and inadequate knowledge about how to further evaluate and treat patients with suspected EIB.

In November 2012, an expert panel composed of 6 nationally recognized allergists and pulmonologists met to discuss unmet needs regarding the detection of EIB in the general population. (Teva Pharmaceuticals sponsored the meeting but had no role in the development of this article.) This article summarizes the panel's findings, and constitutes a call to action to improve widespread screening for EIB and appropriate follow-up for individuals with positive screening results.

## PREVALENCE AND BURDEN OF EIB

EIB is an acute bronchoconstriction triggered by exercise, which may occur in the presence of established asthma or in the absence of other features of chronic asthma.<sup>1,2</sup> Common symptoms of EIB include shortness of breath, wheezing, cough, and chest tightness during or immediately after exercise.<sup>1,2</sup> More subtle symptoms that may be suggestive of EIB include fatigue, feeling out of shape, feeling unable to keep up with peers, symptoms that occur repeatedly in specific environments (such as pools, ice rinks, or freshly mowed fields), performances that fall

<sup>&</sup>lt;sup>a</sup>Department of Internal Medicine, University of Iowa, Iowa City, Iowa

<sup>&</sup>lt;sup>b</sup>Division of Pulmonary and Critical Care Medicine, Department of Medicine, University of Washington, Seattle, Wash

<sup>&</sup>lt;sup>c</sup>Division of Pulmonary, Critical Care, Allergy and Sleep Medicine, The Ohio State University Medical Center, Columbus, Ohio

<sup>&</sup>lt;sup>d</sup>Department of Pediatrics, Division of Allergy and Clinical Immunology, Yale University, New Haven, Conn

eAllergy Asthma Colorado, P.C., Englewood, Colo

<sup>&</sup>lt;sup>f</sup>The William Storms Allergy Clinic, Colorado Springs, Colo

<sup>&</sup>lt;sup>g</sup>BioMedEcon, LLC, Moss Beach, Calif

Teva Pharmaceuticals sponsored the expert panel meeting, which led to this article, but had no role in the development of this article.

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Corresponding author: John M. Weiler, MD, MBA, Department of Internal Medicine, University of Iowa, PO Box 3090, Iowa City, IA 52244. E-mail: jweiler@ compleware.com.

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Abbreviations used
AHR-Airway hyperresponsiveness
ATS-American Thoracic Society
EIB-Exercise-induced bronchoconstriction
EVH-Eucapnic voluntary hyperventilation
FEF <sub>25-75%</sub> -Forced expiratory flow between 25% and 75% of vital
capacity
$FEV_1$ -Forced expiratory volume in 1 second
FRAST-Free-running athletic screening test
NPV-Negative predictive value
PEFR-Peak expiratory flow rate
PPV-Positive predictive value
PRO- Patient reported outcome
SABA-Short-acting $\beta_2$ agonist

consistently below expectations given an athlete's conditioning level, and abdominal discomfort.<sup>3,4</sup> Exercise is one of the most common triggers of bronchoconstriction in people with asthma and may be the first indication of asthma or an indicator of poorly controlled asthma.<sup>5</sup> Approximately 40% to 60% of individuals with asthma have EIB.<sup>6-11</sup> Estimates of the prevalence of EIB in the general healthy population (individuals without underlying asthma) range from approximately 5% to 20%.<sup>1</sup> Elite athletes, particularly those who participate in endurance winter sports, are at greater risk for experiencing EIB without a history of asthma than the general population.<sup>1,12</sup>

EIB reduces participation in sports and physical activities, contributes to poor physical conditioning and obesity, and negatively impacts physical and emotional functioning. Children and adolescents with EIB have significantly lower overall quality of life scores than those without EIB,<sup>13,14</sup> irrespective of previous asthma diagnosis.14 The EIB Landmark Survey found that asthma limited participation in sports, recreational, and outdoor activities in 25% to 30% of children and 50% of adults.<sup>5</sup> Almost one-third of children (32%) and one-half of adults (46%) with asthma reported that they avoid activities because of their exercise-related symptoms.<sup>5,15</sup> Avoidance of exercise and physical activity due to a fear of experiencing EIB symptoms may be the best explanation for the finding of poorer cardiovascular fitness in people with asthma compared with their peers.<sup>16</sup> Low levels of physical activity may contribute to the link between asthma and obesity<sup>17-19</sup> and can adversely affect self-esteem and mental health in both healthy children and those with asthma.<sup>19,20</sup> In contrast, results of studies showed that exercise may increase fitness and exercise capacity in people with EIB, reduce severity of EIB, improve asthma control, and enhance quality of life.<sup>21-2</sup>

