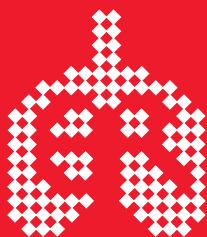


# Diagnosis, Prevention and Treatment of Exercise-Related Asthma, Respiratory and Allergic Disorders in Sports

Edited by

K-H. Carlsen, L. Delgado and S. Del Giacco



**Diagnosis, Prevention and  
Treatment of Exercise-Related  
Asthma, Respiratory and Allergic  
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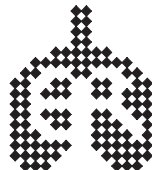
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## INTRODUCTION

K-H. Carlsen\*, J. Cummiskey#, L. Delgado<sup>†</sup>, S. Del Giacco<sup>+</sup>

\*Voksentoppen BKL, Rikshospitalet University Clinic, University of Oslo, Oslo, Norway. #Blackrock Clinic, Blackrock, County Dublin, Ireland. <sup>†</sup>Serviço de Imunologia, Faculdade de Medicina, da Universidade do Porto, Hospital S. João, Porto, Portugal. <sup>+</sup>Dipartimento di Medicina 2, University of Cagliari, Cagliari, Italy.

Asthma and allergy represent increasing problems for the actively competing athlete. The prevalence of exercise-induced asthma (EIA) has increased over the last two decades, especially amongst elite endurance athletes [1–3]; it has been reported that high-level endurance training in particular may increase bronchial hyperresponsiveness (BHR) [4] and cause inflammation in the airways [5]. Intensive endurance training and competition, together with environmental influences, are thought to be causative factors. For winter sports, inhaled cold air represents such an environmental factor; moreover, exposure of competing swimmers to organic chlorine products released from indoor swimming pools is another example of a harsh environment. Furthermore, the increased amount of training and increased level of physical fitness and maximum oxygen uptake reached by present-day elite athletes may, in some cases, make it difficult to discriminate between limitations to maximum exercise set by normal airways and EIA. This underlines the need for developing good diagnostic criteria for EIA and BHR in relation to sports.

It has become a concern that the use of inhaled asthma drugs, especially inhaled  $\beta_2$ -agonists, has become increasingly wide-spread amongst elite athletes and that high-level endurance training in particular may increase BHR [4] and cause inflammation in the airways [5]. In 1993, the Medical Commission of the International Olympic Committee (MC-IOC) restricted the use of inhaled  $\beta_2$ -agonists, even in asthmatic athletes, and only allowed inhalation of the short-acting  $\beta_2$ -agonists (SABA) salbutamol and terbutaline for use in relation to sports by asthmatic athletes. All drugs should be prescribed by a doctor with confirmation of an asthma diagnosis.

Several studies were performed on the effect on performance of both inhaled SABA and long-acting  $\beta_2$ -agonists (LABA), regarding endurance performance and maximal strength, speed and power functions; however, none of these studies could confirm any improvement in performance. Thus, from 1996, the MC-IOC also allowed the use of salmeterol, a LABA, by inhalation; later (2001), inhaled formoterol was allowed by both the MC-IOC and the newly formed World Anti-Doping Agency (WADA) in relationship to participation in sports by asthmatic athletes.

However, due to the frequent use of both SABA and LABA by inhalation, and the fear that  $\beta_2$ -agonists in high systemic doses might increase muscle mass, as indicated by some animal studies [6, 7], further regulations were introduced by the MC-IOC in December 2001, shortly before the Winter Olympic Games in Salt Lake City (UT, USA) 2002. In order to be allowed to use inhaled  $\beta_2$ -agonists, the team doctor had to make a prior application to the commission, together with documentation of increased reversibility to bronchodilators, bronchial hyperresponsiveness and/or exercise-induced bronchoconstriction (EIB). ANDERSON *et al.* [8], who suggested these regulations, described their experiences during the Winter Olympics in 2002.

