Exercise-Induced Bronchoconstriction

Background, Prevalence, and Sport Considerations

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KEYWORDS

• Asthma • Bronchoconstriction • Exercise • Athlete • Prevalence • Sport discipline

KEY POINTS

- Exercise-induced bronchoconstriction (EIB) is defined as the transient airway narrowing that occurs as a result of exercise.
- Current guidelines recommend distinguishing EIB with underlying clinical asthma from the occurrence of exercise-induced bronchial obstruction in subjects without other symptoms and signs of asthma.
- EIB has been reported in up to 90% of asthmatic patients, reflecting the level of disease control, but it may develop even in subjects without clinical asthma, particularly in athletes, children, subjects with atopy or rhinitis, and following respiratory infections.
- The intensity, duration, and type of training have been associated with the occurrence of EIB with higher prevalence rates in endurance sports, winter disciplines, and swimming.
- When properly managed, EIB does not restrict exercise performance and does not prevent competition at elite level.

BACKGROUND

Regular physical activity is strongly recommended by all principal health care systems and evidence-based guidelines as one of the most effective means to prevent chronic diseases and maintain good health.[1] Indeed, extensive evidence exists regarding the beneficial effect of training and rehabilitation programs in respiratory diseases, including asthma.[2] It has been shown that physical activity can improve symptoms, quality of life, exercise capacity, and pulmonary function, as well as reduce airway inflammation and responsiveness in asthmatic subjects.[3–5]

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On the other hand, vigorous physical training may trigger airway symptoms by imposing high demands on the respiratory system and by exposing subjects to increased amounts of inhalant allergens, pollutants, irritants, and adverse environmental conditions.[6] Furthermore, intense physical training may induce a transient status of immune downregulation with a shift toward a prevalent T-lymphocyte helper-2 response, clinically associated with an increased prevalence of atopy and viral upper respiratory tract infections, both representing relevant risk factors for the onset and worsening of asthma.[7,8]

The transient airway narrowing that occurs as a result of exercise is defined exercise-induced bronchoconstriction (EIB).[6] Already in the first century AD, Araeteus the Cappadocian described respiratory symptoms induced by physical exercise: "if from running, gymnastics, or any other work, breathing becomes difficult, it is called asthma."[9] However, a scientific objective interest for this phenomenon can be dated back to 1960, when Jones and coworkers[10] focused on the physiologic response to exercise in asthmatic children and named the airway obstruction after an exercise challenge "exercise-induced asthma" (EIA). Subsequent studies defined the different patterns of response to exercise in asthmatic patients, the effect of type, intensity, and duration of challenges, and the influence of antiasthmatic drugs on EIA.[11] In reviewing these findings, Godfrey[12] concluded that "despite of some exceptions, there has been no evidence that EIA occurs in patients other than asthmatics, and although sporadic cases have been reported where exercise appears to have been the only precipitant of asthma in a patient, careful investigation has usually revealed other clinical and physiological manifestations of bronchial asthma." Although some investigators consider EIA a distinct asthma phenotype,[13] it is quite evident that exercise may trigger bronchial obstruction and clinical symptoms in almost all asthmatic patients, independently from the underlying causes and mechanisms of asthma.[14] However, the concept that exercise may induce bronchial obstruction only in asthmatic patients is currently under debate.[15] In fact, despite the physiologic response to exercise, which usually results in slight bronchodilation, EIB may develop even in subjects without clinical asthma.[9] To bring some clarity to this still controversial issue, a Practice Parameter, jointly developed by the American Academy/College of Allergy Asthma and Immunology,[16] recommended to abandon the term of EIA, and more recently, an American Thoracic Society Clinical Practice Guideline[6] suggests naming EIB with asthma (EIBa), the occurrence of bronchial obstruction after exercise in asthmatic patients, and EIB without asthma (EIBwa), the occurrence of EIB in subjects without other symptoms and signs of clinical asthma.

