**Sports and allergy: How much is too much?**

**SUMMARY**

Physical exertion is a powerful and frequent trigger of different hypersensitivity events. The all-encompassing term exercise-induced (EI) hypersensitivity syndromes include EI-asthma (EIA), EI-bronchoconstriction (EIB), EI-rhinitis, EI-anaphylaxis and EI-urticaria. These are significant problems for those practicing sports both at a recreational and an elite level. Adequate management depends upon its recognition, which allows a correct diagnosis and proper treatment.

The fear of exacerbations often prompts individuals to curtail exercise. However, the evidence for the potential benefit of exercise in asthma and allergic diseases is increasing, with several studies showing improvements in inflammatory, lung function, and even quality-of-life outcomes after a training program. So, physicians should stress the importance of adequate levels of physical activity to patients.

EI-urticaria and EI-anaphylaxis are much less frequent, but yet with an important impact in performance and quality of life. As recurrences might occur under the same conditions, future exercise-related activities are often curtailed and therefore prompt diagnosis and proper identification of triggers are mandatory.

Regular physical exercise and participation in sports are considered to be important components of a healthy life and are recommended for all individuals [1]. There is unquestionable evidence that regular physical activity contributes to the primary and secondary prevention of cardiovascular diseases and several other chronic conditions [2].

Guidelines recommend children above 2 years and youth to participate in at least 60 minutes of enjoyable, moderate-intensity physical activities every day [1]. However, exercise is a powerful and frequent trigger of different hypersensitivity events that impair performance. The all-encompassing term exercise-induced (EI) hypersensitivity syndromes include EI-asthma (EIA), EI-bronchoconstriction (EIB), EI-rhinitis, EI-anaphylaxis and EI-urticaria.

Most asthmatic subjects may experience respiratory symptoms provoked by exercise [3]. Such evidence of asthmatic symptoms occurring during exercise prompted avoidance of physical activity by asthmatics throughout the years, leading to detrimental consequences to physical and social well-being of these patients. Asthma has been associated with reduced physical activity and obesity [4, 5]. More recent data, however, changed this paradigm; evidence that physically active children and youth have higher levels of cardiorespiratory endurance compared to inactive young people [1], turned exercise to become regarded with greater interest for asthmatic patients.

However, while structured exercise on a recreational level has been shown to be beneficial, repeated high-intensity exercise performed by elite athletes has been pointed out to contribute to the development of asthma and bronchial hyperresponsiveness (BHR) [6]. Also, in contrast to moderate or intermittent physical activity, prolonged and intensive exertion causes numerous deleterious changes in immunity that reflects physiological stress and immune suppression [7–9].

EI-rhinitis, characterized by itching, sneezing, rhinorrhea and/or post-nasal drainage, nasal congestion and occasional anosmia provoked by exercise, is frequently accompanied by eye, ear or throat symptoms [10]. Athletes with rhinitis, particularly congestion, often complain about disturbed sleep, daytime somnolence, fatigue and impaired performance [11]. Treating rhinitis, especially reducing nasal congestion, should improve sleep and thereby improve quality of life and, most likely, athletic performance. Controlling rhinitis also may improve asthma control. Certain medications for athletes with asthma and rhinitis who participate in regulated competitions are not allowed.

EI-urticaria and EI-anaphylaxis, the later possibly being related to specific food ingestion (a process named food dependent exercise-induced anaphylaxis – FDEIA), are much less frequent, but yet with an important impact in performance and quality of life. EI-anaphylaxis is a rare, unpredictable event, and the most

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serious and potentially life-threatening syndrome associated with exercise (12); 2–15% of anaphylactic episodes are caused by or associated with exercise (13, 14). As recurrences might occur under the same conditions, consequently, future exercise-related activities are often curtailed. EI-urticaria also appears in athletes without an associated anaphylactic reaction and is frequently driven by physical and environmental stimuli, like high temperatures (cholinergic urticaria) or even cold environments.

The aim of this article is to review the effects of exercise on asthma and allergies focusing in regular patients and also addressing the particular athlete’s asthma phenotype, as well as to provide evidence on new perspectives of beneficial effects of exercise in patients with asthma and/or allergy.

The patient with asthma: to exercise or not to exercise?

