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INNOVATION HUB
Universitas

PATHOLOGIES IN TEAM SPORTS

INFECTION AND SPORTS

1.2 Infection and Sports

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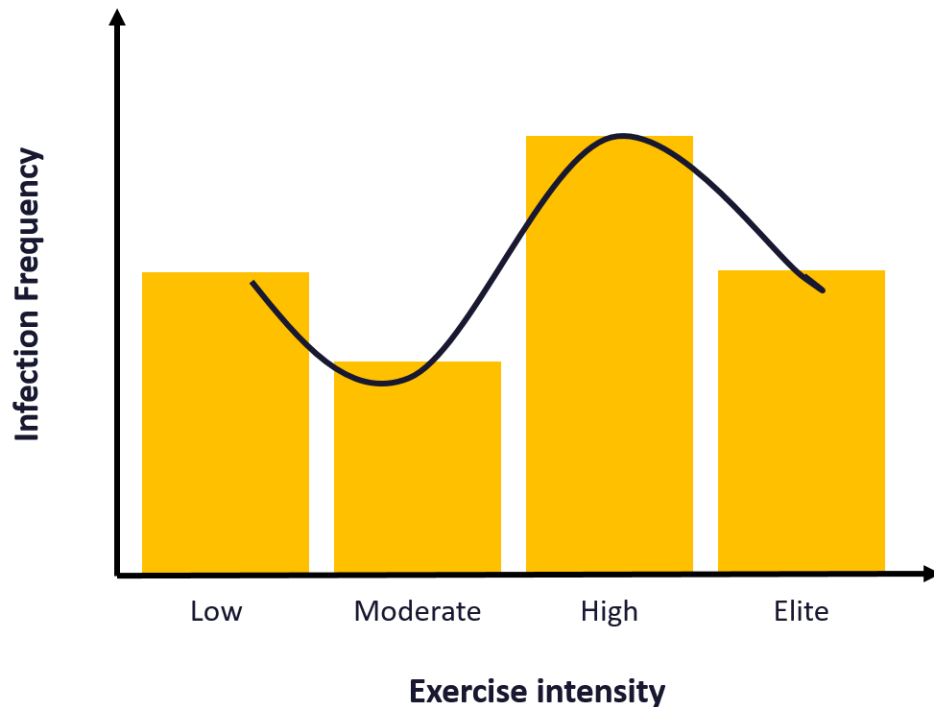
1. Physical Activity and Infection: Defense Mechanisms
2. Infections and athletic performance
3. The body's response to physical exercise during an infectious disease
4. Infectious Disease and Participation in Sports
 - a. Passed on through physical contact: herpes simplex, dermatomycosis, bacterial infections.
 - b. Passed on through young people living together: Respiratory and digestive infections
 - c. Passed on through blood or body fluids: Infectious mononucleosis, hepatitis A, B or C, HIV
5. Infection Prevention for Athletes
 - a. Hygiene precautions
 - b. Immunization
6. Considerations for treating infections in athletes

1. Physical Activity and Infection: Defense Mechanisms

A popularly held belief is that physical conditioning helps prevent disease, while exhaustion or poor physical fitness increases susceptibility to common infections.

Under normal conditions, continued and moderate physical activity improves health. As the physical quality of tissues that make up the locomotor system improves, the adaptation of cardiovascular and respiratory systems to stressful situations facilitates the immune response to infection (Malm, 2006). This has clearly beneficial effects on an individual's psychosocial wellbeing. However, continuous high-intensity exercise compromises the immune system against diseases: it favors the occurrence of mild infections, especially in the upper respiratory tract. Infection evolution is aggravated by physical exercise and negatively influences the evolution of the illness, as depicted below.

Figure 1: S-curve apparent in the relationship between the frequency of infections and the intensity of physical work



Source: adapted from Malm, 2006.

The first line of defense against infections are the anatomical and physiological barriers that prevent pathogens from penetrating the body: skin, mucous membranes, secretions and normal saprophytic microbial flora. Exercise has little influence on these barriers, but skin trauma (abrasions, cellulitis) or hot or cold weather exposure can impact the body's defenses.

If the microorganism impacts these barriers and enters the body, there are secondary non-specific defense mechanisms (phagocytosis, complementary system), as well as specific defenses (humoral and cellular immunity).

Phagocytosis constitutes the second line of protection formed by polymorphonuclear leukocytes and macrophages, which increase during the infectious process, as does their functionality. However, phagocytic activity does not increase with physical exercise.

The complementary system is another of the non-specific mechanisms that is activated during infection; however, there are no changes during athletic activity.

Lymphocytes are first-line defensive cells and, therefore, the most important link between exercise and immune function. It seems that lymphocytes increase with exercise, although its functionality depends on the lymphocytes population: CD4 lymphocytes increase during infection, but there are no changes or they even decrease during training. In contrast, CD8 lymphocytes increase in both cases, so that the CD4/CD8 ratio tends to decrease.

In terms of interferon, interleukin 1 can increase with exercise. It appears that cellular immunity is activated with physical activity, similar to what happens with infection. With regard to immunoglobulins, there is no increase in total or specific immunoglobulins against an antigen during sports practice. However, it has been demonstrated that decreased salivary IgA secretion after physical effort could lead to a predisposition for upper respiratory infections by pathogens, especially viral infections.

