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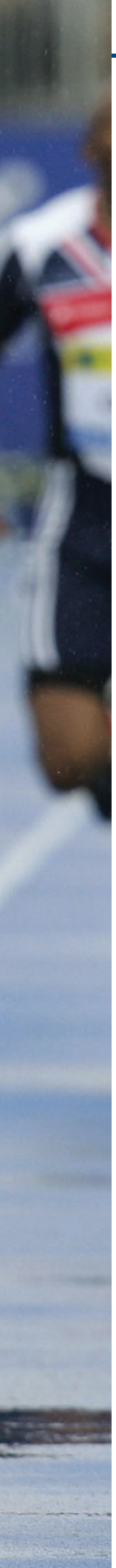

Topical review: Asthma, sports and the Olympic Games

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Summary

Exercise-induced asthma (EIA) is a general concern for growing children and adolescents with asthma. One main objective in the treatment of asthma during childhood, according to most international and national guidelines, is to master EIA. Additionally, among athletes, and especially elite athletes, EIA and bronchial hyperresponsiveness (BHR) are major problems, interfering with the performance of sports and representing a health risk. Athletes, as well as ordinary patients, need an optimal diagnosis and treatment of their asthma. This was shown by BECKER *et al*. [1], who reported deaths linked to athletic performance over a 7-year period in the USA. Out of 263 deaths, 61 were asthma related, and 51% of the deaths were related to organised sports events. Only one of the 61 athletes who died used inhaled steroids [1]. This underlines the need for optimal asthma treatment among competitive athletes.

Due to concern about reports of frequent use of inhaled β_2-agonists, the Medical Commission of the International Olympic Committee (IOC-MC) introduced restrictions in the use of these drugs in relationship to sport in 1993. These rules have been altered several times, with the introduction of applications and approvals for international athletes to be able to use such drugs. Among pulmonologists and allergologists, these rules were felt to be very restrictive, and a joint Task Force was set up by the European Respiratory Society (ERS) and European Academy of Allergy and Clinical Immunology (EAACI). This Task Force recently produced three reports [2–4]. The present article focuses on the problems raised by this report, as well as outlining a pan-European study focusing on asthma and BHR in top athletes.

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The history

As early as 1986, VOY [5] reported from a screening organised by the US Olympic Committee that 67 out of 597 US athletes at the Los Angeles 1984 Olympic Games suffered from EIA or asthma. These asthmatic athletes won 41 medals during the games. WEILER *et al*. [6] reported a prevalence of EIA of 11% among American athletes participating in the 1984 summer Olympic Games, increasing to >20% among the American participants in the 1996 summer games in Atlanta [7], with an asthma prevalence of 45% in cyclists and mountain bikers compared to zero in divers and weightlifters [7]. LANGDEAU *et al*. [8] reported on the prevalence of BHR to methacholine (49%) in 100 competitive athletes from various sports compared with sedentary subjects (28%). The prevalence varied between athletes performing their sports in cold air, dry air, humid air or a combination. LARSSON *et al*. [9] reported in 1993 that 23 out of 42 elite cross-country skiers had a combination of BHR and asthma symptoms compared with only one of 23 referents. Shortly afterward, a questionnaire-based report showed a 14% prevalence of doctor-diagnosed asthma in 155 actively competing skiers, compared

with 5% in twice-matched controls; moreover, the prevalence of asthma diagnosis increased with increasing age in the actively competing skiers [10]. This was followed by reports of high prevalence in Norwegian and Swedish skiers [11], in competitive figure-skaters [12, 13], in elite cold-weather athletes [14] and among participants in the 1998 US Olympic team for winter sports, including gold medallists [15].

FEINSTEIN *et al*. [16] found EIA in nine out of 48 male football players, whereas BHR to methacholine (dose of methacholine causing a 20% fall in forced expiratory volume in one second (FEV_1) <16.3 µmol) was found in 35.5% of the Norwegian national female soccer team [17]. In a study of Canadian professional football players, 56% had a positive bronchodilator test (increase in FEV_1 of 12%) to inhaled salbutamol [18]. HELENIUS and co-workers [19–21] published several studies on Finnish elite track and field athletes. Physician-diagnosed asthma was reported in 17% of long-distance runners, 8% of speed and power athletes and 3% of controls [19]. In another study, total asthma (current asthma, physician-diagnosed asthma or BHR) was found in 23% of athletes compared with 4% of controls; current asthma in 14% compared with 2% of controls; and positive skin–prick test in 48% of athletes compared with 36% of controls [20]. A high prevalence of BHR (48%) to histamine was also found among swimmers [21]. MAIOLO *et al*. [22] reported asthma and atopy prevalences of 15% and 18%, respectively, among 1,060 Italian competing summer athletes. Higher prevalence of asthma among endurance athletes *versus* speed and power athletes has been reported in a Norwegian study [23]. Employing the objective criteria for diagnosing asthma and/or BHR as given by the IOC-MC, DICKINSON *et al*. [24] reported asthma prevalence among British participants in the Olympic Games in 2000 and 2004 to be 21.2% and 20.7%, respectively.

