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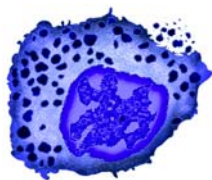
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2. Anaphylaxis: diagnosis and management

Simon G A Brown, Raymond J Mullins and Michael S Gold

Anaphylaxis is a severe immediate-type generalised hypersensitivity reaction affecting multiple organ systems and characterised at its most severe by bronchospasm, upper airway angioedema and/or hypotension. It has also been defined simply as “a serious allergic reaction that is rapid in onset and may cause death”.¹ This review aims to help general practitioners and emergency physicians with their approach to acute management and follow-up care in cases of anaphylaxis.

How common is anaphylaxis?

Anaphylaxis is uncommon but not rare, with new cases arising at rates of between 8.4 and 21 per 100 000 patient-years.²⁻⁴ An Australian survey of parent-reported allergy and anaphylaxis found that 1 in 170 school children had suffered at least one episode of anaphylaxis.⁵ Another Australian study showed that, in areas where native *Myrmecia* ant species are prevalent, 1 in 50 adults have experienced anaphylaxis after stings from native *Myrmecia* species (Box 1) or honeybees.⁶ Deaths from anaphylaxis are uncommon, estimated to occur at a rate of 1 per 3 million population per year.⁷ In areas where sting allergy is common, the death rate may be higher than this. Hospital-based studies suggest a death rate in the order of 1 per 100–200 episodes of anaphylaxis treated in an emergency department.^{8,9}

There is some evidence that the incidence of food allergy and anaphylaxis — like that of allergic rhinitis and atopic dermatitis — may be increasing.¹⁰⁻¹²

What causes anaphylaxis?

Food, insect venoms or medication trigger most cases of anaphylaxis, with a variable proportion of patients experiencing idiopathic anaphylaxis (in which extensive evaluation fails to identify an underlying cause) (Box 2). In emergency department studies, food allergy is the commonest cause in children — responsible for about 80% of anaphylactic reactions in which the cause has been identified¹³ — whereas, in adults, foods are implicated in only 20%–30% of cases.^{8,9} This difference is reflected in mortality statistics: the median ages for lethal reactions to foods and to insect venoms or medications are 22–24 years and 55–67 years, respectively.¹⁴

Summation anaphylaxis

Cofactors are sometimes required before an allergen will provoke a reaction. Factors associated with increased risk of anaphylaxis include intercurrent infection, concomitant medication/foods (particularly α -blockers, β -blockers, angiotensin-converting enzyme [ACE] inhibitors, non-steroidal anti-inflammatory drugs [NSAIDs], alcohol or spicy food), high ambient temperatures and exercise. So-called “summation anaphylaxis” may explain intermittent anaphylaxis despite frequent allergen exposure, and may account for some cases in which a cause has not been established.¹⁵ One of the most common cofactors, predominantly affecting young adults, is physical exercise. Some experience symptoms with exercise alone; others do so only if allergenic foods

ABSTRACT

- Anaphylaxis is a serious, rapid-onset, allergic reaction that may cause death. Severe anaphylaxis is characterised by life-threatening upper airway obstruction, bronchospasm and/or hypotension.
- Anaphylaxis in children is most often caused by food. Bronchospasm is a common symptom, and there is usually a background of atopy and asthma.
- Venom- and drug-induced anaphylaxis are more common in adults, in whom hypotension is more likely to occur.
- Diagnosis can be difficult, with skin features being absent in up to 20% of people. Anaphylaxis must be considered as a differential diagnosis for any acute-onset respiratory distress, bronchospasm, hypotension or cardiac arrest.
- The cornerstones of initial management are putting the patient in the supine position, administering intramuscular adrenaline into the lateral thigh, resuscitation with intravenous fluid, support of the airway and ventilation, and giving supplementary oxygen.
- If the response to initial management is inadequate, intravenous infusion of adrenaline should be commenced. Use of vasopressors should be considered if hypotension persists.
- The patient should be observed for at least 4 hours after symptom resolution and referred to an allergist to assist with diagnosis, allergen avoidance measures, risk assessment, preparation of an action plan and education on the use of self-injectable adrenaline. Provision of a MedicAlert bracelet should also be arranged.