Therefore, we cannot yet answer the question as to whether sports or regular training affect the individual's resistance to infection. The data regarding the protection that physical exercise can exert against this type of disease is not conclusive; it seems that an athlete is no more resistant to infections than a sedentary individual. Moderate exercise improves immunity and decreases the presence of banal infections. However individuals subjected to intense and/or excessive quantities of training—especially if this reaches overtraining levels—suffer infections more frequently and with more intensity.

2. Infections and athletic performance

We should ask ourselves if the infection has the potential to cause serious complications during exercise and whether the symptoms and signs that appear during exercise could reduce athletic performance.

The infection is how the pathogen penetrates and proliferates in the host. The disease is the organic manifestation of the fight between them and depends on the toxins of the virus, the site of infection and, above all, the varying intensity and quality of the host's reaction when it comes to setting in motion all the defense mechanisms.

The presence of infection and the processes that can accompany infections (such as fever, anemia, iron deficiency, decreased clarification of catabolites, liver disease, nephropathy, residual cardiac injury, joint flogosis and painful numbness in the form of myalgia or arthralgia) will

reduce athletic performance, while at the same time putting the athlete's health at some risk (Drobnic, 1997, Friman, & Ilbak, 1992).

3. The Body's Response to Exercise During an Infectious Disease

The evolution of an infection in an athlete is similar to that in a sedentary individual. The incubation time, symptomatology and resolution do not typically vary. However, intense exercise or demand on an athlete's systems puts them to the test when they are affected by an infection, which differs from when people rest. Some neurotropic pathogen infections are potentially more serious or even fatal in very muscular and active individuals, such as poliovirus or Coxsackie virus (Drobnic, 1997, Wesslen et al., 1992, Priemer, Keil, & Kandolf, 1999). In this sense, intense exercise can be very dangerous and is contraindicated during the acute and symptomatic phase of infectious diseases, especially those caused by microorganisms that have a predilection for the tissues that will be activated with exercise, as occurs in polio and in viral myocarditis. However, for infections with a low level of general affectation, recovery can be promoted by low intensity physical activity (Friman, & Ilbak, 1992).

During the acute and convalescent phases of many diseases, physiological responses to physical exercise can be adversely impacted.

Fever alters cardiovascular response during exercise (decreases working capacity, increases heart rate and cardiac output) which can lead to presyncope or syncope, with reduced maximum performance. In addition, orthostatic hypotension can occur during effort recovery and dehydration due to fever could exacerbate these responses.

Body temperature regulation is affected and, combined with dehydration and altered vasomotor response, this can lead to exhaustion or if there is hot weather, it can also lead to heat stroke.

In respiratory infections, the resistance of airways increases, as do the anomalies in the ratio between ventilation and perfusion. Diffusion capacity also decreases. As a result of these processes, exercise tolerance is compromised. Abnormalities in pulmonary function can last for weeks.

4. Infectious Disease and Participation in Sports

A frequent decision that physicians face is when to allow an athlete to return to training or competition after an infectious disease.

A player is more exposed to the infection. Continued contact with contaminated objects or environmental elements facilitates germ entry, especially if the mechanical barrier, that is the skin, is altered (Adams, 2002). Elite athletes must travel throughout a season, which occasionally involves extreme weather changes, changes in schedules and in biorhythms, as well as exposure to different diets, in addition to changes in normal rest patterns. Furthermore, many athletes, during training and sports practice, experience a high rate of shared living in closed groups, since they share poorly ventilated residences, locker rooms and sports halls, not to mention that these spaces may not be very hygienic, which makes them more susceptible to the spread of certain infections.

a) Contagion due to physical contact:

- *Herpes gladiatorum*: a herpes simplex infection type 1 and 2 that is transmitted by contact and friction between two wrestlers. It is a bothersome and contagious infection for opponents. There is no cure, only preventative medication that can be used when there is an outbreak.
- *Tinea corporis*: an infection that can be transmitted in contact sports, caused by *Trichophyton tonsurans* and relatively easy to treat.
- *Pseudomonas* spp.: grows in a humid environment. Folliculitis in athletes occurs who use Turkish baths and saunas. It is transmitted through towels and clothing.

b) Passed on through young people living together:

- Respiratory tract infections: viruses that cause infections such as the common cold, rhinopharyngitis, pharyngotonsillitis, tracheobronchitis, otitis, such as adenovirus, mixed herpes virus, myxovirus, enterovirus, chlamydia, mycoplasma.

Respiratory system infections are more frequent, especially in certain groups of athletes. Activities that put intense demands on the respiratory system, especially in variable environmental

conditions (such as temperature, humidity, pollution, allergens, etc.) test physical adaptation and the immune system. Among cyclists, long-distance runners, mountaineers, swimmers, and similar, the incidence of upper respiratory infections is higher than in the general population, especially at certain moments of the season, due to exposure to different environments, to multiple pathogens and different levels of immune defense (Malm, 2006; Spence et al., 2007).