EIB typically develops within 15 minutes following at least 5 to 8 minutes of high-intensity aerobic training (>85% of maximal voluntary ventilation), although it can also occur during exercise, and spontaneously resolves within 60 minutes.[17] After an episode of EIB, there is often a refractory period of about 1 to 3 hours during which, if exercise is repeated, the bronchoconstriction is less accentuated.[12] The increase in airway osmolarity due to the respiratory water loss and the vasodilation associated with airways rewarming has been reported to be the major determinants of EIB (osmotic and thermal theories).[18,19] Furthermore, a direct damage of the bronchial epithelium caused by viral infections, occupational agents and exercise, as well as an autonomic dysregulation may represent alternative causal mechanisms.[11] Most common symptoms include cough, dyspnea, breathlessness, wheezing, and chest tightness.[6] A careful history taking and physical examination is always recommended.[20] The use of specific questionnaires for screening allergic and respiratory diseases in athletes and exercisers represents a useful and easy-to-use additional diagnostic tool.[21] However, research performed over the years has consistently

shown a poor relationship between the presence of "asthmalike" symptoms and objective evidence of EIB.[22] Furthermore, pulmonary function tests at baseline seem to be poorly predictive of EIB in athletes, often being within the normal ranges even in the presence of disease.[23] Thus, in order to establish a secure diagnosis of EIB, it is critical to perform objective testing to confirm dynamic changes in airway function.[6,24] The differential diagnosis of EIB should take into account several entities, such as physiologic exercise limitations, exercise-induced laryngeal dysfunctions, exercise-induced anaphylaxis, and shortness of breath with exercise due to lung diseases (other than asthma), and metabolic and cardiac diseases.[6,25,26] Management of EIB includes multiple effective pharmacologic and nonpharmacologic strategies,[6,17,27] but should take into high consideration onset of tolerance,[28] side effects,[29] and, in elite athletes, anti–doping regulations.[30]

PREVALENCE

The prevalence of EIB varies from 5% to 20% in the general population and has been reported to be up to 90% in asthmatic subjects, reflecting the level of disease control, with EIBa occurring more frequently in more severe and uncontrolled asthmatic patients.[14] EIBwa is also particularly frequent in athletes,[31] children,[32,33] subjects with rhinitis,[34] and following respiratory infections.[35]

In particular, several studies called attention to an increased occurrence of asthma and EIB in athletes, with prevalence rates widely ranging from 3.7% to 54.8% (**Table 1**) depending on the study population and the criteria used for diagnosis (ie, questionnaires, anti–doping records, baseline spirometry, bronchial provocation challenges). Independently from these potential confounders, studies performed in comparable samples and with similar diagnostic methodologies seem to indicate that the asthma incidence is on the increase: from 9.7% in 1976 to 11.2% in 1984, 16.7% in 1996 and 21.0% in 2000 in the US Olympic delegation.[36–38] More recently, a 12-year study including 4 cross-sectional surveys performed between 2000 and 2012, before Summer and Winter Olympics, showed that the prevalence of asthma in 659 Italian Olympic athletes was 14.7%, with a significant increase from 2000 (11.3%) to 2008 (17.2%).

With regards to a gender effect,[39] a study recently performed in 187 elite athletes (101 swimmers and 86 tennis players) showed a higher prevalence of asthma symptoms in women, although there was no significant difference in the prevalence of EIB when measured through a mannitol and a sport-specific challenge.[40] Norqvist and colleagues[41] also reported that, compared with men, elite female athletes had a higher prevalence of asthma, respiratory symptoms, use of medications, and health care services.

It has been also extensively reported that asthma and allergic rhinitis frequently coexist, with symptoms of rhinitis being reported in 80% to 90% of asthma patients, and asthma symptoms reported in 20% to 40% of patients with allergic rhinitis.[34] Prospective studies also suggest that rhinitis frequently precedes the development of asthma[42] and that many patients with rhinitis alone show nonspecific bronchial hyperresponsiveness after exercise or methacholine, this being a risk factor for developing asthma.[43] Furthermore, it has been proven that the severity of allergic rhinitis and asthma is related and that proper management of allergic rhinitis improves asthma control.[34] In addition, exercise can be a trigger for rhinitis, especially in outdoor sports and even greater with cold dry air exposure in winter sports, for example, the "skier's nose."[44] On the basis of all the above, the Alergic Rhinitis and its Impact on Asthma (ARIA) recommendation[34] to screen every subject with rhinitis for asthma should be also extended to athletes.[45]

Table 1
Prevalence of asthma and exercise-induced bronchoconstriction among athletes

