

21 examination, and testing. Tests reviewed included spirometry, body plethysmography,
22 bronchodilator response, fraction of exhaled nitric oxide, allergy tests, chest x-ray, and bronchial
23 challenge tests; no cardiopulmonary stress testing was performed. The authors determined from
24 examination of the previously obtained data that etiologies of exercise-induced symptoms were
25 different from the referring physician's diagnoses. More than half of the patients were given a
26 final diagnosis of exercise induced asthma, although only a third of the total patient population
27 were tested for exercise induced bronchospasm (EIB). About a third of the patients were
28 diagnosed with extrathoracic and intrathoracic dysfunctional breathing with or without asthma.
29 However, the authors did not provide any definitions for these disorders or the criteria used for
30 reaching those diagnoses.

31 The study by Ersson and colleagues evaluated the prevalence of EIB and laryngeal
32 obstruction in healthy adolescents.² They described 98 attendees of a sports high school who
33 completed a questionnaire about dyspnea with exercise. A history of dyspnea with exercise was
34 reported in 41 while 57 indicated no such history. All underwent a test for EIB defined as a
35 decrease of 10% in the one second forced expiratory volume (FEV₁). Based on the criteria used,
36 EIB was identified in 8 of 41 with dyspnea and in 16 of 57 without dyspnea. Continuous
37 laryngoscopy during exercise was also performed on 75 subjects. Thirty-four had a history of
38 dyspnea on exertion of whom 5 were observed to have exercise-induced laryngeal obstruction
39 (ELO). Three of the 41 without dyspnea were noted to have ELO. The conclusion from this
40 study was that EIB and ELO were poorly predicted by symptoms.

41 Unfortunately, the methodologies used in these reports result in presumptuous
42 conclusions about etiologies of EID because the specific pathophysiology associated with
43 exercise-induced dyspnea (EID) was not examined by either of these recent publications.^{1,2} The

44 actual etiology of EID requires identifying the physiology associated with the patient's exertional
45 dyspnea.^{3,4,5} That requires reproducing the patient's dyspnea during cardiopulmonary monitoring.
46 This includes heart rate, ventilation pattern, oxygen utilization, carbon dioxide production,
47 inspiratory and expiratory airflow, visualization of airway if needed because of decreased
48 inspiratory airflow, and blood gas measurements at the time symptoms are reproduced.⁵ When
49 that was done in 117 otherwise healthy adolescents, diagnoses were not limited to bronchospasm
50 and laryngeal obstruction (Table 1). Of importance is that 74 of 117 of the patients had dyspnea
51 on exertion associated with normal physiological limitation. This typically occurs when
52 anaerobic metabolism, that occurs normally at high levels of exercise, results in lactic acid
53 accumulation. That induces an attempt to compensate for the resulting metabolic acidosis with
54 respiratory alkalosis by increasing respiration. This increased respiratory drive when ventilation
55 physically cannot be further increased is perceived by some subjects as dyspnea.

56 Prevalence of EIB in the normal population and in athletes has been described
57 previously.⁶ EIB was also observed in children with rhinitis but no asthma diagnosis and in the
58 absence of associated dyspnea.⁷ EIB was also reported in children with decreased levels of
59 physical activity and no clinical evidence of asthma.⁸ Burnett and colleagues reported an EIB
60 prevalence of 43% in college athletes, most having no respiratory symptoms.⁹ Thus, EIB occurs
61 in the absence of both dyspnea and asthma. Is EIB of clinical importance in the absence of
62 dyspnea?¹⁰ Does a 10% decrease in FEV₁ from exercise in the absence of associated dyspnea
63 support the diagnosis of exercise-induced asthma? A more stringent criteria using a cutoff value
64 of 15% found dyspnea associated with EIB to be positive in only 11 of 117 children referred
65 because of exercise induced dyspnea (Table 1).³

66 The following conclusions emanate from the above discussion of the two recent
67 publications in Pediatric Pulmonology,^{1,2} our previous work on the subject and review of the
68 literature.