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(most commonly wheat, celery, seafood, nuts, fruit or vegetables) are ingested within a few hours prior to exercise.

What happens in anaphylaxis?

Mast cell leukocyte cytokine cascade

Mast cell activation results in the release of many mediators that include histamine, leukotrienes, tumour necrosis factor and various cytokines. The large numbers of mediators provide redundancy and positive feedback mechanisms whereby other effector cells are recruited to release more mediators, perpetuating the allergic response. This amplification and perpetuation, which has been referred to as a “mast cell leukocyte cytokine cascade”,¹⁶ underscores the importance of physiological antagonism with adrenaline and fluid resuscitation, rather than antagonism of a single mediator such as histamine.

Pathophysiology

Anaphylactic mediators cause vasodilation, fluid extravasation, smooth muscle contraction and increased mucosal secretions. Death may occur from *hypoxaemia* (due to upper airway angioedema, bronchospasm and mucus plugging) and/or *shock* (due to massive vasodilation, fluid shift into the extravascular space and depressed myocardial function).¹⁷ While compensatory tachycardia in response to hypotension is considered a characteristic feature, sudden bradycardia with cardiovascular collapse and cardiac arrest may occur before any skin features become apparent.¹⁸ The cause of this phenomenon is unclear, but it is an important clinical feature to recognise in order to avoid making an initial misdiagnosis of a “panic attack” or “vasovagal reaction” in cases where dyspnoea, nausea, anxiety, and bradycardia may occur just before cardiovascular collapse.

Suspecting the diagnosis

Clinical features

The clinical features of anaphylaxis are summarised in Box 3. Skin features are almost universal if reactions are closely observed, but erythema (and even angioedema) may be subtle and missed if not carefully looked for (Box 4). Respiratory symptoms are more common in children, whereas cardiovascular and cutaneous symptoms dominate in adults.¹³ In part, this may be related to the higher frequency of atopy, asthma and food allergy in children.¹³ Pre-existing lung disease is associated with an increased frequency of respiratory compromise from any cause,^{6,9} and poorly controlled asthma appears to be the main risk factor for childhood death due to food allergy.¹⁹

Confusion, collapse, unconsciousness and incontinence are strongly associated with the presence of hypotension and hypoxia. In adults, the occurrence of dyspnoea, profuse sweating, nausea, vomiting and abdominal pain are also significant, as they correlate with the presence of hypotension.⁹

Does definition matter?

Lack of a universally accepted definition and severity grading system for anaphylaxis, and lack of a reliable biomarker to confirm the diagnosis, has not only hampered research but has also resulted in failure to diagnose and treat anaphylaxis in a consistent and timely manner. A simple definition has been applied by the Australasian Society of Clinical Immunology and Allergy (ASCI):

Anaphylaxis is a rapidly evolving generalised multi-system allergic reaction characterised by one or more symptoms or

1 Jack jumper ant (*Myrmecia pilosula*)



The jack jumper ant is endemic to Australia and a major cause of anaphylaxis in regional south-eastern Australia. Body length (from top of head to tip of abdomen) is approximately 10–12 mm. ◆

2 Causes of anaphylaxis

Common

- Insect stings: most commonly honeybee, Australian native ants, wasps
- Foods: most commonly peanuts, tree nuts, egg, seafood, cows milk, dairy products, seeds
- Medications: most commonly antibiotics, non-steroidal anti-inflammatory drugs
- Unidentified (no cause found)

Less common

- Physical triggers (eg, exercise, cold)
- Biological fluids (eg, transfusions, immunoglobulin, antivenoms, semen)
- Latex
- Tick bites
- Hormonal changes: breastfeeding, menstrual factors
- Dialysis membranes (haemodialysis-associated anaphylaxis)
- Hydatid cyst rupture
- Aeroallergens: domestic/laboratory animals, pollen
- Food additives: monosodium glutamate, metabisulfite, preservatives, colours, natural food chemicals
- Topical medications (eg, antiseptics) ◆

signs of respiratory and/or cardiovascular involvement and involvement of other systems such as the skin and/or the gastrointestinal tract.²⁰

This definition will exclude some atypical yet still life-threatening reactions, and more recently, an international consensus working definition has been proposed to address these issues.¹ However, no definition has yet been subject to prospective validation. Thus it may be important at times to initiate treatment for a suspected case of anaphylaxis with cardiovascular or respiratory compromise, even if consensus diagnostic criteria have not been met.