Type of Sport	Study Population (n)	Prevalence, %	Methodology for Diagnosis	Reference
Olympic teams	US 1998 Olympic team (170)	23.0	Spirometry, exercise challenge	Wilber, 2000
	US 1998 Olympic team (196)	21.9	Questionnaire	Weiler, 2000
	Australian 2000 Olympic team (214)	21.0	Questionnaire	Katelaris et al,[38] 2000
	US 1996 Olympic team (699)	16.7	Questionnaire	Weiler et al,[37] 1998
	Italian Olympic athletes (659)	14.7	Questionnaires, lung function tests	Bonini et al,[11] 2015
	Polish 2008 Olympic team (222)	11.3	Questionnaire, spirometry, methacholine challenge	Kurowski, 2016
	US 1984 Olympic team (597)	11.2	Questionnaire, exercise challenge	Voy,[36] 1984
	Italian 2000 pre-Olympic team (265)	10.9	Questionnaire, spirometry	Lapucci, 2003
	Australian 1976 Olympic team (185)	9.7	Physical examination	Fitch, 1984
	Australian 1980 Olympic team (106)	8.5	Physical examination	Fitch, 1984
	Spanish 1982 Olympic team (495)	4.4	Questionnaire	Drobnic, 1994
Winter sports	Cross-country skiers (42)	54.8	Questionnaire, spirometry, methacholine challenge	Larsson et al,[54] 1993
	Swedish and Norwegian cross-country skiers (171)	42.0/12.0	Questionnaire, spirometry, methacholine challenge	Sue-Chu et al,[55] 1996
	Ice hockey players (88)	21.5	Questionnaire, spirometry, histamine challenge	Lumme, 2003
	Ice hockey players (50)	11.5	Questionnaire, spirometry, methacholine and exercise challenge	Leuppi, 1998
	Cross-country skiers (20)	10.0	Exercise challenge	Pohjantähti, 2005
Swimming	Swimmers (90)	39.0	EVH challenge	Bougault, 2010
	US swimmers (738)	13.4	Questionnaire	Potts, 1996
Track and field	Marathon runners (208)	32.0	Questionnaire	Robson-Ansley et al,[51] 2012
	Finnish runners (103)	15.5	Questionnaire	Tikkanen, 1994

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Table 1
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Type of Sport	Study Population (n)	Prevalence, %	Methodology for Diagnosis	Reference
Various sports	US college athletes (80)	42.5	Questionnaire, exercise challenge	Burnett, 2016
	Summer athletes (162)	22.8	Questionnaire, spirometry, histamine challenge	Helenius et al,[70] 1998
	Swiss athletes (2060)	3.7	Questionnaire	Helbling, 1990
	Figure skaters (124)	35.0	Exercise challenge	Mannix, 1996
	US football players (151)	50.6	Questionnaire, methacholine challenge	Weiler, 1986

Despite extensive epidemiologic data, EIB evolution in athletes has not been yet fully studied. However, in athletes who stopped intensive training, EIB attenuated or even disappeared, whereas symptoms and airway inflammation increased among those who remained active during the follow-up period, irrespective of treatment strategies. Thus, EIB in athletes seems to be only partly reversible, and active training appears to be a causative factor of airway inflammation and symptoms.[46]

SPORT CONSIDERATIONS

The intensity, duration, and type of training have been associated with the occurrence of bronchial symptoms, airway hyperresponsiveness, and asthma in elite athletes (**Table 2**).

Table 2
Sport disciplines and risk of exercise-induced bronchoconstriction

Low-Risk Sports	Medium-Risk Sports	High-Risk Sports
All sports where the exercise lasts <5–8 min	Team sports where continuous exercise rarely lasts more than 5–8 min	All sports where the exercise lasts >5–8 min and/or is performed in special environments (ie, dry/cold air, chlorinated pools)
Track and field: • Sprint (100, 200, and 400 m) • Middle distance (800 and 1500 m) • Hurdles (100, 110, 400 m) • Jumps • Throws	Soccer Rugby American football Basketball Volleyball Handball Baseball Cricket Field hockey	Track and field: • Long distance (5000 and 10,000 m) • 3000 m steeplechase • Walks (20 and 50 km) • Marathon
Tennis Fencing Gymnastics Boxing Golf Weightlifting Body building Martial arts		Cycling Cross-country skiing Downhill skiing Ice hockey Ice skating High-altitude sports Triathlon Pentathlon Swimming Water polo

