The Asthma Center Education and Research Fund
ADVISOR

Exercise-induced asthma

Playing the game—without limits

Vigorous exercise is one of the most common causes of bronchospasm that can affect individuals of any age and fitness level. Symptoms include coughing, wheezing, chest tightness, chist discomfort or burning, and/or shortness of breath—classic asthma symptoms.

Factors contributing to *exercise-induced asthma* (EIA) include the intensity of activity, the degree of airway stability, control of underlying chronic asthma and temperature/humidity of inhaled air. Local air pollution can also play a role in worsening symptoms. EIA is most frequently diagnosed in children and young adults, who are more likely to engage in strenuous activity.

While exercising, the passage of cool, dry air flowing over moist, warm bronchial tubes can cause bronchial heat loss. Many studies have demonstrated that cooling of the airways resulting from increased air movement along the airways is one of the main causes of EIA in susceptible individuals.

Exercise-induced asthma can present alone or coexist with other forms of asthma. However, it is uncommon for EIA to be the only presentation of asthma when one evaluates a patient over time, with elite athletes being a common exception. It is important to confirm the diagnosis objectively, since other respiratory and cardiac disease entities can mimic EIA (e.g., paradoxical vocal cord dysfunction, heart disease, etc. See Table 2), thus delaying proper diagnosis and treatment.

EIA Mechanism

Airway cooling that causes EIA or bronchospasm is thought to be non-immunologic and non-pharmacologic in origin. Inhaled air is conditioned mostly in the upper airway through the addition of moisture and warmth before it arrives deep inside the lungs.

During exertion, respiratory heat exchange increases. As cool or dry air is inhaled, heat is transferred away from the airway mucosa to air passing through the bronchial tree. Inspired air is primarily heated and humidified by the nasal passageway and upper airway to mimic the body's internal environment.

Mucosal moisture evaporation accounts for most of the heat transfer. Dry air holds more moisture as it is heated. In contrast, the opposite effect occurs during expiration, when warmer alveoli air (in the lung air sacs) flows out over the cooler bronchial tree. The result is a heat transfer back to the mucosa.

When large volumes of air move quickly through the airway—as with intense exercise—conditioning of inspired air occurs in the lower airway, rather than in the upper airway. Heat and moisture are added to the inhaled air. The bronchial mucosa temperature is then lowered due to moisture evaporation, and the patient experiences EIA symptoms.

Another possible mechanism contributing to EIA may be an increase in osmolarity of the pericilliary fluid, which can occur during conditioning of inspired air. The loss of mucosal water to the inspired air can cause a transient increase in mucosal osmolarity, which might also cause bronchoconstriction.

The extent of mediator involvement in EIA is not entirely clear. Studies have not consistently demonstrated the release of mediators from mast cells (as with other forms of asthma). In contrast, leukotriene antagonists have consistently decreased bronchospastic responses to exercise, indicating that mediator generation might play a role in some cases.