Differential diagnosis

The many possible causes of hypotension should be considered in patients suffering shock. Rashes and angioedema should not be assumed to be the result of anaphylaxis. A range of conditions may be confused with some of the individual features of anaphylaxis (Box 5).

Acute management

Cornerstones

Acute management of anaphylaxis (Box 6, Box 7) includes the following:

- Place the patient in the supine position (or left lateral position for vomiting patients);
- Give intramuscular adrenaline;
- Resuscitate with intravenous saline (20 mL/kg body weight, repeated up to a total of 50 mL/kg over the first half hour);
- Support the airway and ventilation; and
- Give supplementary oxygen.¹⁷

Intramuscular 1 : 1000 (1 mg/mL) adrenaline at a dose of 0.01 mg/kg (0.01 mL/kg) body weight up to a maximum dose of 0.5 mg (0.5 mL) injected into the lateral thigh (*vastus lateralis*) has the advantage that it can be given without delay, is absorbed more reliably than injections into other locations or subcutaneously,^{21,22} is anecdotally effective in most cases when given early, and avoids the potentially lethal effects of large intravenous bolus injections.¹⁴ The appropriate dose of EpiPen (CSL Limited, Melbourne, VIC) (Box 8) can be used instead, if available. The intramuscular dose can be repeated after 3–5 minutes if required.

Intravenous adrenaline

If resuscitation using intramuscular adrenaline and volume expansion with intravenous saline is ineffective, an infusion of intravenous adrenaline may be required, but this should be done only by experienced hands. Intravenous boluses of adrenaline are poten-

3 Clinical features of anaphylaxis

Mucocutaneous

- Rhinitis
- Conjunctival erythema and tearing
- Flushing
- Itch
- Urticaria
- Angioedema

Abdominal/pelvic

- Nausea*
- Vomiting*
- Abdominal pain
- Pelvic pain (described as being “like uterine contractions”)
- Delayed vaginal discharge

Neurological

- Vascular headache (typically described as “throbbing”)
- Dizziness*
- Collapse, with or without unconsciousness*
- Confusion†
- Incontinence*

Respiratory/chest

- Dysphagia and stridor due to upper airway angioedema†
- Throat and/or chest tightness
- Dyspnoea*†
- Cough
- Wheeze†
- Cyanosis*†

Cardiovascular

- Palpitations
- Tachycardia
- Bradycardia (relative or absolute)
- ECG changes (T and ST changes)
- Hypotension*†
- Cardiac arrest*†

ECG = electrocardiogram.

* These features are associated with hypotension.⁹

† These features are associated with hypoxia.⁹

use is not advised.^{17,31} Until human research clarifies the potential risks and benefits of antihistamines, it is prudent to restrict antihistamine use to oral, selective, non-drowsiness-inducing antihistamines, with or without oral or injectable corticosteroids, for the symptomatic relief of mild skin symptoms. Based on their use in treating asthma, corticosteroids are commonly given to reduce the risk of biphasic anaphylaxis (see below), although there is currently no evidence to support their effectiveness for this purpose.

Investigation

Anaphylaxis remains a largely clinical diagnosis. Serum mast cell tryptase concentration can be determined, but this is an insensitive biomarker for anaphylaxis, although serial measurements (eg, on arrival, 1 hour later and before discharge) may improve sensitivity and specificity.³² An elevated tryptase level may be a useful clue when the diagnosis is uncertain, but a normal result does not exclude anaphylaxis.