- The common cold originates from over 200 different viruses and more than half of these are rhinoviruses. Although the symptoms are usually benign and localized in the upper respiratory tract, they can be complicated by bacterial sinusitis or otitis media.

Is it dangerous to exercise when you have a cold? There is no simple answer, but there are some circumstances in which physical exercise is not recommended. If the athlete has a fever, the combination of excess heat produced by exercise and poor regulation of temperature due to the fever can lead to a thermal injury. The body fights against the cold and fever, the thermoregulatory system returns to normal and heat loss is initiated which could lead to dehydration. It is better to rest and avoid exercise when the athlete has a fever.

It is worth remembering that frequent colds could indicate that an athlete has reached a state of overtraining.

c) Passed on through blood or body fluids:

- Infectious mononucleosis: is a disease caused by the Epstein-Barr virus (EB), it is more common in people aged 30 and under. Characterized by asthenia, pseudomembranous pharyngotonsillitis, cervical or generalized adenopathies, and hepatosplenomegaly is also common.

There is leukocytosis with lymphocytosis and alterations in liver tests. Diagnosis is confirmed by detecting specific IgM immunoglobulins against the EB virus. The disease heals spontaneously, although the virus can persist in the body for months or even years. In some athletes there are two significant complications: first, the splenic fragility in the acute phase of the disease can lead to a rupture of the spleen in response to minimal trauma; second, it may result in chronic fatigue syndrome or post-

infectious asthenia that can last for a long period of time and should be considered when evaluating the patient (and should be taken into account in possible asymptomatic EB virus infections in order to ensure a correct diagnosis).

Some physicians permit aerobic sport moderated to the athlete's tolerance. Contact sports must be avoided until the size of the spleen normalizes.

- Other airborne or enteric viral infections include those caused by the Coxsackie B3 virus, which causes myocarditis, which usually heals spontaneously but is fatal in some cases. Infectious myocarditis can be symptomatic, presenting as arrhythmia or a fatigued state, which is not due to overtraining, but to an infection that needs to be treated. This can sometimes be a result of excessive demands during exercise on a weak heart due to infection or with an inflammatory process occurring in the muscle or conduction tissues.
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- Upper respiratory infections (URI) are disabling for an athlete. These infections may be more frequent in the winter months. The repercussions of a URI on cardiac, respiratory and muscular functions often lead to long-term complications. Prevention includes avoiding sudden effort and focusing on the best possible recovery from the infection. Special attention should be given to athletes with underlying inflammatory processes such as asthma or those who train or compete in specific environments, such as swimming pools, at high altitude, in a polluted environment, and so on.
- Gastrointestinal infections transmitted by poor quality water or food are also prevalent. These infections cause diarrhea and possible dehydration, thus prevention is important.

Infections acquired during athletic activity are due to contamination of visible skin lesions or through contact with another player's blood or body fluids.

- Hepatitis B: protective immunization is an option for athletes, especially those who play contact sports.
- Hepatitis C: insidious onset, sometimes asymptomatic, frequently leads to chronicity, cirrhosis and hepatocellular carcinoma.

- AIDS (acquired immunodeficiency syndrome): the AIDS virus is less abundant in blood and less detectable in secretions such as sweat or saliva compared to hepatitis B. Contagion can increase when an AIDS or HIV carrier has skin lesions. Contagion is possible. The most effective preventive measure is to stop the athlete from playing and treat them until there is no possibility of infection.

5. Infection Prevention for Athletes

Hygiene precautions:

- Personal hygiene.
- Environmental hygiene: particularly in places where there is humidity such as showers, locker rooms, saunas, Turkish baths, chlorinated pools.

Prior information about competitors:

- Skin infections: ideally an athlete with this type of pathology does not participate in contact sports.
- Infections transmittable by contact or by blood and body fluids: withdraw the injured player from play until bleeding has stopped and the wound is disinfected. The physician and physiotherapist must wear gloves and use disposable supplies to avoid contagion.

Active immunization:

There are vaccines that should be mandatory for all team or contact sports participants, such as tetanus, diphtheria and antivirals such as polio, measles and hepatitis B.

For professional athletes who live in high performance centers, in student residences or similar, an annual flu vaccine is recommended.

6. Infection Treatment for Athletes

It is often believed that antibiotics negatively impact performance. Post-infectious asthenia is produced by the infection itself, not by the use of antibiotics.

- Antibiotic treatment of the infection does not reduce performance or cause fatigue. There is no evidence that demonstrates this. Energy levels can be affected in a very secondary way by the side effects of some antibiotics or by individual interactions (intestinal

dysbacteriosis, heartburn, etc.) (Malm, 2006, Drobic, 1997). Reduced athletic performance at the time of antibiotic treatment is the product of the infectious process that requires treatment.

- Antibiotic treatment does not need to be modified for athletes. Germs are not selective. Empirically, for some treatments and in specific acute situations, antibiotic treatment can begin with a double starting dose, in order to reach the CMI more rapidly. Evidence does not indicate that evolution will be dramatically improved, but it is a way to ensure the first few days of treatment are working and thus ensure that the athlete is being well cared for. For athletes who follow hypoproteic diets or are in a dehydration period, the antibiotic dose must be adjusted accordingly.
- Treatment with corticosteroids, when necessary, must comply with current anti-doping regulations. If necessary, request a standard therapeutic use exemption (TUE).

