Exercise-induced anaphylaxis (EIA) can be idiopathic, triggered by a specific allergen, or precipitated by exercise. Since the original case description, EIA has become increasingly recognised as more people participate in physical activity. EIA has been categorised in a variety of formats in the literature. More recently, the most comprehensive categorisation has distinguished five types of EIA, namely, classic, variant-type, familial, food (specific and non-specific) and medication-dependent EIA.

INTRODUCTION
The USA National Institute of Allergy and Infectious Diseases/Food Allergy and Anaphylaxis Network defines anaphylaxis as a "severe, potentially fatal, systemic allergic reaction that occurs suddenly after contact with an allergy-causing substance." Anaphylaxis can be idiopathic, triggered by a specific allergen, or exercise-induced.

Exercise-induced anaphylaxis (EIA) is a syndrome in which patients experience the symptoms of anaphylaxis, which occur only after increased physical activity. Thus, EIA is unique medical emergency since it derives from a physical allergy. EIA has become increasingly recognised as more people participate in physical activity. Since the original case description during the 1970s, more than 1000 cases have been described in the literature up until 2001. The focus of this review is to investigate exercise as a cause of anaphylaxis. The results of investigations at this point indicate that research and related material on EIA is very limited. Furthermore, the vast majority of available literature or research material currently appears to focus on a specific subset of EIA, namely food-dependent EIA. Therefore more research on this potentially fatal and increasingly recognised condition is warranted.

CATEGORIES OF CLINICAL PRESENTATION
EIA has been categorised in a variety of formats in the literature. More recently, the most comprehensive categorisation has distinguished five types of EIA, namely, classic, variant-type, familial, food (specific and non-specific) and medication-dependent EIA. Classic EIA is the most common type. Urticaria or angio-oedema with upper respiratory obstruction and hypotension precipitated by exercise are described as the classic EIA presentation. The variant form of EIA is the least common form, which is similar to classic EIA, except the typical hives are not observed. In their place small punctate skin lesions are described. The variant type of EIA accounts for approximately 10% of cases. Familial EIA has been described involving patients with a family history of EIA. However, further research is required to establish the inheritance pattern.

Two forms of food-dependent EIA have been described, noting that food or exercise alone does not produce symptoms. Specific-food EIA occurs when a particular type of food is known to be the offending allergen. Numerous foods have been implicated, including wheat, raw celery, shellfish, cabbage, peaches, grapes, chicken, hazelnuts and apples. Most events occur within 2-3 hours of ingestion. In non-specific food EIA no particular type of food is identified, but eating any food prior to exercise causes symptoms of EIA. The last type, described as medication-dependent or drug-dependent EIA, occurs in patients who develop the syndrome only after ingesting a specific medication and then participating in physical exercise. Offending medications that have been reported include aspirin, nonsteroidal anti-inflammatory drugs (NSAIDs), cold remedies and antibiotics.

EIA has been reported in children as young as 4 years old, and into adulthood, and there does not appear to be an overwhelming difference between genders or races.

PATHOPHYSIOLOGY
The specific aetiology of EIA is unclear, however results from skin biopsies reveal that skin mast-cell degranulation occurs during symptomatic attacks. It is likely that vasoactive mediators released by mast cells are responsible for the symptoms. Other products of mast-cell degranulation (tryptase and leukotrienes) have also been shown to be present at increased levels in symptomatic patients. The mechanism by which exercise lowers the mast-cell degranulation threshold is unknown. However, it has been theorised that increased sympathetic nervous activity stimulates cholinergic fibres innervating eccrine sweat glands to release acetylcholine, leading to mast-cell degranulation and liberation of vasoactive substances. In food-dependent EIA, the process is influenced by immunoglobulin E (IgE) mast-cell sensitisation by a known or unknown food.

PRECIPITATING FACTORS
EIA may be triggered by any physical activity but most commonly jogging, brisk walking, dancing and aerobic sports are the triggers. Even mild activities have been shown to induce an attack. Most of the available literature cites aerobic-type activities as the trigger for EIA attacks; however, anaerobic activities such as sprinting...
have also been noted. Other factors that have been associated with EIA include menstruation and exercising in warm, humid or cold environments.