Exercise is one of many non-pharmacologic and non-immunologic stimuli that can produce episodes of airway obstruction in asthmatic patients. In fact, physical activity is the second leading cause of acute airway constriction and ranks only behind viral upper respiratory tract infections (URTIs) in this regard (15). Most of the asthmatic subjects without anti-inflammatory treatment experience an asthma attack provoked by exercise (4). EI-asthma is most frequently seen in children and young adults because of their high levels of physical activity (16).

Classical postulated mechanisms behind EIA include the osmotic or airway-drying hypothesis (17). Physical activity increases the need for oxygen, thus increasing ventilation and, therefore, the amount of air passing through the airways to and from the lungs. As water evaporates from the airway surface liquid, it becomes hyperosmolar, thereby providing an osmotic stimulus for water to move from nearby cells (17). This results in shrinkage of nearby cells and the release of inflammatory mediators that causes airway smooth muscle contraction in susceptible individuals. Besides the water loss, increased ventilation also promotes heat loss. So, another explanatory hypothesis focuses on cooling of the airways caused by increased ventilation, which causes reflex parasympathetic nerve stimulation that leads to bronchoconstriction through stimulation of the vagal nerve, initially causing reflex vasoconstriction to conserve heat, followed at the end of the exercise by secondary airway rewarming with vascular bronchial congestion, edema, and further narrowing of the airways (18).

However, the increased water loss due to the rise in ventilation is considered to be more important than the heat loss, as it increases the osmolality of the extracellular fluid of the bronchial mucosal membranes (18). The release of both newly formed mediators and pre-formed mediators induced by changes in osmolarity, and that cause bronchoconstriction, can be inhibited by treatment with anti-inflammatory agents.

Starting anti-inflammatory treatment and obtaining better asthma control has shown to increase both fitness and level of vigorous activity after 1 year of treatment (19, 20). For the asthmatic patient, it is important to control EIA without being dependent upon planned pre-medication before planned exercise training.
Thus, anti-inflammatory treatment becomes important for the daily life activities of our asthmatic patients in order to control EIA and allow full participation in physical activity, play and sporting activities (21). According to GINA guidelines, the presence of symptoms with exercise is a marker of poor asthma control indicating a need for additional controller medications (22). Table 1 summarizes currently available drugs for asthma treatment (23).

**Asthmatic children**

It has been reported that asthma limits the participation of children in physical activity, especially vigorous physical activity (24). Newly diagnosed asthmatic adolescents are less fit and have lower levels of vigorous physical activity than control subjects (19, 20). Asthmatic children suffering from EIA will become passive and participate at a low level in physical activity and play (3). Symptoms every time the child exercises and has Physical Education classes at school leads parents to suggest to doctors that «because he/she is constantly wheezing when he/she runs, he/she should have a note from you excusing the child from Physical Education classes» (25). This starts a vicious circle of respiratory symptoms, inactivity, and physical deconditioning (Figure 1). This is particularly concerning, given the recent evidence of benefits arising from regular exercise practicing.

**FIGURE 1.** The vicious circle of respiratory symptoms and the consequences arising from lack of asthma treatment and control.

<table>
<thead>
<tr>
<th>DRUG</th>
<th>TYPE</th>
<th>NOTES</th>
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</thead>
<tbody>
<tr>
<td>Inhaled corticosteroids</td>
<td>Controller</td>
<td>Presently the most important treatment available. Ciclesonide may be particularly suited to both children and athletes because of fewer side-effects.</td>
</tr>
<tr>
<td>Anti-leukotrienes</td>
<td>Controller</td>
<td>Montelukast protects against EIA without the development of tolerance. Some patients are non-responders. Effect should be controlled through follow-up. Also improves rhinitis.</td>
</tr>
<tr>
<td>Cromones</td>
<td>Controller</td>
<td>More effective than inhaled anti-cholinergics at attenuating EIB-bronchoconstriction, but less than short-acting beta2-agonists.</td>
</tr>
<tr>
<td>Inhaled beta2-agonists</td>
<td>Reliever</td>
<td>Short-acting: Useful for pretreatment before exercise and for reliever treatment of dyspnea. Regular use may cause tolerance development.</td>
</tr>
<tr>
<td></td>
<td>Reliever and/or controller</td>
<td>Long-acting: Useful with uncontrolled EIA both in schoolchildren and adolescents. Regular use may result in tolerance development. Should not be used without concomitant inhaled corticosteroids.</td>
</tr>
<tr>
<td>Inhaled anti-cholinergics</td>
<td>Reliever</td>
<td>May be particularly useful in elite athletes owing to possible cholinergic involvement in pathogenesis.</td>
</tr>
<tr>
<td>Omalizumab</td>
<td>Controller</td>
<td>Approved for treatment of moderate to severe allergic asthma. Not studied for EIA.</td>
</tr>
</tbody>
</table>