Observation

The time course of anaphylaxis can be classified as “uniphasic”, “protracted” or “biphasic”.³³ Although most reactions respond rapidly to treatment and do not recur (uniphasic reactions), an observation period is recommended. This is because, in some patients, symptoms may fail to improve or may worsen as the effect of adrenaline wears off (protracted anaphylaxis) or may return after early resolution (biphasic reaction). No clinical feature consistently identifies patients at risk of a biphasic reaction. Expert consensus is that a reasonable length of observation after symptom resolution is 4–6 hours in most patients, with more prolonged observation in those with severe or refractory symptoms and those with reactive airway disease, as most

tially dangerous and should not be used unless cardiac arrest is imminent. Controlled intravenous infusions of adrenaline were shown to be safe and effective in one prospective Australian study.¹⁸ An infusion protocol derived from this study has been published elsewhere.¹⁷

Management of persistent airway tract obstruction and/or hypotension

If the patient is still unresponsive after the treatments outlined above, there are several further options:

- *Persistent bronchospasm* may respond to treatment with additional bronchodilators. If intubation is required, continuous puffs of salbutamol through an aerosol port directly into the ventilation circuit may help to “break” severe bronchospasm.
- *Persistent stridor* may respond to continuous nebulised adrenaline (5 mg in 5 mL [ie, five 1 mg ampoules]) in addition to parenteral adrenaline. Surgical airway intervention (cricothyrotomy) may be required.
- *Persistent hypotension* may be due to either profound vasodilation or cardiac failure. Anecdotally, vasodilation may respond to vasopressors such as metaraminol or vasopressin.^{26–28} In patients who have pre-existing heart failure or are taking β -blockers, a phosphodiesterase inhibitor such as glucagon may be tried.^{29,30}

Ancillary medications

Medications such as antihistamines, H₂ receptor antagonists, corticosteroids and antileukotrienes have no proven impact on the immediate and dangerous effects of anaphylaxis, although they may ameliorate mild allergic reactions confined to the skin. The only registered antihistamine for parenteral use in Australia, promethazine, can worsen vasodilation and hypotension, and its

4 Facial erythema and oedema, seconds before the onset of severe anaphylaxis with hypotension



Flushing and oedema can be transient, subtle and easily overlooked. Sometimes the only clue may be “normal” (warm, well perfused) skin in the setting of circulatory collapse, when pallor and poor perfusion would be the norm. In cases of acute-onset bronchospasm or hypotension, look carefully for these features and ask relatives or friends if they have noticed any changes. (Reproduced with permission from the patient.)

fatalities associated with anaphylaxis occur in these patients.¹

Poorly controlled asthma is the main risk factor for death in children. Age over 35 years and previous severe reactions are the main risk factors for hypotension and death in adults.

After the acute episode

Before examining the surrounding circumstances to define a cause for the patient's symptoms (Box 2), it is important to first determine whether anaphylaxis occurred by carefully reviewing the available documentation. Short-lived bouts of urticaria and/or angioedema lasting less than 12 hours should prompt suspicion of an allergic cause, although on their own they do not satisfy a definition of anaphylaxis. As typical cutaneous features may be absent in up to 20% of cases, anaphylaxis should be considered in the differential diagnosis of any episode of severe, acute-onset respiratory distress, bronchospasm or cardiovascular collapse (Box 9).

Details of exposure to potential triggers, including occupational allergens (eg, latex) and cofactors, in the preceding 8 hours should be recorded while memory of the event is fresh. Almost all anaphylactic reactions to insect venoms or to food or medication occur within 1 and 6 hours, respectively.²

Medical practitioners should record the presence of known food or drug hypersensitivity and consider the possibility of accidental exposure. Ask patients about symptoms of contact urticaria (eg, during food preparation) or itching in the mouth and throat after eating certain foods (oral allergy syndrome). The latter indicates an allergy to structurally similar proteins in pollen and in some fruit and vegetables.² If an insect sting has occurred, factors that may help identify the cause are the insect's appearance, the presence of a stinger left in the skin (pathognomonic for honeybee sting) and the location where the sting occurred (stings by jack jumper ants or bulldog ants are more common in bushland).