- 69 • A modest degree of EIB does not confirm the diagnose of asthma and has ~~no~~ little
70 clinical relevance if not concurrently associated with the patient's symptoms of
71 dyspnea,
- 72 • Identification of ELO not concurrently associated with the patient's symptoms of
73 dyspnea has ~~no~~ little clinical relevance to an individual with EID,
- 74 • Since ELO can occur from different anatomical abnormalities with different treatment
75 implications, the specific abnormality should be identified by direct visualization.
- 76 • Results that test only for specific causes of EID require that the patient's dyspnea be
77 concurrent with results of that test,
- 78 • The various etiologies of EID in Table 1 can be best identified by reproducing the
79 patient's symptoms of dyspnea during cardiopulmonary stress testing.

80 **Table 1.** Diagnoses among 117 children referred to the University of Iowa Pediatric Allergy and
81 Pulmonary Division because of exercise-induced dyspnea between 1996 and 2003. Treadmill
82 exercise sufficient to reproduce symptom were performed with continuous cardiopulmonary
83 monitoring.³
84

Disorder identified	Number of patients
Exercise-induced bronchospasm	11
Vocal cord dysfunction	13
Restrictive physiology	15
Exercise-induced laryngomalacia	2
Exercise-induced hyperventilation	1
Exercise-induced supraventricular tachycardia	1
Normal physiologic limitation	74

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2 ¹ Pedersen ESL, Ardura-Garcia C, de Jong CCM, et al. Diagnosis in children with exercise-induced
3 respiratory symptoms: A multi-center study. *Pediatr Pulmonol*. 2021 Jan;56(1):217-225.
4

5 ² Ersson K, Mallmin E, Malinowski A, et al. Prevalence of exercise-induced bronchoconstriction and
6 laryngeal obstruction in adolescent athletes. *Pediatr Pulmonol* 2020 Dec;55(12):3509-3516.

7 ³ Abu-Hasan M, Tannous B, Weinberger M. Exercise-induced dyspnea in children and adolescents: if
8 not asthma then what? *Ann Allergy Asthma Immunol* 2005;94:366-371.
9

10 ⁴ Weinberger M, Abu-Hasan M. Perceptions and pathophysiology of dyspnea and exercise intolerance.
11 *Ped Clinics N America* 2009;56:33-48.
12

13 ⁵ Bhatia R, Abu-Hasan M, Weinberger M. Exercise-induced dyspnea in children and adolescents:
14 Differential diagnosis. *Pediatric Annals*, 2019;48(3)e121-127.
15

16 ⁶ Randolph C. An update on exercise-induced bronchoconstriction with and without asthma. *Curr*
17 *Allergy Asthma Rep* 2009;9(6):433-438.
18

19 ⁷ Canonica W, Anderson SD, Bjermer L, et al. Exercise-induced asthma, respiratory and allergic
20 disorders in elite athletes: epidemiology, mechanisms and diagnosis: part I of the report from the Joint
21 Task Force of the European Respiratory Society (ERS) and the European Academy of Allergy and
22 Clinical Immunology (EAACI) in cooperation with GA2LEN. *Allergy* 2008;63(4):387-403.
23

24 ⁸ Anthracopoulos MB, Fouzas S, Papadopoulos M, Antonogeorgos G, et al. Physical activity and
25 exercise-induced bronchoconstriction in Greek schoolchildren. *Pediatr Pulmonol* 2012;47(11):1080-
26 1087.
27

28 ⁹ Burnett DM, Burns S, Merritt S, Wick J, Sharpe MR. Prevalence of exercise-induced
29 bronchoconstriction measured by standardized testing in healthy college athletes. *Respir Care*
30 2016;61(5):571-576.
31

32 ¹⁰ Weinberger M, Abu-Hasan M. Is exercise-induced bronchoconstriction exercise-induced asthma?
33 *Respiratory Care*. Invited editorial 2016;61:713.
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