Conclusions:

- Intense exercise reduces defenses against infection.
- Moderate exercise can reduce defenses.
- Physical exercise can negatively impact the healing process of an acute infection, and can negatively affect the evolution of the infection.
- Both chronic and acute infections can reduce physical performance.
- There are preventative measures to avoid infection in sports.
- Antibiotics do not cause asthenia or decrease physical performance.

Allergies and Sports

Dr. Montse Bellver - Dr. Franchek Drobic

1. Exercise-induced respiratory disorders
 - a. Pathogenesis of exercise-induced asthma
 - b. Diagnosis of exercise-induced respiratory disorders
 - c. Treatment of exercise-induced asthma, bronchoconstriction and rhinitis
 - d. Allergy and asthma in athletes: information for non-specialist physicians
2. Exercise-induced urticaria and anaphylaxis
 - a. Pathogenesis

- b. Cholinergic urticaria: clinical features
- c. Anaphylaxis: clinical features
- d. Diagnosis
- e. Treatment

Allergies and Sports

Physical exercise is fundamental to a child's overall education and it is a healthy activity for adults. For an asthmatic child, suitable physical exercise is helpful from a medical and psychological point of view, as it favors adaptability, independence and communication between the asthmatic child and their environment.

Suffering from an allergic illness does not exclude anyone from practicing sport. There are many elite athletes who are also allergy-sufferers who are not seriously affected in terms of their engagement in elite sports. (Durán, 2011, <https://goo.gl/3h4mqW>).

Allergic illnesses that worsen or show symptoms with physical exercise include bronchial asthma, urticaria, mainly cholinergic, and anaphylaxis.

Exercise-induced (EI) hypersensitivity disorders are a serious problem for both recreational and competitive athletes. These affect the respiratory (asthma, bronchospasm and rhinitis), cutaneous (urticaria and angioedema) and cardiovascular (anaphylaxis) systems. Although most patients survive hyperresponsiveness, exercise is likely to cause a reoccurrence of the same conditions and, consequently, future exercise may often need to be reduced. In many cases, these disorders are associated with allergic sensitivities (immunoglobulin IgE). A group of experts from the European Academy of Allergy and Clinical Immunology and the American Academy of Allergy, Asthma and Immunology met to discuss the pathogenesis of these disorders and how to diagnose and treat them. They consequently published a consensus report. The goal was to provide physicians with guidance for diagnosing, understanding and managing hypersensitivity disorders, to allow their patients to return safely to exercise-related activities.

Exercise-induced respiratory disorders

Exercise-induced asthma is defined as obstruction of the lower airway with coughing, wheezing or dyspnea in patients with underlying asthma (Bousquet et al., 2007). The same clinical features in individuals without asthma is defined as bronchoconstriction. It is debatable whether EI-asthma and EI-bronchoconstriction are different, as they have similar symptoms and share the same physiopathological mechanism. An asthma crisis significantly affects an athlete's performance.

Exercise-induced asthma (EIA) manifests itself in almost all uncontrolled asthmatics and in most children with asthma (Bacharier et al., 2008). EIA or bronchoconstriction is not only more prevalent in elite athletes (Haahtela, Larsson, & Bonini, 2005), particularly in those who participate in endurance sports such as cross-country skiing, swimming, road cycling and long distance running, but also in sprinters and endurance sports in special environments, such as ice hockey and trail runners, more so than in recreational athletes (Parsons et al., 2007; Weiler, & Ryan, 2000).

Exercise-induced rhinitis is characterized by itching, sneezing, runny nose, nasal congestion and occasional anosmia caused by exercise (Bonini et al., 2006). This disorder is usually accompanied by symptoms that affect the eyes, ears or throat. Underlying noninfectious rhinitis can be classified, according to its etiology, as allergic (IgE-mediated) and non-allergic and intermittent or persistent and mild, moderate or severe (ARIA classification) (Bonini et al., 2006). The prevalence of underlying rhinitis in athletes and non-athletes is comparable. Allergic rhinitis affects 25% of adults in Europe and up to 40% of children worldwide (Bousquet et al., 2008, Bjorksten, Clayton, Ellwood, Stewart, & Strachan, 2008). Children are typically encouraged to participate in sports. The sleep patterns of athletes with rhinitis, particularly with congestion, are often affected, with daytime sleepiness, fatigue and impaired performance.

Pathogenesis of exercise-induced asthma:

Exercise increases ventilation and, as a result, dehydrates the airways (right flow diagram), which increases the osmolarity of the airway's surface water layer. This hyperosmolarity activates epithelial cells and mast cells, leading to the release of mediators, which in turn causes the smooth muscle of the respiratory tract to contract and mucus

hypersecretion. Athletes with EI-asthma or bronchoconstriction have increased cellular markers of inflammation in the respiratory tract and increased levels of histamine, tryptase, leukotrienes and chemokines. These are the same biomarkers that are usually observed in asthma. In addition, heat loss with cooling of the respiratory tract (left flow diagram) stimulates the tract receptors and induces vasoconstriction. Reactive hyperemia occurs with reheating, which is associated with vascular congestion and tissue edema, further decreasing airflow. EIA can also be modulated by preexisting atopy with bronchial hyperreactivity and airway inflammation, by autonomic dysregulation associated with intensive training and by sport-specific environmental factors.