Carlsen and colleagues[47] first reported that the exercise load was related to the degree of bronchial hyperreactivity in both asthmatic and healthy swimmers. Some years later, the same investigators showed that the maximum decrease in forced expiratory volume at 1 second (FEV_1) after a treadmill test performed at 85% of maximal predicted heart rate (220, age) was significantly lower than the one recorded following a challenge at 95% (8.84% vs 25.11%; $P<.001$). Furthermore, although only 9 subjects (40%) fell $\geq$10% in FEV_1 after an exercise load at 85%, all the 20 subjects (100%) developed EIB after a 95% exercise test.[48]

Moreover, the longitudinal changes in the methacholine concentration needed to determine a 10% FEV_1 decrease in cross-country skiers were negatively correlated with the changes in the volume of physical activity only at an intensity level greater than 90% of maximal heart rate.[49] In addition, Stensrud and colleagues[50] observed increased airway reactivity to methacholine in elite athletes with increasing age and training volume.

Asthma is then most commonly found in athletes performing endurance activities, such as long-distance running, cycling, triathlon, and pentathlon. For example, in the study of Robson-Ansley and colleagues,[51] 32% of 208 runners from the 2010 London Marathon had asthma according to the validated Allergy Questionnaire for Athletes.[21] The high prevalence of EIB among endurance athletes has been mainly attributed to an increased minute ventilation through the mouth (bypassing the nasal filter) and exposure to allergens and pollutants.[52,53] In major national and international competitions, local pollen counts and forecasts (ie, www.polleninfo.org) should be therefore always made available in advance to athletes, their coaches, and medical teams.

Environmental factors also play a relevant role for athletes practicing winter sports. More than 1 out of 2 (54.8%) Swedish cross-country skiers were shown to have EIB in the study of Larsson and colleagues.[54] Similarly, the prevalence of bronchial hyperresponsiveness and clinical d asthma was 42% and 43%, respectively, in the 53 Swedish cross-country skiers studied by Sue-Chu and colleagues.[55] Such a high prevalence of asthma and EIB reported among Nordic and ice rink athletes has been attributed to the high ventilation of cold dry air during training and competition, in combination with the elevated emission of pollutants from fossil-fuelled ice resurfacing machines.[56,57]

Swimming has been long considered a safe and recommended sport activity for subjects with asthma because of the inhalation of humid air[58]; however, despite conflicting data,[59] an increased risk of EIB with swimming and pool attendance has been reported.[60,61] Furthermore, an association was shown between the number of chlorinated pools in the country and the prevalence of childhood asthma, independently from environmental conditions and subjects' socioeconomic status.[62] Bernard and colleagues[63] also reported that asthma development during adolescents was clearly associated with cumulative pool attendance before the age of 7. Competitive swimmers show a high prevalence of asthma and EIB,[64–66] with increased levels of leukotriene B4, a mixed eosinophilic-neutrophilic airways inflammation and evidence of bronchial epithelial damage.[63,67] These findings are thought to be the result of repeated hyperventilation challenges together with the exposure to chlorine-based derivatives, commonly used to disinfect swimming pools, such as trichloramine. This hypothesis is further supported by studies on occupational asthma in swimming pool workers and lifeguards[68] and by studies comparing exposures to non–chlorinated pools (copper-silver pools) versus chlorinated pools.[69]

At last, it is of interest to report that when the risk factors "type of sport" and "atopy" are combined in a logistic regression model, the relative risk of asthma is considerably

high: 25-fold in atopic speed and power athletes, 42-fold in atopic long-distance runners, and 97-fold in atopic swimmers compared with nonatopic control subjects.[70]

SUMMARY

Although regular physical activity is strongly recommended for a proper prevention and management of chronic diseases, including asthma, evidence has been accumulating that intense and repeated exercise is associated with a higher prevalence of EIB both with and without underlying clinical asthma. EIB has been reported to be particularly frequent in swimming, endurance, and winter sports. Furthermore, in athletes, EIB seems to be only partly reversible, representing exercise itself as a causative factor of airway inflammation and symptoms. However, it is reassuring that, when properly diagnosed and optimally treated,[71] athletes with EIB are able to participate on the highest level with their peers with even more chances to succeed and win medals than others in the Olympic Games and other major international competitions.[72]