How?

Why exercise-induced asthma?

Two hypotheses attempt to explain the relationship between physical activity and EIA. One relates to cooling of the airways due to the increased ventilation during exercise, the other to increased water loss from the respiratory tract, also caused by increased ventilation during exercise. Airway cooling due to respiratory heat loss during exercise is thought to cause vasoconstriction in bronchial vessels, followed by a secondary reactive hyperaemia with resulting oedema and airway narrowing [25]. Conversely, the high ventilation rates of top athletes (>280 L per min) during exercise can cause water loss as relatively dry inhaled air becomes saturated prior to exhalation. The resulting increase in osmolarity of the periciliary fluid lining the respiratory mucosal membranes is thought to cause mediator release, increased airway inflammation and bronchial constriction [26]. The use of inhaled mannitol as a tool to diagnose BHR strengthens this hypothesis [27].

Why EIA and BHR in athletes?

That high-intensity exercise may cause an increase in BHR was first demonstrated in Norwegian competitive swimmers after a swimming exercise of 3,000 m [28] and then in young skiers during the competitive season [10]. Heavy endurance training, especially when performed in an adverse environment, presents stress to the mucosal membrane of the airways. This was elegantly shown by SUE-CHU and co-workers [29, 30] in bronchial biopsies from heavily training young skiers who did not have asthma, but had increased airway responsiveness to cold air. They described increased airway inflammation with lymphoid aggregates and increased tenascin expression (as measured through the thickness of the tenascin-specific immunoreactivity band in the basement membrane). Similar findings were recently described experimentally in exercising *versus* sedentary mice [31]. Also inflammatory changes in induced sputum have been reported among competitive swimmers [21].

Thus, heavy and repeated physical endurance training over prolonged periods of time in combination with nonoptimal environmental

conditions may contribute to the development of asthma and BHR among top athletes.

The environment

Repeated competitions and endurance training in adverse environmental conditions are thought to contribute to the development of asthma and BHR among top athletes. Examples are the development of BHR and EIA among cross-country skiers exposed to cold air [9, 32] and among competitive swimmers exposed to organic chlorine products from the water in indoor pools [21]. LARSSON *et al*. [33] showed that cold air inhalation increased the number of inflammatory cells in bronchoalveolar lavage. In children, BERNARD and co-workers [34, 35] found that time spent in swimming pools during early childhood was related to development of asthma and signs of lung involvement by increased serum levels of surfactant proteins [34] and reduced levels of Clara cell protein [35]. Respiratory tract infections also increase bronchial responsiveness in actively training athletes [36].

Thus, the combination of heavy repeated exercise with an unfavourable environmental milieu is probably important for the development of asthma among top athletes.