There is now accumulating evidence that physical training may have positive effects on asthma (21, 26–32). A systematic review of eight studies of asthmatic subjects undertaking physical training included 226 asthmatics above 8 years-old and concluded that physical training improved cardiopulmonary fitness (26). Later, other systematic reviews reported similar findings (28, 29). Several studies also reported improved quality of life of asthmatics in the actively training groups (21, 27, 30, 32, 33), not only in children but also in their caregivers (33). Regarding inflammatory outcomes, regular training reduced total and house dust mite-specific IgE levels in asthmatic children (34). Airway responsiveness assessed by exercise or methacholine challenge was reduced in asthmatic children after 3 months of aerobic training or after a swimming program (32, 35). In addition, in asthmatic adults, lower sputum eosinophilia as well as exhaled nitric oxide levels after 3 months of aerobic training has been shown (36).

So, given the current evidence, physical activity should be recommended as a supplementary therapy to medication in asthmatic subjects (27, 37). Asthmatic patients can be physically active and fit and may participate in sports activities, provided they receive optimal treatment for their asthma [18] and so, treating and preventing EIA has become one of the main objectives among all guidelines [22, 38–40]. The role of the school, and in particular her Physical Education teacher, is important, and their understanding...
of asthma may need to be explored and improved, particularly around access to medication (25). All too often, it remains the case that children have difficulty accessing their medication, a problem that can be amplified on the playing field or playground, with teachers considering that children may be using their asthma and its symptoms as an excuse to avoid games or sports (25). Educational programs for teachers to help dealing with these conditions may be helpful (41). This would avoid the withdrawal from exercise that sometimes children and their families request from doctors and which should be resisted. In the meanwhile, it is important to be sure of the correct diagnosis. Methods to diagnose EIA and the possible differential diagnosis are presented in table 2 and table 3 (see page 10), respectively.

**Prescription of exercise: which sport for the asthmatic?**

This is a common question that asthmatic patients pose to their doctor, after being encouraged to exercise. The most important answer is to assure the patient that as long as the asthma is well-controlled, any sport can be chosen and he/she should practice the one that is the most enjoyed. Though no limitations in sport selection should arise for patients with EIA, symptoms may be decreased by selecting a sport based on its low asthmogenic potential (42).

Sports with low risk for asthma are the ones in which the physical effort is of short duration and in which high ventilatory levels are not reached. Medium-risk sports are team sports in general, in which the alternation of aerobic and anaerobic phases, as well as the relatively brief periods of continuous high-intensity exercise (in any case usually lower than 5–8 min) result in a lower risk of bronchial hyperreactivity. High-risk sports are endurance and winter sports (3). Swimming should be encouraged since it has been previously shown that it causes a lung growth greater than normal in children and adolescents [43], improves their lung function [44] and teaches airway control [45]; also, the hot and humid conditions of swimming training have been pointed out as less asthmogenic. Although concerns have been raised regarding a potential risk of asthma with an increased swimming pool attendance in children [46], later others refuted this hypothesis [44]; also, the hazards seem to be mostly related to chlorinated disinfection by-products [47], so other methods of disinfection may be preferable [48]. In addition, it is also important to avoid strenuous exercise during temporarily increased exposure to «biological stress» – this can be increased aeroallergen load, extreme cold air environment, or strenuous exercise too close to a recent viral respiratory tract infection (3).

The doctor should be responsible to ensure that asthma is not a limitation to exercise. With an early and precise diagnosis, and an early start of anti-inflammatory treatment, EIA may usually be well controlled and considering the available evidence, exercising should be prescribed as a supplementary therapy to medication in asthmatic subjects (27, 37). However, although clinicians working in the field of allergy and respiratory diseases are aware of this evidence, they need more training in such counselling (49).