REFERENCES

1. Latimer-Cheung AE, Toll BA, Salovey P. Promoting increased physical activity and reduced inactivity. Lancet 2013;381(9861):114.
2. Moreira A, Bonini M, Pawankar R, et al. A World Allergy Organization international survey on physical activity as a treatment option for asthma and allergies. World Allergy Organ J 2014;7(1):34.
3. Moreira A, Delgado L, Haahtela T, et al. Physical training does not increase allergic inflammation in asthmatic children. Eur Respir J 2008;32(6):1570–5.
4. Eichenberger PA, Diener SN, Kofmehl R, et al. Effects of exercise training on airway hyperreactivity in asthma: a systematic review and meta-analysis. Sports Med 2013;43:1157–70.
5. Del Giacco SR, Garcia-Larsen V. Aerobic exercise training reduces bronchial hyper-responsiveness and serum pro-inflammatory cytokines in patients with asthma. Evid Based Med 2016;21(2):70.
6. Parsons JP, Hallstrand TS, Mastronarde JG, et al. An official American Thoracic Society clinical practice guideline: exercise-induced bronchoconstriction. Am J Respir Crit Care Med 2013;187(9):1016.
7. Walsh NP, Gleeson M, Shephard RJ, et al. Position statement. Part one: immune function and exercise. Exerc Immunol Rev 2011;17:6.
8. Lakier Smith L. Overtraining, excessive exercise, and altered immunity: is this a T helper-1 versus T helper-2 lymphocyte response? Sports Med 2003;33(5):347.
9. Del Giacco SR, Firinu D, Bjermer L, et al. Exercise and asthma: an overview. Eur Clin Respir J 2015;2:27984.
10. Jones KS, Buston MH, Wharton MJ. The effect of exercise on ventilator function in the child with asthma. Br J Dis Chest 1962;56:78–86.
11. Bonini M, Palange P. Exercise-induced bronchoconstriction: new evidence in pathogenesis, diagnosis and treatment. Asthma Res Pract 2015;1:2.
12. Godfrey S. Exercise-induced asthma. In: Clark TJH, Godfrey S, editors. Asthma. London: Chapman and Hall; 1977. p. 57–8.
13. Wenzel SE. Asthma: defining the persistent asthma phenotypes. Lancet 2006; 368:804–13.
14. Global INitiative on Asthma. Available at: http://ginasthma.org/. Accessed April 28, 2017.
15. Bonini S. EIB or not EIB? That is the question. Med Sci Sports Exerc 2008;40(9): 1565–6.

16. Weiler JM, Anderson SD, Randolph C, et al. Pathogenesis, prevalence, diagnosis, and management of exercise-induced bronchoconstriction: a practice parameter. Ann Allergy Asthma Immunol 2010;105:S1–47.
17. Smoliga JM, Weiss P, Rundell KW. Exercise induced bronchoconstriction in adults: evidence based diagnosis and management. BMJ 2016;352:h6951.
18. Anderson SD, Daviskas E. The mechanism of exercise-induced asthma is …. J Allergy Clin Immunol 2000;106:453–9.
19. McFadden ER. Hypothesis: exercise-induced asthma as a vascular phenomenon. Lancet 1990;1:880–3.
20. Price OJ, Hull JH, Ansley L, et al. Exercise-induced bronchoconstriction in athletes - a qualitative assessment of symptom perception. Respir Med 2016;120:36–43.
21. Bonini M, Braido F, Baiardini I, et al. AQUA: allergy questionnaire for athletes. Development and validation. Med Sci Sports Exerc 2009;41(5):1034–41.
22. Ansley L, Kippelen P, Dickinson J, et al. Misdiagnosis of exercise-induced bronchoconstriction in professional soccer players. Allergy 2012;67(3):390–5.
23. Bonini M, Lapucci G, Petrelli G, et al. Predictive value of allergy and pulmonary function tests for the diagnosis of asthma in elite athletes. Allergy 2007;62(10):1166–70.
24. Hull JH, Ansley L, Price OJ, et al. Eucapnic voluntary hyperpnea: gold standard for diagnosing exercise-induced bronchoconstriction in athletes? Sports Med 2016;46(8):1083–93.
25. Ansley L, Bonini M, Delgado L, et al. Pathophysiological mechanisms of exercise-induced anaphylaxis: an EAACI position statement. Allergy 2015;70(10):1212–21.
26. Nielsen EW, Hull JH, Backer V. High prevalence of exercise-induced laryngeal obstruction in athletes. Med Sci Sports Exerc 2013;45(11):2030–5.
27. Bonini M, Di Mambro C, Calderon MA, et al. Beta-2 agonists for exercise-induced asthma. Cochrane Database Syst Rev 2013;(10):CD003564.
28. Bonini M, Permaul P, Kulkarni T, et al. Loss of salmeterol bronchoprotection against exercise in relation to ADRB2 Arg16Gly polymorphism and exhaled nitric oxide. Am J Respir Crit Care Med 2013;188(12):1407–12.
29. Salpeter SR, Buckley NS, Ormiston TM, et al. Meta-analysis: effect of long-acting beta-agonists on severe asthma exacerbations and asthma-related deaths. Ann Intern Med 2006;144(12):904–12.
30. The world anti-doping agency. Available at: www.wada-ama.org/. Accessed April 28, 2017.
31. Carlsen KH, Anderson SD, Bjermer L, et al. Exercise-induced asthma, respiratory and allergic disorders in elite athletes: epidemiology, mechanisms and diagnosis: part I of the report from the Joint Task Force of the European Respiratory Society (ERS) and the European Academy of Allergy and Clinical Immunology (EAACI) in cooperation with GA2LEN. Allergy 2008;63(4):387–403.
32. Randolph C. Exercise-induced bronchospasm in children. Clin Rev Allergy Immunol 2008;34(2):205–16.
33. Ventura MT, Cannone A, Sinesi D, et al. Sensitization, asthma and allergic disease in young soccer players. Allergy 2009;64(4):556–9.
34. Bousquet J, Van Cauwenberge P, Khaltaev N, Aria Workshop Group, World Health Organization. Allergic rhinitis and its impact on asthma. J Allergy Clin Immunol 2001;108(5 Suppl):S147–334.
35. Sandrock CE, Norris A. Infection in severe asthma exacerbations and critical asthma syndrome. Clin Rev Allergy Immunol 2015;48(1):104–13.