Diagnosis of asthma, EIA and BHR in athletes

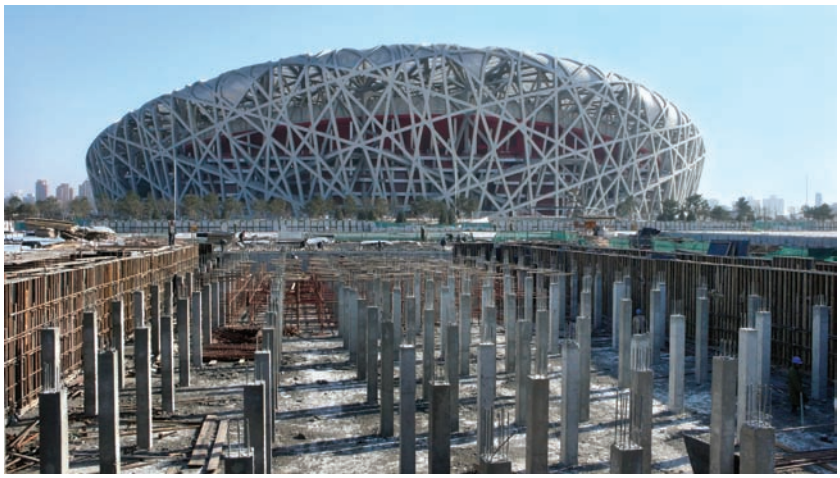
The diagnosis of asthma is clinical and should be based upon history of symptoms, physical examination of signs indicating the presence of bronchial obstruction and variability in lung function spontaneously or due to bronchodilators (table 1) [37]. The main symptoms of asthma are recurring episodes of bronchial obstruction. The term "current asthma" is used when at least one episode of asthma has occurred during the previous year. The competing athlete frequently reports the presence of respiratory symptoms in relationship to exercise, but the diagnosis of asthma or EIA may be difficult due to the variability and nonspecificity of symptoms [14, 38]. An exact clinical history, examination with lung function measurements before and after inhalation of a β_2-agonist (requiring an increase in FEV1 of 12%), before and after a standardised exercise-test such as treadmill run and/or a cold-air inhalation test and measurement of BHR by methacholine inhalation are parts of the diagnostic process. One important part of the diagnostic process is to follow up the patient to evaluate the effect of treatment.

EIA may be diagnosed in different ways; running provokes exercise-induced bronchoconstriction more easily than cycling. A heavy exercise load is recommended. In the current author's laboratory, a motor-driven treadmill is employed with an inclination of 5.5%, which rapidly increases speed until a steady heart rate of ~95% of calculated maximum is reached and maintains this for 4–6 min. The widespread use of inhaled steroids necessitates this level of exercise [39]. Maximum heart rate per minute is approximately calculated by subtracting the age of the patient in years from 220, and can be measured electronically. The running is performed with a room temperature of ~20°C and a relative humidity of ~40%. Lung function (FEV1) is measured before running, immediately after cessation of running, and 3, 6, 10, 15 and 20 min after running. A fall of 10% is taken as a sign of EIA. When adding an extra stimulus to the exercise test, by combining running on a treadmill with the inhalation of dry cold air at -20°C, the sensitivity of the test is markedly increased while maintaining a high degree of specificity [40]. Other tests used for the diagnosis of exercise-induced bronchoconstriction and BHR are eucapnic hyperventilation [41] and

Table 1 Diagnosis of exercise-induced asthma or bronchial responsiveness in relationship to sports

Diagnostic procedure	Required result by IOC-MC
Clinical history of respiratory symptoms and clinical examination	Positive clinical history
Lung function (spirometry or maximum expiratory flow volume loops). Reversibility to inhaled bronchodilator	Increase in FEV_1 after inhaled bronchodilator
Exercise-induced bronchoconstriction by standardised exercise test	FEV_1 decrease of 10% from before to after standardised exercise challenge
Bronchial hyperresponsiveness to methacholine (histamine presently not allowed by IOC-MC)	PD_{20} <2 mol, PC_{20} < 4 mg per ml Other values when on inhaled steroids
Eucapnic hyperventilation test or mannitol inhalation test	Reduction in FEV_1 of 15% or more
Exercise field test	Reduction in FEV_1 of 10% or more

Results given relate to the present rules for approving permission for use of inhaled steroids and/or inhaled β_2-agonists in sports as given by IOC-MC with regards to the Beijing Olympics. As change of existing rules may be issued, the responsible physician should keep informed through the websites of the World Anti-doping Agency and IOC for the Olympic Games. A clinical history in combination with a positive bronchodilator response or a positive response to EIA test or other test of bronchial responsiveness is required. PD_{20}: provocative dose causing a 20% fall in FEV_1; PC_{20}: provocative concentration causing a 20% fall in FEV_1.



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mannitol bronchial provocation, determining the inhaled dose causing a 15% decrease in FEV_1 [42].

Differential diagnoses

There are several differential diagnoses to EIA, including exercise-induced laryngeal inspiratory stridor (also called exercise-induced vocal cord dysfunction) [43, 44] and hyperventilation during exercise. These conditions should be borne in mind, as many such patients have been given unnecessary drugs for treatment of asthma, including both inhaled steroids and β_2-agonists, which will have no effect upon the exercise-induced laryngeal stridor. Exercise-induced laryngeal stridor is more common among female athletes during adolescence. Marked inspiratory stridor during maximal exercise with a flattening of the maximal inspiratory flow–volume curve [45] is typical, in contrast to EIA, in which case the dyspnoea occurs after exercise, and is expiratory due to the obstruction of the lower airways. Other differential diagnoses include exercise-induced arterial hypoxaemia [46–48] and swimming-induced pulmonary oedema [49].