**Allergies in relation to exercise Rhinitis**

Nasal efficiency during exercise is usually improved by autonomic reflexes: dynamic exercises reduce nasal resistance (50), because of an increase in nasal sympathetic tone, causing constriction of nasal blood...
vessels through α-adrenoreceptor stimulation. So, an initial decongestion of mucosa occurs, and it is maintained nearly 30 min after stopping exercise. However, this reduction of nasal resistance can lead to mucosa dehydration and a rebound increase in nasal secretion to compensate it (51). Also, in patients with rhinitis isometric exercises induce a clear increase of nasal resistance and the normal reduction of nasal resistance as a response to standing is absent (52).

Until now, it has not been possible to confirm the association of rhinitis symptoms and exercise performance (53). However, it seems reasonable

<table>
<thead>
<tr>
<th>METHOD</th>
<th>PROTOCOL</th>
<th>POSITIVITY CRITERIA</th>
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<tbody>
<tr>
<td>Bronchodilation test</td>
<td>FEV1, before and 15 minutes after inhalation of a standard beta-2 agonist</td>
<td>FEV1 increase from baseline ≥ 200 mL, and ≥ 12% of predicted</td>
</tr>
<tr>
<td>Bronchial provocation challenges</td>
<td></td>
<td></td>
</tr>
<tr>
<td>– Methacholine test</td>
<td>Provocative dose (PD20) or concentration (PC20) of inhaled methacholine inducing a FEV1 decrease from baseline ≥ 20%</td>
<td>PC20 ≤ 4 mg/ml or PD20 ≤ 400 μg [cumulative dose], or ≥ 200 μg [noncumulative dose] in those not taking ICS. PC20 ≤ 16 mg/ml or PD20 ≤ 1600 μg [cumulative dose] or ≤ 800 μg [noncumulative dose] in those taking ICS for at least 1 month</td>
</tr>
<tr>
<td>– Eucapnic voluntary hyperpnoea</td>
<td>FEV1, before and within 30 min of 6 min dry [or dry and cool] air inhalation at 85% of predicted maximum voluntary ventilation</td>
<td>≥ 10% decrease in FEV1 from baseline</td>
</tr>
<tr>
<td>– Hypertonic saline inhalation</td>
<td>FEV1, before and after inhaling 22.5 ml of 4.5 g % NaCl</td>
<td>≥ 15% decrease in FEV1 from baseline</td>
</tr>
<tr>
<td>– Mannitol inhalation</td>
<td>Provocative dose of inhaled mannitol inducing a FEV1 decrease from baseline ≥ 15% (PD15M)</td>
<td>PD15M ≥ 635 mg of mannitol</td>
</tr>
<tr>
<td>– Exercise challenge [field or laboratory]</td>
<td>FEV1, before and within 30 min of exercise challenge achieving heart rate ≥ 85% for at least 4 min</td>
<td>≥ 10% decrease in FEV1 from baseline</td>
</tr>
</tbody>
</table>

FEV1: Forced expiratory volume in one second; ICS: inhaled corticosteroids; NaCl: sodium chloride.

**TABLE 2.** Diagnostic methods and positivity criteria to document exercise-induced bronchoconstriction in athletes [adapted from Couto et al. (97)].

**TABLE 3.** Most common differential diagnoses of exercise–induced asthma. Exercise–induced arterial hypoxemia and swimming–induced pulmonary edema are only observed in elite athletes, while all the other conditions may be diagnosed in regular asthmatic patients [adapted from Couto et al. (97)].

