Exercise-induced bronchoconstriction update—2016



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The first practice parameter on exercise-induced

bronchoconstriction (EIB) was published in 2010. This updated practice parameter was prepared 5 years later. In the ensuing years, there has been increased understanding of the pathogenesis of EIB and improved diagnosis of this disorder by using objective testing. At the time of this publication, observations included the following: dry powder mannitol for inhalation as a bronchial provocation test is FDA approved however not currently available in the United States; if baseline pulmonary function test results are normal to near normal (before and after bronchodilator) in a person with suspected EIB, then further testing should be performed by using standardized exercise challenge or eucapnic voluntary hyperpnea (EVH); and the efficacy of nonpharmaceutical interventions (omega-3 fatty acids) has been challenged. The workgroup preparing this practice parameter updated contemporary practice guidelines based on a current systematic literature review. The group obtained supplementary literature and consensus expert opinions when the published literature was insufficient. A search of the medical literature on

PubMed was conducted, and search terms included pathogenesis, diagnosis, differential diagnosis, and therapy (both pharmaceutical and nonpharmaceutical) of exercise-induced bronchoconstriction or exercise-induced asthma (which is no longer a preferred term); asthma; and exercise and asthma. References assessed as relevant to the topic were evaluated to search for additional relevant references. Published clinical studies were appraised by category of evidence and used to document the strength of the recommendation. The parameter was then evaluated by Joint Task Force reviewers and then by reviewers assigned by the parent organizations, as well as the general membership. Based on this process, the parameter can be characterized as an evidence- and consensus-based document. (J Allergy Clin Immunol 2016;138:1292-5.)

Key words: Exercise-induced bronchoconstriction, exerciseinduced bronchospasm, exercise-induced asthma, exercise-induced bronchoconstriction pathogenesis, diagnosis, differential diagnosis and therapy, nonpharmacologic, pharmacologic

Board; has consultant arrangements with Adamis Pharmaceutical, Canadian Transportation Agency, Nutricia, Nestle/Gerber, and Aimmune; is an Associate Editor for the Annals of Allergy, Asthma, and Immunology; and has received payment for lectures from the American College of Allergy, Asthma, and Immunology, Reach MD, Thermo Fisher Scientific, California Society for Allergy and Immunology, the Allergy and Asthma Network, New England Society for Allergy, UCLA/Harbor Heiner Lectureship, Medscape, Western Michigan School of Medicine, Canadian Society of Allergy and Clinical Immunology, and the Pennsylvania Society for Allergy and Immunology. D. Khan has consultant arrangements with Aimmune; has received grants from the NIH, has received payment for lectures from Genentech, and has received royalties from UpToDate. D. Lang has consultant arrangements with Genentech/Novartis, Adamis, Merck, Meda, GlaxoSmithKline, and AstraZeneca; has received grants from Genentech/Novartis and Merck; and has received payment for lectures from Genentech/Novartis. J. Oppenheimer has consultant arrangements with GlaxoSmithKline, Mylan, and Meda: has received fees for participation in review activities from Ouintiles and PRA: has received money from UpToDate and Annals of Allergy; is a member of the American Board of Allergy and Immunology; and is employed by the Pulmonary & Allergy Associates Atlantic Health System. J. M. Portnoy has received payment for lectures from Mylan and Thermo Fisher. D. Schuller declares that she has no relevant conflicts of interest. S. Tilles received grant support from Merck, Genentech, Novartis, Teva, Mylan, NIAID, Circassia, Astellas, and AstraZeneca. D. Wallace has consultant arrangements with Neohealth, Sanofi, Allergan, and Kaleo and has received payment for lectures from Mylan and MEDA. The rest of the authors declare that they have no relevant conflicts of interest. Received for publication February 24, 2016; revised May 13, 2016; accepted for publi-

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Disclosure of potential conflict of interest: J. Weiler is employed by CompleWare and has stock/stock options with CompleWare and ICRC. J. D. Brannan has received rovalties from Pharmaxis. C. C. Randolph is a member of the American College of Asthma, Allergy & Immunology Board of Regents; has consultant arrangements with Genentech; has received payment for lectures from TEVA, GlaxoSmithKline, AstraZeneca, and Merck; has received travel support from TEVA; and owns an eucapnic voluntary hyperpnea machine purchased from Richard Rosenthal. T. S. Hallstrand has received grants from the National Institutes of Health (NIH), has consultant arrangements with Genentech, has received payment for lectures from Teva, GlaxoSmithKline, AstraZeneca, and Merck; has received travel support from Teva; and owns a eucapnic voluntary hyperphoea testing machine purchased from Richard Rosenthal. W. Silvers has received payment for lectures from Teva. W. Storms has consultant arrangements with Amgen, AstraZeneca, Bausch & Lomb, Merck, Sunovion, and TEVA; has received grants from Amgen, Genentech/Novartis, GlaxoSmithKline, Circassia, Meda, Mylan, Sanofi, Sunovion, and TEVA; and has received payment for lectures from AstraZeneca, Genentech/Novartis, Bausch & Lomb, Merck, Sunovion, and TEVA, D. I. Bernstein is a member of the American Board of Allergy and Immunology; has consultant arrangements with TEVA, Circassia, and Merck; has received grants from Merck, TEVA, Johnson & Johnson, Novartis, Pearl Therapeutics, Genentech, Pfizer, GlaxoSmithKline, Allergy Therapeutics, and Amgen; has received payment for lectures from AstraZeneca and Merck; and has received payment for development of educational presentations from AstraZeneca. J. Blessing-Moore has received travel support from the American Academy of Allergy, Asthma & Immunology and has received payment for lectures from AstraZeneca, Merck, Genentech/Novartis, Alcon, and Mylan. M. Greenhawt has received a grant from the Agency for Healthcare Research Quality (1K08HS024599-01, Career Development Award); has received travel support from the National Institute of Allergy and Infectious Diseases and the Joint Taskforce on Allergy Practice Parameters; is on the scientific advisory council for the National Peanut

These parameters were developed by the Joint Task Force on Practice Parameters (JTFPP), representing the American Academy of Allergy, Asthma & Immunology (AAAAI); the American College of Allergy, Asthma & Immunology (ACAAI); and the Joint Council of Allergy, Asthma & Immunology.