Diagnosis of exercise-induced respiratory disorders:

It is worth considering whether patients with EIA have underlying asthma that is aggravated by exercise due to poor asthma management. The methacholine challenge test can demonstrate bronchial hyperreactivity, even when the baseline spirometry is normal and does not necessarily correlate with exercise hyperreactivity. SABAs (short-acting beta2 agonists) can reverse exercise-induced bronchospasm.

The methods and thresholds for documenting EI-bronchoconstriction are different for recreational athletes and competitive athletes. For recreational athletes, free running for children or a simple 10 minute jog (1 km) for adults may be enough to diagnose EI-bronchoconstriction (10% decrease in FEV1). For competitive athletes, exercise should reach 90% of maximum heart rate or 40-60% of maximum ventilation for 6-8 minutes on a treadmill or exercise bike (Crapo et al., 2000; Bonini et al., 2007). The relevant authorities have established precise criteria for diagnosing asthma which will continue to be updated.

The criteria established by the International Olympic Committee to document EI-bronchoconstriction in athletes for Beijing 2008 is as follows:

- An increase in FEV1 with a bronchodilator > 12% of the baseline or a predicted FEV1 that exceeds 200 ml.
- A $\rightarrow$ 10% FEV1 decrease from the beginning, in response to exercise or voluntary eucapnic hyperpnea.
- A $\pm$ 15% FEV1 decrease from the beginning after inhaling 22.5 ml of 4.5 g% NaCl (sodium chloride) or £ 635 mg of mannitol.
- A $\pm$ 20% FEV1 decrease from the beginning in response to methacholine: PC20 £ 4 mg/ml or PD20 £ 400lg (cumulative dose)

or £ 200lg (non-cumulative dose) in athletes who do not take inhaled corticosteroids (ICS) and PC20 £ 16 mg/ml or PD20 £ 1600lg (cumulative dose) or £ 800lg (non-cumulative dose) in athletes who take ICS for at least 1 month¹.

The diagnosis of EI-rhinitis is clinical, but it can be confirmed with a stress test and objective measurements of nasal obstruction (maximum nasal flow, rhinomanometry and acoustic rhinometry), by mucociliary clearance and due to the symptoms. However, stress tests are not standardized or validated as diagnostic tools for EI-rhinitis. Underlying allergic or nonallergic rhinitis is diagnosed using medical history, physical examination and evaluation of specific IgE, through skin and laboratory tests. A nasal allergen test is sometimes useful, although it is primarily a research tool. Rhinitis and asthma often occur together and each must be considered independently of which is clinically more evident (Bousquet et al., 2008).

Treatment of exercise-induced asthma and bronchoconstriction.

Most drugs that are effective in the treatment of chronic asthma are also effective in the treatment of EI-asthma and EI-bronchoconstriction. Good management of underlying asthma minimizes airway narrowing during exercise (Bousquet et al., 2007; Weiler et al., 2007). If EI-asthma worsens it may be a sign of inadequate management of the underlying asthma and treatment should be reviewed. Controlling rhinitis can also improve asthma management. Reduced nasal congestion should improve sleep and therefore, improve an athlete's quality of life and, most likely, athletic performance. Certain medications are prohibited for athletes with asthma and rhinitis who participate in regulated competitions.

Short-acting beta2 agonists (SABA) are effective in reversing EI-asthma or bronchoconstriction and are also used in prevention. Effectiveness of inhaled SABAs (salbutamol and terbutaline) for this disorder is optimal 20

¹ In the case of an athlete with diagnosed, well-managed asthma, who registers a negative result in the bronchial challenge tests, but still seeks approval for the use of inhaled beta2 agonists, the following documents must be included in their medical record: medical consultations for the treatment of asthma, visits to the hospital emergency department, admissions for acute exacerbations of asthma and treatment with oral corticosteroids. Additional information that may help includes: the age of asthma onset, a detailed description of asthma symptoms both day and night, triggers, use of medications, history of atopic or childhood asthma disorders and physical examinations, along with the results of skin or RAST tests to document allergic hypersensitivity. Negative bronchial challenge and the results of allergy tests should also be included with the documents presented to the International Olympic Committee.

minutes after inhalation and decreases within a few hours.

Long-acting beta2 agonists (LABA) (formoterol and salmeterol) provide up to 12 hours of protection after a single inhalation. However, only formoterol acts as fast as SABAs. Therefore, to reverse EI-asthma or bronchoconstriction, formoterol or a SABA should be chosen, but not salmeterol. Inhaled beta2 agonists can mask worsening airway inflammation and should never be used regularly without an inhaled glucocorticoid (Bousquet et al., 2007). In addition, tachyphylaxis occurs with the regular use of beta2 agonists (Lang, 2007), which reduces its protective effect against EI-asthma or bronchoconstriction, even if it is used together with an inhaled corticosteroid (Bousquet et al., 2007). Therefore, avoiding the daily use of inhaled beta2 agonists will optimize their rescue or preventive effect when they are most needed.