<table>
<thead>
<tr>
<th>CONDITION</th>
<th>SYMPTOMS AND OCCURRENCE</th>
<th>PHYSICAL SIGNS</th>
<th>OBJECTIVE EVIDENCE</th>
<th>OTHER USEFUL TIPS</th>
</tr>
</thead>
<tbody>
<tr>
<td>EIA</td>
<td>Chest tightness, wheezing, cough, shortness of breath, generally occurring within 5 to 30 minutes after intense exercise (sometimes during)</td>
<td>Expiratory dyspnea</td>
<td>Reversibility on lung function testing</td>
<td>Improvement occurs either spontaneously or after inhaled bronchodilator</td>
</tr>
<tr>
<td>Vocal cord dysfunction</td>
<td>Throat tightness, shortness of breath, increased inspiratory effort, stridor and wheeze Only during maximum exercise, and stopping right after (unless hyperventilation) Most often occurs in teenage girls</td>
<td>Stridor</td>
<td>Flattened inspiratory flow volume loop during stridor</td>
<td>No effect of asthma medication Consider direct fibre–optic laryngoscopy during exercise to check for paradoxical vocal cord movement and to differentiate from laryngomalacia</td>
</tr>
<tr>
<td>Poor physical fitness</td>
<td>Dyspnea and muscular stiffness related to expectations and training level</td>
<td>High heart rate after low–grade exercise load</td>
<td>Normal lung function and negative provocation challenges</td>
<td>Exercise rehabilitation or training can improve aerobic fitness and endurance and can shift the lactate/ventilatory threshold so more work is required before lactate accumulates and ventilation increases. Improved aerobic fitness through exercise training can thus decrease the hyperpnoea and dyspnea associated with exercise</td>
</tr>
<tr>
<td>Exercise–induced hyperventilation [pseudo–asthma syndrome]</td>
<td>Dyspnea and chest tightness during exercise</td>
<td>Hyperventilation</td>
<td>Increased end–tidal carbon dioxide</td>
<td>Symptoms are not directly related to bronchial obstruction but with hypocapnia and a possible abnormal ventilatory homeostasis during exercise</td>
</tr>
<tr>
<td>Exercise–induced arterial hypoxemia</td>
<td>Occurs in well–trained athletes with high VO2max</td>
<td>Respiratory distress</td>
<td>Reduction in arterial oxygen saturation</td>
<td>Primarily due to diffusion limitations and ventilation–perfusion mismatch</td>
</tr>
<tr>
<td>Swimming–induced pulmonary edema</td>
<td>Shortness of breath and cough during or immediately after swimming associated with evidence of pulmonary edema</td>
<td>Sputum production Hemoptysis Reduction in arterial oxygen saturation Respiratory distress</td>
<td>None or restrictive spirometric pattern persisting for up to 1 week</td>
<td>Crackles, râtil or ‘junky’ feelings deep in the chest associated with breathing effort and cough</td>
</tr>
</tbody>
</table>

EIA: exercise induced asthma; VO2max: maximum oxygen uptake
that distorted airflow dynamics and ventilation caused by allergic rhinitis and nasal obstruction have a negative effect, particularly in high-intensity activities (53). Allergic rhinitis affects approximately 25% of adults in Europe and up to 40% of children globally (54, 55); so, naturally, many people practicing exercise will be suffering from this situation, which will reduce their capacity for exercise.

The environment where the exercise is performed is also an important determinant. Practicing sports outdoor increases the exposure to pollen and pollutants. In swimmers, it is essential to consider the contact with chlorine derivatives (56, 57). On the other hand, cold air induces glandular hypersecretion and nasal discharge in normal subjects (under parasympathetic control), and this response is more severe in patients with rhinitis (58). So, although some patients experience improvement in rhinitis with exercise (through an increase in nasal sympathetic tone), rhinitis may worsen under certain environmental conditions (56).

In elite athletes, rhinitis seems to be more frequent, with prevalence ranging from 13% up to 35%, depending on the sport and environmental conditions (10, 59). El-rhinitis is characterized by itching, sneezing, rhinorrhea and/or postnasal drainage, and/or nasal congestion provoked by exercise (60). Rhinitis is frequently accompanied by eye, ear or throat symptoms. Athletes with rhinitis, particularly congestion, often have disturbed sleep, daytime somnolence, fatigue and impaired performance. Allergic rhinitis has been shown to have negative effects on performance scores – ability to train and compete (56).

Early recognition and diagnosis of allergic rhinitis is mandatory so that adequate treatment may be promptly started, to improve nasal symptoms and prevent El-rhinitis avoiding the negative effects on exercise practice. Allergy testing is recommended in order to provide relevant measures of allergen avoidance and specific immunotherapy if needed. In athletes, it is important to choose drugs without affecting athletic performance while complying with antidoping regulations.