Investigation

In-vitro testing for allergen-specific IgE (using a radioallergosorbent test [RAST] or ImmunoCAP [Phadia AB, Uppsala, Sweden]) is a useful initial screening test for a variety of allergens. In-vitro testing has limitations because the test lacks sensitivity and is limited by the range of allergens available and the ability to claim Medicare rebates for only four allergens at a time.

Skin prick testing, to assess sensitisation to food, and skin prick testing (or sometimes intradermal testing), to assess allergy to medications or insect venom, are more sensitive than in-vitro testing. As these carry a small risk

5 Differential diagnosis of anaphylaxis

Tissue swelling

- Idiopathic urticaria
- Isolated angioedema*
- Idiopathic
- ACE inhibitor-induced
- Acquired or hereditary C1 esterase inhibitor deficiency

Conditions mimicking upper airway oedema

- Dystonic reactions mimicking symptoms of a swollen tongue after taking metoclopramide, prochlorperazine or antihistamines
- Acute oesophageal reflux (sudden onset of painful throat "swelling")

Flushing syndromes

- Peptide-secreting tumours (eg, carcinoid syndrome, VIPomas[†])
- Alcohol-related
- Medullary carcinoma of thyroid
- "Red man syndrome"[‡]

Neurological syndromes

- Epileptic seizure
- Stroke

Other causes of collapse

- Vasovagal episodes
- Systemic inflammatory response syndrome
- Shock (septic, cardiogenic, haemorrhagic)

Acute respiratory distress

- Asthma
- Panic disorders
- Globus hystericus
- Laryngospasm
- Vocal cord dysfunction

Miscellaneous

- Scombroid fish poisoning
- Serum sickness
- Pheochromocytoma
- (Systemic mastocytosis[§])

ACE = angiotensin-converting enzyme.

* Isolated angioedema lacks any other organ or systemic features and thus by definition is not anaphylaxis.

† Neuroendocrine tumours that secrete vasoactive intestinal polypeptide. ‡ "Red man syndrome" is flushing and erythema associated with infusion of vancomycin (or occasionally other antibiotics). It is thought to be due to histamine release, and may be related to dose or infusion rate.

§ Although included here to prompt a consideration of this underlying disease, systemic mastocytosis is, strictly speaking, a cause of anaphylaxis. ◆

of inducing anaphylaxis, they should only be carried out in an environment in which resources for treating anaphylaxis are available. Measurement of total IgE and in-vitro testing using food mixes frequently provide misleading or irrelevant results and should not be requested.

There is currently no test to confirm tick bite allergy. Skin testing for jack jumper ant allergy is not yet available outside the Royal Hobart Hospital in Tasmania, although an in-vitro test is available from SouthPath Laboratories in South Australia (this detects only 80% of cases, and, while the subject of ongoing research, there is no validated test to detect allergy to related ant species).

Some drug reactions (eg, to NSAIDs, radiographic contrast agents) are independent of IgE, and there are numerous difficulties in assessing some cases of antibiotic allergy. To establish a diagnosis in cases in which the causative agent is in doubt, challenge testing under controlled conditions may sometimes be required, although a negative challenge test does not always exclude the diagnosis.

There is no scientific validity for "alternative" therapies such as cytotoxic or Vega testing, hair analysis and kinesiography, and their use should be discouraged.³⁴

Long-term management

Anaphylaxis to insect stings can be prevented with venom immunotherapy,²³ which reduces the risk of anaphylaxis from repeated stings and is associated with an improved quality of life compared with carrying an EpiPen alone.²⁴ Attempts to modify the severity of food allergy using similar techniques have thus far failed, although novel methods of inducing tolerance hold some promise for the future.³⁵

For most patients, anaphylaxis is a disorder for which the risk of relapse is chronic but the event itself is unpredictable.² The mainstays of long-term management of anaphylaxis include:

- Specialist assessment.
- Identification and avoidance of triggers and cofactors, if possible. Common triggers of anaphylaxis include food, stinging insects and medication. Exercise, alcohol consumption and taking NSAIDs are common cofactors.
- Avoidance of medications that may complicate management.
- Training patients to recognise early warning symptoms and to carry self-injectable adrenaline (EpiPen) (after being trained in its use).
- Provision of a written anaphylaxis action plan.