Treatments with inhaled glucocorticoids or leukotriene antagonists control underlying asthma and reduce EI-asthma or EI-bronchoconstriction in most patients (Weiler et al., 2007; Koh, Tee, Lasserson, & Irving, 2007). Zileuton is a leukotriene synthesis inhibitor and montelukast, zafirlukast and pranlukast are antagonists of the CysLT1 receptor. It is important to note that tachyphylaxis with antileukotrienes and inhaled glucocorticoids has not been reported (Bousquet et al., 2007).

H1-antihistamines and cholinergic antagonists have minimal effects on EI-asthma or bronchoconstriction, whereas chromones administered before exercise reduce EI-bronchoconstriction by 30%.

Xanthines, calcium channel blockers and inhaled furosemide have moderate mitigating effects on EI-bronchoconstriction, but side effects generally mean they are not a preferred treatment (Bousquet et al., 2007; Weiler et al., 2007).

In difficult to manage EI-asthma or bronchoconstriction, the combination of inhaled glucocorticoids, oral leukotriene antagonists or inhaled beta2 agonists can be beneficial (Bousquet et al., 2007).

Intranasal corticosteroids, both in non-allergic and allergic rhinitis, reduce all symptoms, including congestion, and improve sleep quality (Hughes et al., 2003). Non-sedating antihistamines mitigate itching, sneezing and rhinorrhea (but not congestion) in allergic rhinitis (Tanner, Reilly, & Meltzer, 1999).

Nasal sprays containing a sedating antihistamine (azelastine) reduce symptoms but diffuse through the mucosa and cause drowsiness (Golden et al., 2000, Chicharro, Lucia, Vaquero, & Pérez, 1998). Intranasal decongestants act quickly, however, they cause rebound congestion (rhinitis medicamentosa) if used regularly. An intranasal anticholinergic (ipratropium) rapidly inhibits rhinorrhea and is the first-line rescue therapy or prophylactic treatment when rhinorrhea is the predominant symptom.

Intranasal chromones are not effective rescue agents and provide minimal benefit when administered before exercise. CysLT antagonists benefit both rhinitis and asthma.

Other therapeutic options beyond pharmacotherapy in the treatment of EI-asthma, EI-bronchoconstriction and EI-rhinitis include avoiding allergens or irritants, as well as immunotherapy in patients with specific allergies (Bousquet et al., 2007). A mask that heats inhaled air may be helpful when exercising in cold air. Infections, gastroesophageal reflux, sinusitis and exposure to pollutants and tobacco smoke must be managed. Heating and cooling exercises can reduce EI-asthma or bronchoconstriction. In accordance with pathophysiology, hydration should be encouraged.

Which medications for asthma and rhinitis are regulated at sporting events?

- Stimulants are prohibited during competitions, including oral and nasal decongestants (ephedrine, methylephedrine). Intranasal decongestants (oxymetazoline, phenylephrine, propylhexedrine) are allowed although they are monitored.
- Beta2 agonists are forbidden, unless an exemption for therapeutic use of asthma inhalants is obtained for the first time, despite the fact that inhaled beta2 agonists do not improve the performance of athletes without asthma. Oral beta2 agonists, which are ineffective in EI-bronchoconstriction, are prohibited in regulated competitions.
- Sedative antihistamines, although not prohibited, impair performance and should be avoided.
- Oral and parenteral glucocorticoids are prohibited, while the use of topical intranasal glucocorticoids is allowed. However glucocorticoids inhaled in competitions need abbreviated therapeutic use exemption.
- Diuretics, such as furosemide, are prohibited as they can mask

the presence of other prohibited drugs. An exemption for therapeutic use is not valid if an athlete's urine contains a diuretic in association with a threshold or sub-threshold level of a prohibited substance (Fédération Internationale de Football Association [FIFA], 2006).

Allergy and asthma in athletes: information for non-specialist physicians

- Early detection and correct diagnosis are fundamental for successful management of exercise-induced (EI) hypersensitivity disorders.
- Asthma or EI-asthma symptoms and baseline spirometry are not very predictive of EI-asthma in competitive athletes.
- Exercise, methacholine, mannitol or hypertonic saline solution or an eucapnic voluntary hyperpnea test performed by experienced personnel are more useful.
- Treatment of underlying asthma and rhinitis should follow the available guidelines. Underlying rhinitis must be evaluated and treated in patients with EI-asthma, since it increases the severity of asthma and EI-asthma.
- Combinations of various types of drugs are often necessary to completely control EI-asthma in athletes, but for those participating in competitions, the latest World Anti-Doping Agency regulations (<http://www.wada-ama.org/en/>) and the International Olympic Committee regulations (http://www.olympic.org/uk/organisation/commissions/medical/index_uk.asp) must be taken into account.
- If EI-asthma does not respond to treatment, a differential diagnosis must be made, considering EI-vocal cord dysfunction, EI-arterial hypoxemia, pulmonary edema induced by swimming, poor physical condition, other pulmonary disorders and cardiovascular diseases.
- In the case of anaphylaxis during exercise, carefully document food intake history during the preceding 24 hours, paying special attention to wheat products and seafood.
- Athletes at risk of EI-anaphylaxis must have an action plan to deal with future events, including suspending exercise at the first sign or symptom, having an EpiPen (epinephrine injection) immediately available and knowing how to use it, and using the Trendelenburg position for hypotension symptoms.