**Exercise induced anaphylaxis**

EI-anaphylaxis is a physical allergy, brought on by exercise (61). It is a rare, unpredictable event, and the most serious and potentially life-threatening syndrome associated with exercise (12); 2–15% of anaphylactic episodes are caused by or associated with exercise (13, 14). Symptoms include fatigue, pruritus, warmth, flushing, urticaria, and can progress to angioedema, wheezing, rhinitis, gastrointestinal symptoms and cardiovascular collapse (62). Contributing factors may include the use of non- steroid anti-inflammatory drugs, exposure to high pollen levels, insect stings, extremes of temperature and humidity or even stress or menses. In a subgroup, EI-anaphylaxis is related to specific food ingestion (a process named food dependent exercise-induced anaphylaxis – FDEIA), whereby exercise must occur after ingestion of a food allergen to which the subject is sensitive or, in other cases, after ingestion of any food (60, 63).

When a diagnosis of EI-anaphylaxis is established, doctors should teach patients on how to recognize their first symptoms and signs and immediately discontinue exercise. They should learn to assume the Trendelenburg position to facilitate perfusion of vital organs and learn to auto-inject adrenaline. Adrenaline is considered, according to evidence based-medicine, the first-line treatment for anaphylaxis (64–69). Intramuscularly auto-injected into the lateral thigh, it improves airflow and vascular integrity (11). Sporting facilities must have adrenaline available in their emergency kit. Systemic adrenaline is part of the Prohibited Substances list for use in sports. Its use requires a Therapeutic Use Exemption [TUE] (70).

**Exercise induced urticaria**

EI-urticaria is frequently driven by physical and environmental stimuli. The most common forms to take into account in the context of exercise include cold urticaria and cholinergic urticaria (51–53). Cold urticaria occurs after exposure to cold objects/air/ fluid/ wind and is a very bothersome condition for swimmers, but also for other sports related to cold exposure (71). In some cases, it induces severe systemic symptoms like anaphylaxis. Cholinergic urticaria occurs within minutes after elevation of the body temperature, regardless whether passive (hot shower) or active (exercise). Solar, aquagenic, vibratory, dermatographic and/or pressure physical urticarias also may occur but are less frequent. Other sports-related rashes can arise through contact with allergens, like some types of clothing, gymnastic or weight lifting chalk, judo
carpet, billiard cue and adhesives for athletic tape (72). Second-generation antihistamines are the first line treatment for most of these subtypes of urticaria and also for skin itch symptoms (73, 74) as they provide symptomatic relief of itching, reduce the number, size and duration of individual hives and significantly improve quality of life (74).

EI-urticaria is not severe, yet has an important impact in performance and quality of life. In athletes, namely in high competitive levels, the older antihistamines compromise psycho-motor skills crucial for them, namely reaction time and visual discrimination (75, 76), so choosing a non-sedating antihistamine is mandatory. Balancing between disease control and antihistamines side-effects in the sports performance is needed.

Competitive sports and asthma: a complex interaction

In recent years there has been a special focus on the increased occurrence of asthma and BHR among top athletes within endurance sports (77). In 1989, an increase in nonspecific bronchial responsiveness after heavy endurance training was found in young competitive swimmers (78). Later, reports were published concerning increased prevalence of asthma and BHR among top cross-country skiers (79, 80). These and other studies confirmed that both BHR and airway inflammation increased through heavy endurance training (78–82). In the Olympic arena, such reports were confirmed by the observed prevalence of EIA of 11 % among the American 1984 summer Olympic athletes (83) increasing to >20 % among the American participants in the 1996 summer Olympic Games, and especially high among cyclists and mountain bikers (84). The use of asthma drugs and, in particular, inhaled beta2-agonists, was shown to be highest in cross-country skiing and speed-skating followed by cycling, Nordic combined (the combination of both cross-country skiing and ski jumping) and swimming during the last three summer Olympic and the last three winter Olympic Games (85).

So, it is nowadays well established that elite athletes have an increased risk for asthma, especially those who take part in endurance sports and in winter sports (60, 85, 86). Many studies have been performed in Olympic or elite-level athletes that have documented high prevalence of EIB, varying between 30 and 70 %, depending on the population studied and methods implemented (42, 87). EIA is actually the most common chronic condition among Olympic athletes (85), with obvious implications for their health, competing performance and quality of life.