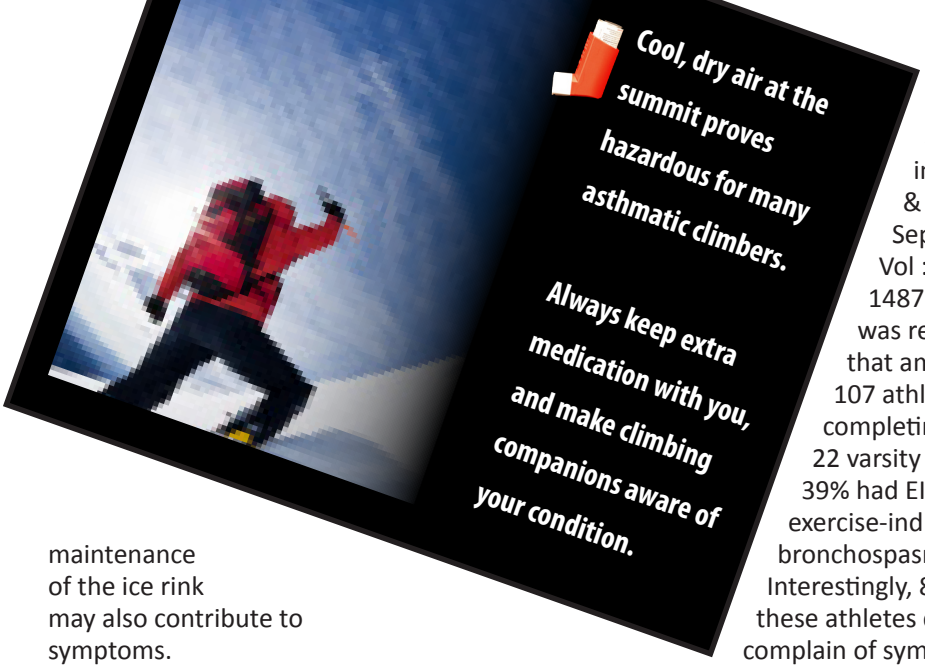
Clinical Features

During exercise, the bronchial tree dilates to accommodate increased air flow as exertion intensifies. As soon as exercise ends, the airways immediately begin to constrict, reaching a peak narrowing within 5 to 10 minutes, which could lead to clinical symptoms. The intensity of exercise, environmental temperatures and humidity all affect the severity of EIA.

Although most EIA attacks resolve quickly, a few patients may subsequently suffer a second wave of bronchospam, a short time after the first episode of EIA. This is known as a ***late-onset reaction***. EIA is usually self-limited in duration. Symptoms usually begin 5-10 minutes after completion of exercise, and attacks typically resolve within 30 minutes. However, a few patients have observed that their symptoms actually begin during exercise.

The type of exercise performed directly affects the intensity and duration of an EIA episode. Sustained hyperpnea (deep, rapid breathing during intense, prolonged aerobic activity)—often experienced while running—will be more likely to induce EIA than a sport that produces intermittent bursts of hyperpnea, such as baseball or tennis. In addition, activities such as bike-riding and swimming are less likely to induce EIA than running. Swimming appears to be the least asthmagenic sport, which may in part be related to the inhalation of humidified air. (An exception to this might be exposure to chlorine and other chemicals which may act as a trigger of asthma symptoms.)

With respect to environmental conditions, intense exertion will produce more severe symptoms when cold air is inhaled. This might occur in outdoor sports in the winter, or in an ice rink. Air pollution exhaust from equipment used in maintenance of the ice rink may also contribute to symptoms.



Although exercise is the most common cause of EIA, cooling of the airways can also result from inhaling cold air, laughing, crying, coughing, talking, singing, yelling, screaming, or sexual activity.

Testing and diagnosis of EIA

A diagnosis of EIA can be objectively confirmed with an exercise challenge in which a decrease of 12-15% or more of the FEV_1 or peak flow is observed following exercise. Bronchial challenges with exercise or methacholine may not identify EIA in all well-conditioned, elite athletes. However, a decrease in pulmonary function can be observed following the intense exercise associated with the athlete's sport when the testing is performed before and after the specific activity.

Unique types of EIA

A. EIA management for elite athletes

Exercise-induced asthma is far more prevalent than previously recognized. In a recent study by Parsons (Journal of Medicine & Science in Sports & Exercise, Sept 2007, Vol :39 pp 1487), it was reported that among 107 athletes completing in 22 varsity sports, 39% had EIA or exercise-induced bronchospasm (EIB). Interestingly, 89% of these athletes did not complain of symptoms, nor was there a prior history of asthma. EIB is not easily detectable in most people, but elite athletes may notice a difference in their performance if the condition is present. Only pulmonary function tests can indicate the presence of EIB.

Fact: The Olympic International Committee requires a physician to objectively diagnose an athlete with asthma if the athlete wishes to use asthma medication during competition.

Testing and diagnosis of EIA in elite athletes

Symptoms of asthma alone cannot be relied upon to diagnose asthma in an athlete, since other medical problems can cause similar symptoms (see Table 2). Objective pulmonary tests are required, which may include spirometry, peak flow readings, and/or bronchial provocation tests (see Table 1).

Elite athletes may have pulmonary functions far above the normal predicted values, therefore, normal spirometry may be misleading in such individuals by underestimating the presence of bronchospasm. Checking pulmonary function over time as well as pre- and post-exercise will be more valuable than a single evaluation in identifying the presence of asthma. Evidence of significant post-bronchodilator improvement of spirometry supports the diagnosis of asthma. Finally, in the absence of objective documentation of airflow limitation, a bronchial provocation test (see Table 1) may establish the

presence of airway hyper-responsiveness confirming the diagnosis of asthma. If the results of these tests are negative, other disorders should be considered (see Table 2 for differential diagnosis).