36. Voy RO. The US Olympic Committee experience with exercise-induced bronchospasm, 1984. Med Sci Sports Exerc 1986;18:328–30.
37. Weiler JM, Layton T, Hunt M. Asthma in United States Olympic athletes who participated in the 1996 summer games. J Allergy Clin Immunol 1998;102:722–6.
38. Katelaris CH, Carrozzi FM, Burke TV, et al. A springtime olympics demands special consideration for allergic athletes. J Allergy Clin Immunol 2000;106:260–6.
39. Pignataro FS, Bonini M, Forgione A, et al. Asthma and gender: the female lung. Pharmacol Res 2017;119:384–90.
40. Romberg K, Tufvesson E, Bjermer L. Sex differences in asthma in swimmers and tennis players. Ann Allergy Asthma Immunol 2017;118(3):311–7.
41. Norqvist J, Eriksson L, Söderström L, et al. Self-reported physician-diagnosed asthma among Swedish adolescent, adult and former elite endurance athletes. J Asthma 2015;52(10):1046–53.
42. Settipane RJ, Hagy GW, Settipane GA. Long-term risk factors for developing asthma and allergic rhinitis: a 23-year follow-up study of college students. Allergy Proc 1994;15:21–5.
43. Braman SS, Barrows AA, De Cotiis BA, et al. Airway hyperresponsiveness in allergic rhinitis: a risk factor for asthma. Chest 1987;91:671–4.
44. Silvers WS, Poole JA. Exercise-induced rhinitis: a common disorder that adversely affects allergic and non-allergic athletes. Ann Allergy Asthma Immunol 2006;96(2):334–40.
45. Bonini S, Bonini M, Bousquet J, et al. Rhinitis and asthma in athletes: an ARIA document in collaboration with GA2LEN. Allergy 2006;61(6):681–92.
46. Helenius IJ, Rytilä P, Sarna S, et al. Effect of continuing or finishing high-level sports on airway inflammation, bronchial hyperresponsiveness, and asthma: a 5-year prospective follow-up study of 42 highly trained swimmers. J Allergy Clin Immunol 2002;109:962–8.
47. Carlsen KH, Oseid S, Odden H, et al. The response to heavy swimming exercise in children with and without bronchial asthma. In: Morehouse CA, editor. Children and exercise XIII. Champaign (IL): Human Kinetics Publishers, Inc; 1989. p. 351–60.
48. Carlsen KH, Engh G, Mørk M. Exercise-induced bronchoconstriction depends on exercise load. Respir Med 2000;94(8):750–5.
49. Heir T, Larsen S. The influence of training intensity, airway infections and environmental conditions on seasonal variations in bronchial responsiveness in cross-country skiers. Scand J Med Sci Sports 1995;5:152–9.
50. Stensrud T, Mykland KV, Gabrielsen K, et al. Bronchial hyperresponsiveness in skiers: field test versus methacholine provocation? Med Sci Sports Exerc 2007;39:1681–6.
51. Robson-Ansley P, Howatson G, Tallent J, et al. Prevalence of allergy and upper respiratory tract symptoms in runners of the London marathon. Med Sci Sports Exerc 2012;44(6):999–1004.
52. Helenius I, Haahtela T. Allergy and asthma in elite summer sport athletes. J Allergy Clin Immunol 2000;106:444–52.
53. McCreanor J, Cullinan P, Nieuwenhuijsen MJ, et al. Respiratory effects of exposure to diesel traffic in persons with asthma. N Engl J Med 2007;357:2348–58.
54. Larsson K, Ohlsén P, Larsson L, et al. High prevalence of asthma in cross country skiers. BMJ 1993;307(6915):1326–9.
55. Sue-Chu M, Larsson L, Bjermer L. Prevalence of asthma in young cross-country skiers in central Scandinavia: differences between Norway and Sweden. Respir Med 1996;90(2):99–105.