**DIAGNOSIS**

EIA is unpredictable and difficult to diagnose. Symptoms vary greatly. In a study conducted by Shaddick et al., comprising 279 EIA patients, the most frequently occurring symptoms at the time of an EIA attack were generalised pruritus and urticaria, flushing and angioedema. However, symptoms suggesting vascular compromise, including tachycardia and loss of consciousness, headache, gastrointestinal colic and nausea, upper respiratory obstruction and even dysphagia, were also described (Table I).

The diagnosis of EIA can often be made on the basis of the patient history. A history of exercise-induced warmth, erythema and pruritus with or without urticaria is highly suggestive of exercise-induced urticaria or anaphylaxis. Progression of symptoms to dysphagia, dyspnoea, wheezing, dizziness or syncope is also consistent with EIA. Symptoms typically last from 30 minutes to 4 hours after the cessation of exercise. Frequency of attacks may vary considerably, from a single episode to several episodes annually. It appears that in the majority of individuals the frequency of EIA attacks tends to decrease or remain the same over time.

### Table I. Frequency of EIA symptoms in 279 subjects

<table>
<thead>
<tr>
<th>Symptom</th>
<th>%</th>
</tr>
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<tbody>
<tr>
<td>Pruritus</td>
<td>92</td>
</tr>
<tr>
<td>Urticaria</td>
<td>86</td>
</tr>
<tr>
<td>Angio-oedema</td>
<td>72</td>
</tr>
<tr>
<td>Flushing</td>
<td>70</td>
</tr>
<tr>
<td>Shortness of breath</td>
<td>51</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>34</td>
</tr>
<tr>
<td>Chest tightness</td>
<td>33</td>
</tr>
<tr>
<td>Loss of consciousness</td>
<td>32</td>
</tr>
<tr>
<td>Diaphoresis</td>
<td>28</td>
</tr>
<tr>
<td>Headache</td>
<td>28</td>
</tr>
<tr>
<td>Nausea/diarrhoea/colic</td>
<td>28</td>
</tr>
<tr>
<td>Choking/throat constriction/hoarseness</td>
<td>25</td>
</tr>
</tbody>
</table>

The course of EIA during pregnancy has not been well studied. It is however recommended that postpartum patients with EIA consider resuming exercise gradually.

Partial benefits have been demonstrated by administering antihistamines in an attempt to prevent EIA. Furthermore, the use of cromolyn, a mast-cell stabiliser has shown variable results. Future treatment regimens may include the use of leukotriene-modifying agents; however their effectiveness remains to be determined.

Because patients with EIA might be competitive athletes, physicians should take care to avoid medications that are banned by sport-governing bodies and the World Anti-Doping Agency (WADA) and make use of the Therapeutic Use Exemption (TUE) guidelines if such pharmacological agents are used. A list of medications requiring TUE and guidelines for application can be found at www.wada-ama.org.

Patient education should also form an important part of treatment. Patients must understand the emergent nature of EIA and should be advised to exercise with an emergency epinephrine pen-syringe available and a partner who is able to administer basic life support and epinephrine.

**CONCLUSION**

Anaphylaxis is the most urgent and potentially the most significant condition evaluated and managed by allergists. EIA is a chronic, episodic condition in which patients experience the symptoms of anaphylaxis only after increased physical activity. EIA has been recognised with increasing frequency since its original description. The symptoms of EIA may range from mild urticaria with warmth and flushing to life-threatening laryngeal oedema and vascular collapse. Activities requiring more cardiovascular demand appear to be more likely to provoke an attack than less strenuous activities. Because symptoms vary greatly, many persons with EIA are unaware of their condition, and therefore it often goes undiagnosed. For patients with EIA management typically consists of modification of exercise relative to intensity, duration and weather conditions and abstaining from food before exercise. Patients should also be advised to always carry an epinephrine kit and exercise with a partner.
Declaration of conflict of interest

The authors declare no conflict of interest.

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