Table 1

Bronchial provocation tests used to diagnose asthma in athletes

- Methacholine challenge
- Exercise challenge
- Mannitol inhalation
- Eucapnic voluntary hyperpnea
- Hypertonic saline challenge

Treatment of EIA in elite athletes

Medical treatment of asthma in elite athletes must comply with World Anti-Doping Agency (WADA) regulations, or the athlete risks being disqualified during competition.

Two of the most common and effective categories of medication used to treat athletes with asthma are β_2-agonists and inhaled corticosteroids, **both of which are on the 2009 WADA prohibited list for athletic competition.** Fortunately, properly diagnosed athletes with asthma can receive an exemption, allowing them to use these asthma medications.

Using a prohibited medication to treat asthma in competitive sports requires a *therapeutic use exemption* (TUE). If an athlete requires a prohibited medication for competition, then he or she must complete a *declaration of use* form along with supporting documents provided by a physician indicating the diagnosis of asthma and specifying the necessary treatment. A TUE has a limited period of use of 4 years and requires yearly confirmation.

Inhaled corticosteroids are the most effective drugs for long-term control of chronic asthma. Inhaled β_2-agonists (e.g., albuterol) are the most effective drugs for immediate inhibition of EIA and relief of intermittent symptoms of asthma.

However, when used frequently, tolerance (or tachyphylaxis) to β_2 inhalers develops rapidly. Athletes who frequently use short-acting β_2-agonists should be advised that their effectiveness may decrease. Strategies to avoid these problems could include: limiting β_2-agonists to pre-exercise and infrequent use, as well as preventative treatments such as inhaled corticosteroids to treat underlying asthma.

In addition, long-acting β_2-agonists (salmeterol, fenoterol) should not be used as monotherapy, but may be used concomitantly with inhaled corticosteroids in combination preparations such as (Advair or Symbicort) with the required TUE.

Tips for Athletes

Hydration Drink plenty of fluids throughout the day, not just during exercise.

Warming up In addition to the slow build-up of intensity before vigorous exercise, athletes should spend time before a season begins running or doing other high-intensity exercise in the heat of the day to get acclimated.

Pre-treatment The single most important thing an athlete with EIA should remember is to always keep a bronchodilator inhaler handy, for use 10-20 minutes before exercise. Generally, using an inhaler once before, and once during exercise is no cause for concern. However, using an inhaler more frequently during a session could indicate unstable asthma, and the athlete should be monitored.

Cooling down after exercise

Gradually slowing down activity after intense exertion often helps limit post-exercise symptoms of EIA.