The AAAAI and ACAAI have jointly accepted responsibility for establishing "Exercise-induced bronchoconstriction update—2016." This is a complete and comprehensive document at the current time. The medical environment is a changing environment, and not all recommendations will be appropriate for all patients. Because this document incorporated the efforts of many participants, no single individual, including those who served on the JTFPP, is authorized to provide an official AAAAI or ACAAI interpretation of these practice parameters. Any request for information about or an interpretation of these practice parameters by the AAAAI or ACAAI should be directed to the Executive Offices of the AAAAI or the ACAAI.

The JTFPP understands that the cost of diagnostic tests and therapeutic agents is an important concern that can appropriately influence the workup and treatment chosen for a given patient. The JTFPP recognizes that the emphasis of our primary recommendations regarding a medication can vary, for example, depending on third-party payer issues and product patent expiration dates. However, because a given test or agent's cost is so widely variable and there is a paucity of pharmacoeconomic data, the JTFPP generally does not consider cost when formulating practice parameter recommendations. In extraordinary circumstances, when the cost benefit of an intervention is prohibitive, as supported by pharmacoeconomic data, commentary can be provided. These parameters are not designed for use by pharmaceutical companies in drug promotion.

The Joint Task Force (JTF) is committed to ensuring that the practice parameters are based on the best scientific evidence that is free of commercial bias. To this end, the parameter development process includes multiple layers of rigorous review. These layers include the workgroup convened to draft the parameter, the Task Force Reviewers, and peer review by members of each sponsoring society. Although the task force has the final responsibility for the content of the documents submitted for publication, each reviewer comment will be discussed, and reviewers will receive written responses to comments when appropriate.

To preserve the greatest transparency regarding potential conflicts of interest, all members of the JTF and the Practice Parameters Work Groups will complete a standard potential conflict of interest disclosure form, which will be available for external review by the sponsoring organization and any other interested person. In addition, before confirming the selection of a workgroup chairperson, the JTF will discuss and resolve all relevant potential conflicts of interest associated with this selection. Finally, all members of parameter workgroups will be provided a written statement regarding the importance of ensuring that the parameter development process is free of commercial bias.

All published practice parameters are available at http://www. allergyparameters.org

EIB EXECUTIVE SUMMARY

The first practice parameter on exercise-induced bronchoconstriction (EIB) was published in 2010. This update is required by the National Clearinghouse and JTF consistent with the requirement of an update every 5 years. In the ensuing years, since the first publication of the EIB practice parameter, there has been increased understanding of the pathogenesis of EIB and improved diagnosis of this disorder by using objective pulmonary function tests. At the time of this publication, dry powder mannitol for inhalation is no longer available in the United States but is available in many other countries.

If baseline pulmonary function test results are normal to near normal (before and after bronchodilator) in a person with suspected EIB, then further testing should be performed by using a standardized exercise challenge or eucapnic voluntary hyperpnea (EVH).

Since 2010, the efficacy of nonpharmaceutical interventions, such as omega-3 fatty acids, has been challenged and needs validation.

This updated 2016 practice parameter was commissioned by the JTF to capture recent advances in the field of EIB, as elucidated in the most recent literature.

The chair of this workgroup, Dr John Weiler, convened workgroup members who are recognized as experts in the field of EIB. The members have been reviewed for conflicts of interest by the JTF, and conflicts of interest have been listed by the JTF on the JTF Web site at http://www.allergyparameters.org.

During the development of this practice parameter, at the request of the JTF, the workgroup also recruited a patient advocate to provide a dimension from the patient's perspective.

The workgroup was asked to update contemporary practice guidelines based on a current systematic literature review. The workgroup obtained supplementary literature, and consensus expert opinions were used when published literature was insufficient.

A search of the medical literature on PubMed was conducted, and all reference categories were included. Search terms included pathogenesis, diagnosis, differential diagnosis, and therapy (both pharmaceutical and nonpharmaceutical) of exercise-induced bronchoconstriction, or exercise-induced asthma (which is no longer a preferred term); asthma; and exercise and asthma.

References assessed as relevant to the topic were evaluated to search for other relevant references. Published clinical studies were appraised by category of evidence and used to document the strength of the recommendation (see category of evidence and strength of recommendation ratings). The parameter was then evaluated by JTF reviewers and then by reviewers assigned by the AAAAI and ACAAI, as well as the general memberships of the AAAAI and ACAAI. Based on this process, the parameter can be characterized as an evidence- and consensus-based document.

The pathophysiology of EIB has been elucidated in the last 2 decades. Strenuous exercise is known to create a hyperosmolar environment by introducing dry air in the airway with compensatory water loss, leading to transient osmotic change on the airway surface. The hyperosmolar environment leads to mast cell degranulation with release of mediators, predominately leukotrienes, but also including histamine, tryptase, and prostaglandins. In addition, eosinophils can also be activated, producing further mediators, including leukotrienes. In turn, this might lead to bronchoconstriction and inflammation of the airway, as well as stimulation of sensory nerves, with neurokinin release stimulating release of the gel-forming mucin MUC5AC. The water content of the inspired air, the level of ventilation achieved and maintained during exercise, or both are the major determinants of EIB. The major trigger for bronchoconstriction in

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