6 Emergency management of anaphylaxis

EMERGENCY MANAGEMENT OF ANAPHYLAXIS**1 Stop administration of causative agent (if relevant), assess reaction severity and treat accordingly**

Call for assistance

Give adrenaline IM (lateral thigh) 0.01 mg/kg (maximum dose 0.5 mg)

Set up IV access

Lay patient flat (elevate legs if tolerated)

Give high flow oxygen + airway/ventilation support if needed

IF HYPOTENSIVE, ALSO:

Set up additional wide-bore IV access (ie, 14G or 16G in adults) for normal saline infusion

Give IV normal saline bolus 20 mL/kg over 1–2 min under pressure

2 If there is inadequate response, an immediate life-threatening situation, or deterioration:

Start an IV adrenaline infusion, as per hospital guidelines/protocol

OR

Repeat IM adrenaline injection every 3–5 min, as needed

IM = intramuscular. IV = intravenous. Adapted with permission from: Brown SGA. Anaphylaxis: clinical concepts and research priorities. *Emerg Med Australas* 2006; 18: 155-169.¹⁷

- Identification of at-risk patients with a MedicAlert bracelet and entry of an allergy alert into hospital or health care network clinical information systems.

A number of resources for patients and health care professionals, including guidelines for dealing with anaphylaxis in specific settings such as schools and childcare centres, prescribing guidelines and written action plans, are available on the ASCIA website (<http://www.allergy.org.au/anaphylaxis>). The EpiPen doses commonly recommended by specialist bodies (such as ASCIA) differ from those in the package insert. ASCIA recommends prescribing EpiPen Junior (0.15 mg) for patients weighing 10–20 kg and EpiPen (0.3 mg) for patients weighing over 20 kg.

Wearing a MedicAlert bracelet (Australia MedicAlert Foundation, Adelaide, SA) may give attending medical or paramedical personnel access to additional information about known allergies, reduce the risk of administration of allergenic medication, and facilitate earlier recognition and treatment of anaphylaxis.

Despite their widespread clinical use, medications such as antihistamines and corticosteroids have no proven efficacy in preventing or treating anything other than mild cutaneous allergic symptoms. Furthermore, the cost of maintaining or using these medications in people with anaphylaxis due to other causes needs to be balanced against the cost of purchasing an additional EpiPen. Large doses of adrenaline may be required to treat hypotensive anaphylaxis,¹⁸ so Australians living in remote areas may need additional supplies beyond the single EpiPen unit subsidised by the current Pharmaceutical Benefits Scheme for individuals over

17 years of age. Even if an initial EpiPen injection has been effective, patients should seek emergency medical care without delay. Patients who live or work in remote areas should consider having access to means of summoning emergency assistance, such as a mobile telephone or, in some cases, an emergency satellite beacon.

7 Evidence-based practice tips*

- Recommended acute management of a patient with anaphylaxis is to place the patient in a supine position and give adrenaline and intravenous volume resuscitation (Level IV).¹
- Intramuscular injection into the lateral thigh (*vastus lateralis*) is preferred to injections into arm or deltoid muscles or subcutaneously, because of better absorption (Level III-1).^{21,22}
- A controlled intravenous infusion of adrenaline is a safe and effective management for anaphylaxis (Level III-3).¹⁸
- A reasonable length of observation after symptom resolution is 4–6 hours in most patients, with more prolonged observation recommended in patients with severe or refractory symptoms (Level IV).¹
- Venom immunotherapy prevents anaphylaxis to insect stings and significantly improves quality of life compared with carrying injectable adrenaline (EpiPen) alone (Level II).^{23,24}

*Based on National Health and Medical Research Council levels of evidence.²⁵

8 EpiPen administration



The grey “locking” cap is first removed. This enables the device, so that, when the opposite (black) end is pressed against the lateral thigh, the needle is activated and the adrenaline injected.