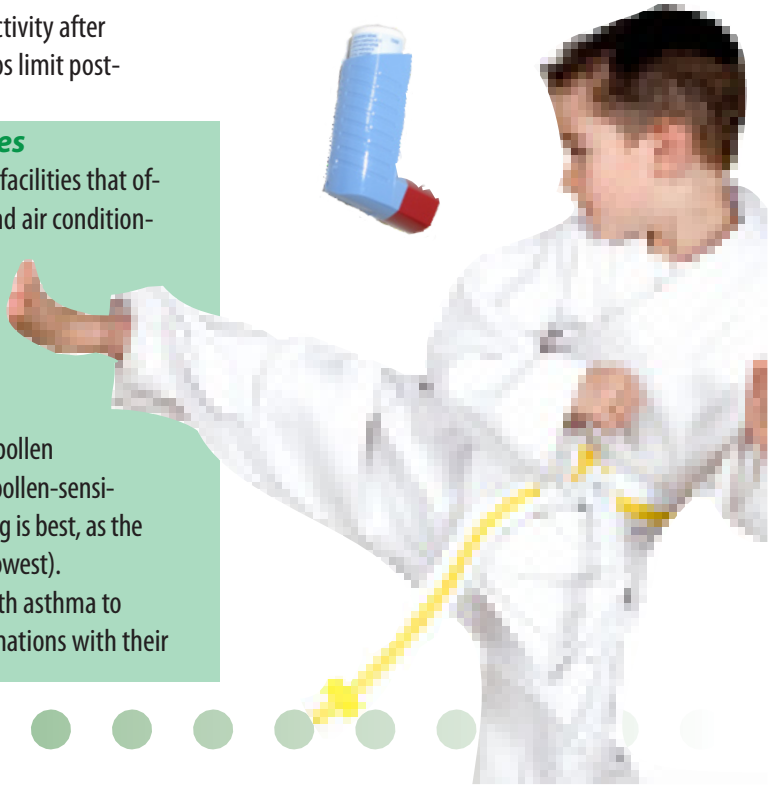
Preventive measures

- Utilize indoor practice facilities that offer good ventilation and air conditioning should be taken into account for at least part of an exercise session.
- Schedule practices during times at which pollen counts are lowest (for pollen-sensitive individuals, evening is best, as the pollen counts are the lowest).
- Encourage athletes with asthma to have follow-up examinations with their physician regularly.
- Avoid air pollution that might be present in ice rinks, swimming pools, indoor facilities, and exposure to high pollen levels or antigens in sensitive individuals.
- Those with a strong allergic component might seek immunotherapy in order to lower their sensitivity to allergen exposure.

B. Scuba diving & asthma

Most national or international organizations involved in scuba diving (e.g., Divers Alert Network (DAN), National Association of Underwater Instructors (NAUI) do not recommend diving for individuals with asthma.

However, thousands of patients with mild asthma do dive safely, provided the severity and details of their asthma are properly assessed by an asthma specialist with pulmonary function tests. Asthma should be stable with no significant risk factors at the time of the dive.



Well-controlled asthmatics may dive if they have allergic asthma or mild/ intermittent asthma. However, if cold air triggers symptoms or they have significant EIA, diving may not be the best choice as a sport. If an individual has had a recent asthma attack or symptoms are currently active, screening spirometry should be performed as part of a pre-dive evaluation. The individual should not dive until airway function returns to normal and symptoms resolve.

A significant risk associated with scuba diving is air-trapping in the lungs, leading to pulmonary barotrauma and/or air embolism, either of which could be fatal. Equally dangerous is an acute episode of asthma while diving. In theory, mucous in the airways may allow inspired air to pass as the diver descends, but it then traps the air in the lungs on ascent. On ascent, the trapped air will expand and could rupture lung tissues or create an air embolism. An acute asthma attack during a dive can also cause severe dyspnea, which can result in a hazardous or fatal situation. Further, the disabled diver may represent a danger to other divers attempting to help.

Asthmatics should not dive if a therapeutic bronchodilator has been necessary in the last 48 hours or any chest symptoms have been present. Individuals who have permanent lung damage from long-standing asthma or COPD—with or without emphysema—should not dive.

Patients should not dive who have:

- **Significant exercise or cold-induced asthma**
- **Asthma symptoms that are active around the time of a planned dive**
- **Need for a 'rescue' or 'reliever' medication regularly**
- **Evidence of persistent air trapping on complete pulmonary function tests**

The Asthma Center Education and Research Fund (theasthmacenter.org) recommends that asthmatics who wish to scuba dive undergo a complete evaluation of asthma by a specialist. Comprehensive pulmonary function tests evaluate for evidence of increased residual volume or air-trapping.

C. Mountain climbing & asthma

Patients with uncontrolled asthma may have great difficulty breathing at altitudes of 5000 feet or higher. The decreased oxygen concentrations at such significant elevations can affect the rate and depth of breathing, even with modest exertion. In addition, cold temperatures often accompany higher altitudes, which can also trigger asthma symptoms.

In contrast, higher altitudes are associated with less humidity, offer lower dust mite exposure, and less aeroallergen exposure. These conditions might benefit some patients with allergic asthma.

Asthmatic patients should reconsider mountain-climbing when their condition is not well-controlled, if they have experienced an asthma attack recently, or a rescue inhaler is used frequently. These individuals should seek clearance from a physician before climbing.