Exercise induced urticaria and anaphylaxis

Exercise-induced anaphylaxis is a physical allergy caused by vigorous and sometimes moderate exercise (Castells, Horan, & Sheffer, 2003). In these patients, exercise is not invariably accompanied by an anaphylactic reaction, but only on certain occasions or in certain circumstances and can often be disconcerting for the patient. Some people develop food-dependent EI-anaphylaxis, whereby they exercise several hours after the ingestion of a food allergen which the individual is sensitive to, or, in some cases, after the ingestion of any kind of food (Morita, Kunie, & Matsuo, 2007; Du, 2007). Symptoms of fatigue, pruritus, heat, flushing and urticaria can progress to angioedema, wheezing, rhinitis, gastrointestinal symptoms and cardiovascular syncope (Sampson et al., 2006). Favorable factors may include the use of aspirin or NSAID (non-steroidal anti-inflammatory drugs), exposure to high levels of pollen, insect bites, extreme temperatures and humidity or even stress or menstruation.

The most frequent food allergies are due to wheat (60%) and seafood (18%), but can also be due to peanuts, walnuts, milk, eggs (Morita et al., 2007; Romano et al., 2001), fruits and vegetables. Loss of susceptibility to EI-anaphylaxis over time is unusual, but in a 10-year study, episode severity stabilized for 46%, decreased for 47% and worsened for 7% (Castells et al., 2003).

Pathogenesis of exercise-induced urticaria and anaphylaxis

Anaphylaxis and urticaria develop after the release of mediators such as histamine, CysLT and PGD₂ that are vasodilators, increase vascular permeability and contract the smooth bronchial muscle. These mediators are secreted via mast cells and basophils, which can be activated by allergens (Schwartz, 2006). EI-anaphylaxis and urticaria associated with food-specific IgE can develop in this way.

In EI-anaphylaxis associated with food, exercise increases the entry of recently ingested but incompletely digested food proteins, including allergens, into the body's circulation. Then they migrate to perivascular and tissue spaces, where the mast cells armed with the Allergen-specific IgE reside (Morita et al., 2007). Increased absorption of allergens derived from wheat gliadin occurs experimentally with exercise or taking aspirin. For those with EI-anaphylaxis without a food allergy, the pathogenesis is less clear. Some cases occur only with exercise; others with exercise after the ingestion of any kind of food. Anaphylaxis during exercise may also coincide with an insect bite (Schwartz, Yunginger, & Schwartz, 1995) or with an underlying disease, such as systemic mastocytosis (Fricker,

Helbling, Schwartz, & Muller, 1997; Haeberli, Bronnimann, Hunziker, & Muller, 2003), or with activating mutations in the tyrosine kinase kit, which increases the risk of anaphylaxis in general (Simons et al., 2007). Some cases of EI-anaphylaxis develop in athletes with cholinergic urticaria (which elevates body temperature during exercise), with cold-induced urticaria, and with chronic urticaria, which has IgG anti-IgE autoantibodies that worsen during exercise. Other cases of EI-anaphylaxis or urticaria may occur in the context of idiopathic anaphylaxis (Greenberger, 2007).

Clinical features: cholinergic urticaria

Cholinergic urticaria is characterized by small round wheals, surrounded by red skin. The appearance of wheals is accompanied by itchiness of the skin which may be more or less intense. It tends to resolve spontaneously, in minutes or hours.

Cholinergic urticaria is typically triggered by physical exercise and also by perspiration, heat and anxiety. In the case of very intense physical effort, the wheals appear disseminated across the surface of the skin.

Cholinergic urticaria can be prevented through adequate warm-up, avoiding exposure to high temperatures and taking preventive medication, usually antihistamines, before exercise. Avoiding excessive perspiration also helps prevent this problem.

Some patients experience a transient outbreak of urticaria, which disappears spontaneously during continued physical effort. In any case, it is best to stop exercising when the first symptom appears, which is usually generalized itching. Cholinergic urticaria outbreaks resolve completely in minutes or hours. (Basomba, n.d., pp. 8-9).

Clinical features: anaphylaxis

Anaphylaxis is the most serious response in allergies, since it involves several organs of the body simultaneously.

An anaphylactic reaction is easily identifiable by its rapid development (seconds or minutes) and by the intensity of its manifestation. After contact with the triggering allergen, the sensitized patient develops, almost instantaneously, generalized itching (it is common for itching to start on the palms of the hands and soles of the feet), disseminated urticaria (hives), facial swelling (angioedema), coughing, wheezing and chest fatigue (bronchial asthma crisis). In the most severe cases there is a sudden drop in blood pressure (hypotension), heart palpitations (tachycardia) and laryngeal edema (edema of the glottis), which can eventually lead to loss of consciousness. The severity of the condition requires adequate and immediate treatment of the anaphylactic reaction; an exhaustive and detailed investigation must be carried out as soon as possible by an allergist.