56. Sue-Chu M, Henriksen AH, Bjermer L. Non-invasive evaluation of lower airway inflammation in hyper-responsive elite cross-country skiers and asthmatics. Respir Med 1999;93:719–25.
57. Rundell KW. High levels of airborne ultrafine and fine particulate matter in indoor ice arenas. Inhal Toxicol 2003;15:237–50.
58. Goodman M, Hays S. Asthma and swimming: a meta-analysis. J Asthma 2008; 45:639–47.
59. Valeriani F, Protano C, Vitali M, et al. Swimming attendance during childhood and development of asthma: meta-analysis. Pediatr Int 2017;59(5):614–21.
60. Bernard A, Carbonnelle S, de Burbure C, et al. Chlorinated pool attendance, atopy, and the risk of asthma during childhood. Environ Health Perspect 2006; 114:1567–73.
61. Andersson M, Hedman L, Nordberg G, et al. Swimming pool attendance is related to asthma among atopic school children: a population-based study. Environ Health 2015;14:37.
62. Nickmilder M, Bernard A. Ecological association between childhood asthma and availability of indoor chlorinated swimming pools in Europe. Occup Environ Med 2007;64:37–46.
63. Bernard A, Nickmilder M, Dumont X. Chlorinated pool attendance, airway epithelium defects and the risks of allergic diseases in adolescents: interrelationships revealed by circulating biomarkers. Environ Res 2015;140:119–26.
64. Fisk MZ, Steigerwald MD, Smoliga JM, et al. Asthma in swimmers: a review of the current literature. Phys Sportsmed 2010;38(4):28–34.
65. Stadelmann K, Stensrud T, Carlsen KH. Respiratory symptoms and bronchial responsiveness in competitive swimmers. Med Sci Sports Exerc 2011;43:375–81.
66. Mountjoy M, Fitch K, Boulet LP, et al. Prevalence and characteristics of asthma in the aquatic disciplines. J Allergy Clin Immunol 2015;136(3):588–94.
67. Moreira A, Delgado L, Palmares C, et al. Competitive swimmers with allergic asthma show a mixed type of airway inflammation. Eur Respir J 2008;31:1139–41.
68. Rosenman KD, Millerick-May M, Reilly MJ, et al. Swimming facilities and work-related asthma. J Asthma 2015;52(1):52–8.
69. Bernard A, Nickmilder M, Voisin C, et al. Impact of chlorinated swimming pool attendance on the respiratory health of adolescents. Pediatrics 2009;124:1110–8.
70. Helenius IJ, Tikkanen HO, Sarna S, et al. Asthma and increased bronchial responsiveness in elite athletes: atopy and sport event as risk factors. J Allergy Clin Immunol 1998;101:646–52.
71. Bonini M, Bachert C, Baena-Cagnani CE, et al, ARIA Initiative, in collaboration with the WHO Collaborating Center for Asthma, Rhinitis. What we should learn from the London Olympics. Curr Opin Allergy Clin Immunol 2013;13(1):1–3.
72. McKenzie DC, Fitch KD. The asthmatic athlete: inhaled beta-2 agonists, sport performance, and doping. Clin J Sport Med 2011;21(1):46–50.