Tips before climbing:

- Have your asthma carefully evaluated beforehand
- Slow the pace of ascent when shortness of breath occurs
- Stay well-hydrated and eat small snacks throughout the day to minimize the chance for other altitude-related illnesses
- Have duplicate asthma medicines readily available
- Keep inhaler warm by storing in an inside coat pocket
- Make other climbing participants aware of your condition

Refractory period after warm-up

By warming up with light exercise prior to vigorous exercise, airways gradually become less sensitive to increased ventilation from intense exertion. However, be advised that warming up does not prevent other triggers from inducing asthma. Warm-up times to prevent EIA will vary from individual to individual. An effective warm-up usually consists of 10 -20 minutes of gradually increasing exercise intensity. Following a warm-up, the body enters a refractory or protective state of about 30-40 minutes, during which intense exercise does not provoke EIA.

Treatment

Know your triggers. If symptoms occur most often during strenuous activity in cold, dry air, one may need to exercise indoors during the winter or wear a scarf or warming face mask when exercising outside. Allergen-sensitive individuals should consider adjusting exercise routines during high-pollution and high-allergen days. Do not exercise when you feel fatigued or have a cold or other illness known to trigger your asthma.

Practice prevention. Improved physical conditioning has been shown to decrease the incidence of asthma attacks. For this reason, those with asthma are encouraged to continue exercising. The following measures can help preven an EIA attack:

- Warm up and cool down effectively

- Avoid exertion when you have a respiratory tract infection, such as a cold, flu, or bronchitis.
- Avoid exertion in extremely cold weather.
- If you smoke, quit.
- If you have allergies, avoid exertion when a reaction is likely to be triggered, as when the pollen count is high or the pollution index is high.
- Consider immunotherapy (allergy shots) if allergies provoke your asthma, as a way of reducing your sensitivity to aeroallergens.

Control existing conditions.

If EIA coexists with underlying asthma, then bring the underlying asthma under excellent clinical control utilizing environmental controls, medications including anti-inflammatory medications, and perhaps immunotherapy. Also, optimize management asthma-triggering co-morbidities such as sinusitis and gastroesophageal reflux.

Pre-treat with medication.

- **Inhaled β_2 short-acting agonists** are the drugs of choice. They should be taken 30 minutes prior to exercise when possible. These bronchodilators work rapidly (within 10-30 minutes) to open the breathing passages. They relax the muscles of the breathing passages, dilating them and decreasing the resistance to exhaled airflow, making it easier to breathe.
  - ❍ Effective in about 80-90% of people with EIA
  - ❍ Effects last as long as 4-6 hours
  - ❍ Does not address underlying cause of EIA
  - ❍ Side effects include rapid heartbeat and shakiness
  - ❍ Most frequently used: Albuterol (Proventil, Ventolin, Pro-air), Levalbuterol (Xopenex)
- **Long-acting β_2-agonist** (salmeterol, fenoterol) can provide protection for up to 12 hours, but should not be used as monotherapy.
- **Leukotriene antagonist** (Singulair, montelukast, Accolate and Zyflo (zileuton) can help control asthma
- **Anticholinergics** (Atrovent) are inferior due to their long onset of action and modest effect compared to β_2-agonists.
- **Cromolyn sodium** (Intal) is effective but has a short duration of action and is inferior in action to β_2-agonists
- **Theophylline** (slow onset, not as effective as β_2-agonists)
- **Corticosteroids** are not effective in preventing isolated EIA, but can contribute to controlling chronic bronchial asthma

Table 2:

Differential Diagnosis

There are a number of medical conditions that can mimic the symptoms of EIA.

- ❍ Deconditioning
- ❍ Cardiac disease
- ❍ Non asthmatic pulmonary disease
- ❍ Paradoxical vocal cord adduction
- ❍ Intra thoracic space occupying lesions
- ❍ Tracheal narrowing (tumor, tracheomalacia, largyngomalacia, tracheal stenosis)
- ❍ Muscle disorders

Summary

EIA is frequently under-diagnosed and undertreated. This is particularly true in athletic competition. A combination of warming up, pre treatment with asthma medications, avoidance of triggers, optimizing chronic asthma treatment, and cooling down post-exercise allows most asthma patients to participate in sports at some level and even allows elite athletes to compete at their highest capacity successfully.

The physicians on our board are clinicians, teachers and researchers and are on the staff of Drexel University College of Medicine and Pennsylvania Hospital. We have written extensively in professional and lay journals, textbooks, and monographs and frequently honor requests to lecture to other physicians and public groups.