Pathogenic mechanisms

Pathogenic mechanisms probably differ in the athlete compared to asthmatic patients (88). Several elite athletes who are diagnosed with EIA have neither personal nor family history of asthma. At rest, they seldom experience asthma symptoms (89), which rather occur during high-intensity exercise. EIB that occurs in athletes which develops during their sports career without other features of clinical asthma has peculiar clinical and pathologic features. So, accordingly, it has been recently proposed designating EIB with asthma (EIB_A) the occurrence of bronchial obstruction after exercise in asthmatic athletes, and EIB without asthma (EIB_wA), the occurrence of bronchial obstruction induced by exercise in athletes without other symptoms and signs of clinical asthma (90). The explanatory model in athletes probably comprises the interaction between environmental training factors, including allergens and ambient conditions such as temperature, humidity and air quality; and athlete’s personal risk factors.

Diagnosis

In athletes, diagnosing asthma is particularly relevant because of potential implications on performance both in training and competition, since airway narrowing during exercise compromises ventilatory capacity and efficiency (91, 92). Additionally, asthma has been pointed out as a significant risk factor for unexplained death in young and healthy subjects (93), and a high proportion of asthma-related deaths has been reported in athletes associated with a sporting event (94). Besides, a subgroup of athletes who are asymptomatic present objective evidence of EIB (95), which raises the question of its potential underdiagno-
sitis and the resulting underperformance. On the other hand, untreated asthma results in chronic sustained inflammation associated with persistent epithelial damage, which contributes to airway remodeling and fibrotic changes, fixed obstruction and progressive lung function decline over time [96].

However, the evaluation of airway damage poses several issues unique to this population [97]. The first issue regards symptoms, as they have been shown to be poor predictors of asthma in athletes [98–100]. The heavy training with the extremely high level of physical fitness and VO2max reached turns difficult to discriminate between physiological and pathologic limitations to maximum exercise [86]. On the other hand, some athletes will not reveal their symptoms due to fear that their asthma disclosure will be detrimental. Therefore, objective evidence of airway damage and asthma is recommended in these subjects [101]. Baseline spirometry is poorly predictive of asthma in competitive athletes [97]. They often record lung function values higher than the general population; they may appear to be within the «normal» range, although, in reality, show a pulmonary deficit on the basis of what is expected for an athlete [11, 102]. Diagnostic methods and positivity criteria to document EIA in athletes are presented in table 2. Other chronic disorders that are possible differential diagnosis related to asthma in athletes are presented in table 3. Heart diseases and other respiratory disorders should be also considered. Obesity, which may represent a differential diagnosis to EIA in the common asthmatic patient, is rare in athletes.

Despite this increased prevalence, it is reassuring that many asthmatic competitive athletes are able to participate on an equal level with their peers in the Olympic Games and in other top level international competitions. Special precautions, however, must be taken with respect to The World Anti-Doping Agency’s (WADA) rules related to the use of medication in sports. It is athlete’s responsibility to know the rules and to abide by them. However, as these guidelines often change, sometimes annually, even with minor changes, the physician caring for subjects who are active in sports should also be updated [91]. Information can be assessed in WADA’s website [103].

Athletes practicing regular strenuous exercise may be at increased risk of URTIs during periods of heavy exercise and for a couple of weeks following competition events [104, 105]. Prolonged, high intensity exercise temporarily impairs the immune competence while moderate activity may enhance immune function. It has been suggested that the relationship between exercise and URTI follows a «J-curve», with moderate and regular exercise improving the ability to resist infections [106–108], while heavy acute or chronic exercise decreasing it [109–111]. The relationship between URTI and exercise is affected by poorly known individual determinants such genetic susceptibility, neurogenic mediated immune inflammation and epithelial barrier dysfunction [9].

Conclusion
EI-hypersensitivity syndromes include EI-asthma, EI-bronchoconstriction, EI-urticaria, which are all significant problems for both recreational and competitive athletes. Appropriate management of exercise induced symptoms is mandatory in order to allow patients to partake in regular exercise training, which in the specific case of asthmatic patients has been shown to be beneficial. Therefore, concerted efforts are needed towards educating clinicians to promote physical activity and weight management, as a supplementary treatment for asthma and allergies.

Despite the increased risk of asthma and immune depression in elite athletes, the physical, mental health, and lifestyle benefits of participation in the sport are numerous and with optimal treatment healthy participation in sports at the elite level can be improved and enjoyed.

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