Asthma treatment and performance

Recommendations

Despite epidemiological evidence regarding the increased prevalence of EIA and BHR among top athletes, the frequent use of asthma drugs has led to concern about possible improvement of performance by asthma drugs, particularly by inhaled β_2-agonists. Thus, in 1993 the IOC-MC restricted the use of asthma drugs in sport. Among the β_2-agonists, only salbutamol and terbutaline were allowed for use in sport, and only by the inhaled route. Only athletes with a confirmed diagnosis of asthma were allowed to use these drugs. These regulations have since been changed several times. Shortly before the Salt Lake City Winter Olympics in 2002, the IOC-MC introduced new rules for the use of inhaled β_2-agonists and inhaled steroids [50]. Applications had to be made beforehand, and results of laboratory tests such as exercise tests, bronchial provocation tests with methacholine, eucapnic hyperventilation tests or documented reversibility to inhaled β_2-agonists had to be submitted [51]. Several allergologists and pulmonologists felt these rules to be too strict as they focused upon the specificity of asthma diagnosis and not upon sensitivity [52], and a Task Force was set up jointly by the ERS and EAACI. This Task Force published a monograph [4], viewing the topic from different angles and recently a two-part report covering the problem of asthma and allergy among athletes, pathogenetic mechanisms and recommendations with regard to the diagnosis of asthma and BHR among athletes, as well as the recommended treatment has also been published [2, 3]. In the present manuscript, the treatment will not be handled, as the treatment of the athlete with asthma or other respiratory problems should follow the common guidelines after appropriate diagnosis, taking into consideration the rules set up by the doping authorities (the World Anti-doping Agency (WADA) and, for the Olympic Games, IOC-MC). As the regulations for the use of asthma drugs among athletes have been repeatedly changed, physicians treating asthmatic athletes and children and adolescents with asthma should keep up to date with the present regulations. This may be done by consulting the website of the WADA, at www.wada-ama.org, for international sports; or as regards the Olympic Games, the website of the IOC [53]. Applications for the use of asthma drugs at the Olympic Games may be made by filling in an electronic form on the IOC website; for other international sports by filling in the written forms for a Therapeutic Use Exemption and submitting them to WADA and/or the relevant international sporting association.

Carrying on the work: Beijing and beyond

Presently, we have a broad impression of the problem of asthma and EIA in athletes. We still

need further knowledge about the topic and about how different types of sports are affected. Ahead of the upcoming Olympic Games in Beijing, much concern has been expressed by athletes and sports organisations about the possible harmful effects of the environmental air pollution in Beijing. Whereas some athletes with asthma may choose not to risk competing in Beijing, other athletes who do wish to compete feel, and possibly are, at risk of developing asthma or suffering exacerbations of their asthma during the games. The Norwegian Olympic Committee was much concerned about this problem and asked the current author to examine all Norwegian athletes qualifying for the Beijing Olympics for respiratory problems, in order to initiate treatment when needed following the regulations given by IOC-MC, and to follow the athletes to and through the Beijing Olympics. This led to a study related to asthma and bronchial responsiveness among athletes of different types of sports and then further to a pan-European study initated through GA^{2}LEN, the European Network of Centres of Excellence. Ten European countries are now taking part in this study. The main aim will be to investigate the prevalences of asthma, bronchial responsiveness and allergy in the different types of summer sports. There will also be a respiratory laboratory in Beijing, and air pollution levels will be recorded. A questionnaire, the

Allergy Questionnaire for Athletes [54], will be evaluated as a tool to assess EIA, bronchial responsiveness and allergic sensitisation by employing objective measurement, *e.g.* bronchial provocation tests to methacholine, skin-prick tests, serum-specific immunoglobulin Es, exhaled nitric oxide and research procedures such as sampling exhaled breathe condensate. A sub-sample will assess the use of methacholine bronchial provocation in comparison to the use of mannitol bronchial provocation as tools for the assessment of asthma and bronchial responsiveness among the athletes. The study, already ongoing, represents an example of European cooperation across borders and will create a basis for further research.

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