Many respiratory physicians caring for top athletes felt that the regulations were too strict and the procedures required for documentation were too demanding on resources,

particularly as no improvement in performance has been demonstrated when using inhaled  $\beta_2$ -agonists or anti-inflammatory drugs. In contrast, there is general agreement that the use of inhaled  $\beta_2$ -agonists should be limited amongst athletes and not permitted in healthy subjects [9]. From January 1, 2004, the WADA has also restricted the use of inhaled steroids, thereby also limiting the availability of anti-inflammatory treatment. There is concern that overly strict criterion for the diagnosis of asthma, which in clinical practice is a clinical diagnosis, could lead to underdiagnosis and undertreatment of asthma amongst athletes. Recommendations for diagnosis and treatment should be in accordance with general clinical guidelines, such as the Global Initiative for Asthma guidelines.

Amongst the aims that the MC-IOC has set up for Sports Medicine, there is the aim that all participants should have equal conditions, and that care should be taken to ensure that sports should not cause any long-lasting harm or disease to the participants [10]. Therefore, asthmatic athletes should receive optimal treatment both symptomatically and prophylactically for their asthma.

Due to these concerns, the European Academy of Allergy and Clinical Immunology and the European Respiratory Society have established a joint Task Force to outline the problem of asthma and allergy in sports, establish definitions for asthma, EIA and EIB in relation to sports. The primary objective of the present Monograph (written by the Task Force) is to outline the problem of allergy and asthma related to sports, establish diagnostic criteria for the diagnosis of asthma and EIA in relation to sports and, finally, to set up guidelines for the treatment of asthma and EIA and other exercise-related respiratory problems in relation to sports. The diagnostic criteria and treatment guidelines should be set up from recognised evidence-based methods, as given by HARBOUR and MILLER [11], taking into account the quality of the cited studies and assessing existing levels of evidence as the basis for the grading of the recommendations given [11].

It should be remembered that athletes are examples and idols to the children and adolescents in our communities. The proper use of asthma medications, without the danger of being accused of doping, is important for the asthmatic athlete, but it also has an effect upon the general view of asthma treatment in the community. Furthermore, knowledge obtained from studies performed on elite competitive athletes may influence future treatment of asthmatic children and adolescents.

## References

1. Larsson K, Ohlsen P, Larsson L, Malmberg P, Rydstrom PO, Ulriksen H. High prevalence of asthma in cross country skiers. *BMJ* 1993; 307: 1326–1329.
2. Heir T, Oseid S. Self-reported asthma and exercise-induced asthma symptoms in high-level competitive cross-country skiers. *Scand J Med Sci Sports* 1994; 4: 128–133.
3. Helenius IJ, Tikkanen HO, Haahtela T. Occurrence of exercise induced bronchospasm in elite runners: dependence on atopy and exposure to cold air and pollen. *Br J Sports Med* 1998; 32: 125–129.
4. Carlsen KH, Oseid S, Odden H, Mellbye E. The response to heavy swimming exercise in children with and without bronchial asthma. *In*: Oseid S, Carlsen K-H, eds. *Children and Exercise XIII*. Champaign, IL, USA, Human Kinetics Publishers, Inc., 1989; pp. 351–360.
5. Sue-Chu M, Karjalainen EM, Altraja A, et al. Lymphoid aggregates in endobronchial biopsies from young elite cross-country skiers. *Am J Respir Crit Care Med* 1998; 158: 597–601.
6. Dodd SL, Powers SK, Vrabas IS, Criswell D, Stetson S, Hussain R. Effects of clenbuterol on contractile and biochemical properties of skeletal muscle. *Med Sci Sports Exerc* 1996; 28: 669–676.

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7. Suzuki J, Gao M, Xie Z, Koyama T. Effects of the beta(2)-adrenergic agonist clenbuterol on capillary geometry in cardiac and skeletal muscles in young and middle-aged rats. *Acta Physiol Scand* 1997; 161: 317–326.
8. Anderson SD, Fitch K, Perry CP, *et al.* Responses to bronchial challenge submitted for approval to use inhaled beta2-agonists before an event at the 2002 Winter Olympics. *J Allergy Clin Immunol* 2003; 111: 45–50.
9. Bonini S, Brusasco V, Carlsen K-H, *et al.* Diagnosis of asthma and permitted use of inhaled beta2-agonists in athletes. *Allergy* 2004; 59: 33–36.
10. Samaranch JA. The Olympic Book of Sports Medicine. London, Blackwell Scientific Publications, 1988; pp. vi–vii.
11. Harbour R, Miller J. A new system for grading recommendations in evidence based guidelines. *BMJ* 2001; 323: 334–336.