The causes of anaphylaxis are very diverse; the most frequent and thus significant causes are food and medicines. (Basomba, n.d., pp. 9-10).

Diagnosing exercise-induced urticaria and anaphylaxis.

Anaphylaxis must be diagnosed in accordance with the clinical criteria agreed upon in 2005 (Sampson et al., 2006). Food and exercise and the timing of same during the 24 hours prior to the episode should be documented in the medical record. IgE responses to relevant allergens should be tested using skin tests (including fresh fruits and vegetables) and laboratory tests. An exercise challenge, with or without food, is another option. The differential diagnosis of EI-anaphylaxis includes heart and respiratory diseases along with appropriate tests. Periodic retesting for a loss of sensitivity to food and exercise is recommended, as the natural evolution of food-dependent EI-anaphylaxis is unpredictable (Du, 2007).

Cholinergic and cold-induced urticarias are also closely linked to exercise (Powell et al., 2007; Zuberbier et al., 2006). Cold urticaria occurs on contact with cold air, fluids or objects, which puts swimmers or skiers at greater risk. Drowning due to cold-induced anaphylaxis can occur in cold water. Cold-induced urticaria can be confirmed by placing an ice cube on the skin for up to 20 minutes to test whether urticaria appears

during rewarming of the skin. Cholinergic urticaria occurs minutes after an increase in body temperature, for passive (hot shower) or active (exercise) reasons, and may progress to include angioedema, bronchospasm and hypotension. The diameter of cholinergic urticarial welts are less than 5 millimeters, while those associated with EI-anaphylaxis are substantially larger. Solar, aquatic, vibratory, dermatographic and physical urticarias due to pressure may also be associated with EI-anaphylaxis.

Treating exercise-induced urticaria and anaphylaxis

Treatment for exercise-induced anaphylaxis and urticaria focuses on preventing and treating the acute process (Sampson et al., 2006; Simons et al., 2007).

Prophylactic management focuses on avoiding triggers, particularly foods. Specific food allergens should be avoided for at least six hours before exercise. As a general rule, affected patients should refrain from physical effort for two hours after eating, regardless of any other consideration. A dietitian will help manage exposure. "It should be remembered that the intake of minimal, sometimes unnoticed quantities of such foods are enough to trigger an anaphylactic response" (Basomba, n.d., p.11).

When EI-anaphylaxis occurs after the ingestion of food, an abstinence interval of between two to four hours is generally sufficient, but individual variation is considerable.

For children with food allergies, their teachers, close friends and family members will need specialized information. Avoid beta blockers, angiotensin converting enzyme inhibitors, and angiotensin receptor blockers, as these medications can increase anaphylaxis severity. Aspirin and NSAIDs increase gastrointestinal permeability and should also be avoided. Prophylaxis with H1 and H2 antihistamines can mitigate urticaria (Powell et al., 2007), but not the cardiovascular and respiratory manifestations of anaphylaxis.

The goal of immediate treatment is to improve cardiovascular (hypotension) and respiratory manifestations as these are the main causes of death (Sampson et al., 2006). A personal emergency plan must be established, which could include a medical identification alert device and exercising with a trained partner. Patients must learn to recognize their first symptoms and signs of EI-anaphylaxis and stop exercising

immediately.

Before the first symptoms, the initial reaction is usually itching, characteristically in the palms of the hands and soles of the feet. The patient must stop exercising and sit or lie down on the floor if they feel dizzy. (Basomba, n.d., pp. 11-12).

The anaphylactic response must be treated immediately if there are signs of severity, difficulty swallowing or breathing or syncope. In general, it is necessary to subcutaneously administer epinephrine and associated intramuscular glucocorticoids simultaneously (Basomba, n.d.). The patient and the people close to them must be trained in how to use these medications. If these medications are not available, the patient must be immediately transported to a medical center.

Some patients experience a temporary improvement of symptoms before relapsing after a few hours. Therefore, if the initial condition was severe, an observation period in the following hours is advisable, preferably in a hospital setting. (Basomba, n.d., p. 12).

"If the patient carefully follows all preventive measures, performing physical exercise is a safe activity. However, it is always advisable to carry the necessary medication in case of a reaction "(Basomba, n.d., p.11).

The Trendelenburg position must be learned, as it facilitates the perfusion of vital organs against hypotension. Epinephrine (EpiPen or EpiPen Jr.) must be injected intramuscularly into the lateral thigh to improve airflow and vascular integrity. Once medical emergency personnel are involved, anaphylaxis should be managed in accordance with published guidelines.

There is a quantitatively small group of patients who suffer from anaphylaxis of unknown origin (or Idiopathic Anaphylaxis). Despite an exhaustive exploration, no allergic factor is detected and thus the cause remains unclear. (Basomba, n.d., p. 11).

"The only effective prevention for these patients is avoiding the precipitating factors of the reaction, as is sometimes the case with physical exercise" (Basomba, n.d., p.11), associated with the ingestion of foods that provoke a response.



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