## THE CHALLENGES OF DIAGNOSING EIB Underdiagnosis

Research findings indicate that EIB is frequently underdiagnosed, possibly due to insufficient awareness of EIB and its burden and the lack of a questionnaire to screen effectively for this condition. Many individuals who report symptoms suggestive of EIB or who objectively test positive for EIB have never been formally diagnosed with EIB. In a general population survey, 26% of respondents reported experiencing respiratory symptoms with exercise, but only 5% had been diagnosed with EIB by a physician.<sup>5</sup> Among 39% of collegiate athletes who objectively tested positive for EIB, only 14% had received a physician diagnosis of asthma or EIB.<sup>24</sup> Almost 80% of elite athletes who had a positive result to bronchoprovocation testing had not been diagnosed with EIB.<sup>25</sup> Together, these findings suggest that EIB is underdetected in a variety of populations.

#### **Overdiagnosis**

Overdiagnosis of EIB also may occur when physicians base their diagnosis on history and presentation alone, and do not confirm with an objective diagnostic test.<sup>1,2</sup> Among 142 children who presented with dyspnea that had been previously attributed to asthma, the symptom was reproduced in 117 during exercise testing, but only 11 (8%) met criteria for EIB.<sup>26</sup> Most children who did not meet criteria for EIB demonstrated normal physiologic limitation, with poor conditioning identified as the cause of dyspnea in 35% of this group. A survey of athletic trainers affiliated with National Collegiate Athletic Association programs revealed that two-thirds diagnosed EIB on a history of symptoms alone and that only 17% used objective testing.<sup>27</sup> In another study, only half of professional soccer players who had a physician diagnosis of EIB had objective evidence of EIB.<sup>28</sup> Among 148 athletes referred to an asthma clinic for evaluation, 24% had previously been diagnosed with EIB, but only 8% had prior objective testing for EIB.<sup>29</sup> When this sample was objectively tested for EIB, only 50% of the patients previously diagnosed with EIB had their diagnosis confirmed. Among 52 children referred to a respiratory specialist clinic for poorly controlled EIB, only 15% met diagnostic criteria for EIB upon objective testing.<sup>30</sup> In contrast, the remaining children were diagnosed with vocal cord dysfunction (27%), poor physical fitness (23%), habit cough (14%), and no abnormality (21%).

Prescribing a trial of short-acting  $\beta 2$  agonists (SABA) for patients who report symptoms of EIB without objectively establishing the diagnosis appears to be a common practice. In a survey of US family practitioners and pulmonologists, approximately 80% of family practitioners and 50% of pulmonologists reported that they would prescribe SABAs without ordering any diagnostic testing for a patient who presents with exercise-related respiratory symptoms without a history of asthma.<sup>31</sup> Although it may be convenient to prescribe SABAs based on symptoms alone, this practice may result in suboptimal care for some patients. Patients who do not actually have EIB and who fail to respond to treatment with SABA or other asthma medication may be subjected to the burden of inappropriate therapy, persistent impairment, and a delay in appropriate diagnosis and treatment.<sup>12</sup>

#### **Diagnostic testing**

The most recent American Thoracic Society (ATS) EIB clinical practice guidelines recommend laboratory exercise testing, a standardized exercise challenge performed on treadmill (preferably) or bicycle ergometer, to diagnosis EIB (see Figure 1 for the complete algorithm for evaluating patients with suspected EIB).<sup>2</sup> In a laboratory exercise challenge, exercise intensity is ramped up over 2 to 4 minutes until the target heart rate (80%-90% of the predicted maximum) is reached; the test ends when the patient has exercised at the target ventilation or heart rate for 4 to 6 minutes (for a total exercise time of approximately 10 minutes).<sup>2</sup> During challenge, relative humidity is controlled so that the subject inspires dry air.<sup>32</sup> Lung function tests are performed before exercise and serially after exercise for up to 30 minutes to determine if EIB is present and to quantify the severity of the disorder.<sup>2</sup>

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