The correct point of injection is the outer thigh. The needle is designed to penetrate thick clothing. A common error is to press the grey end against the thigh while pressing the thumb onto the black tip, thus injecting the adrenaline into the thumb. To prevent this, we advise patients to always grip the device as shown. ♦

When to refer

Specialist evaluation is recommended after a diagnosis of possible anaphylaxis — to identify or confirm the cause, to educate regarding appropriate avoidance strategies, to help in drafting an emergency action plan and to advise whether immunotherapy is appropriate. There is anecdotal evidence that certain medications used to manage blood pressure and heart problems (α -blockers, β -blockers and ACE inhibitors) may worsen anaphylaxis or interfere with the action of adrenaline administered in an

9 Case scenario*

A 63-year-old man experienced sudden cardiovascular collapse at 02:00 in his home. This had been preceded by urticaria and a desire to open his bowels. He was hypotensive, but responded to treatment by paramedics (two 0.5 mg doses of intramuscular adrenaline into the lateral thigh, 5 minutes apart, and rapid intravenous infusion of 2 L saline).

Earlier that evening, he had eaten a buffet meal consisting of bread, various meats, vegetables, salads, sauces and alcohol, had been dancing, and had taken ibuprofen for a headache before retiring to bed at midnight. Concurrent medical problems included ischaemic heart disease (treated daily with a β -blocker).

The patient was observed in the emergency department for 24 hours. There were no ECG changes, and there was no melaena or rise in troponin level. His serum mast cell tryptase level was later reported as 25 $\mu\text{g/L}$ on arrival in the emergency department, falling to 15 $\mu\text{g/L}$ at the time of discharge, confirming the diagnosis of anaphylaxis.

Management

Allergy testing showed no convincing evidence of food hypersensitivity. The diagnostic possibilities of food or drug hypersensitivity were considered, with or without involvement of cofactors like alcohol, exercise and consumption of an NSAID.

The long interval between exercise and onset of a reaction was considered to make exercise an unlikely cofactor. In-hospital graded challenge with ibuprofen was negative. A provisional diagnosis of idiopathic anaphylaxis was made, although it was not possible to completely exclude an unidentified food allergen or summation anaphylaxis (eg, unidentified food allergen \pm NSAID \pm exercise).

The initial difficulties in resuscitation, requiring two doses of adrenaline and fluid resuscitation, were considered partially attributable to β -blockade. After discussions with his cardiologist, it was concluded that the patient could be safely given an alternative cardiac medication and that the risk from untreated anaphylaxis outweighed the theoretical risk of adrenaline triggering myocardial ischaemia.

The patient was advised to carry and use injectable adrenaline (EpiPen) in an emergency, and to document the circumstances in any future reactions to assist in identifying an avoidable trigger.

ECG = electrocardiogram. NSAID = non-steroidal anti-inflammatory drug.

* This is a fictional case scenario based on similar real-life cases. ♦

emergency. However, this poorly defined risk needs to be balanced against the *proven* benefits that these medications provide. For patients taking cardiac medications, the relative risks and benefits of their use should be considered in consultation with an allergist and/or other specialists.

Despite the frightening nature of anaphylactic episodes, compliance with advice to avoid known triggers and to carry and use injectable adrenaline is nowhere near 100%.² Denial and “acting out” by teenagers is also common, and peer pressure or bullying at school may prompt some patients to take unnecessary risks. Review from time to time or after further episodes offers an opportunity to re-educate patients on the use of EpiPen and to ensure that the device is renewed at appropriate intervals. Psychological morbidity and negative impact on quality of life are not uncommon in patients and their caregivers, and some require emotional support and counselling as well as medical advice.

Fact or fiction — true or false?

1. Adrenaline should not be given to patients with anaphylaxis who are pregnant, elderly, or taking α -blockers or β -blockers (T/F)
2. Intravenous bolus injection of adrenaline is safe (T/F)
3. Even in an emergency department (where intravenous infusion is an option), intramuscular injection of adrenaline is an appropriate first-line treatment for anaphylaxis (T/F)

1. False. Although some caution with the dose may be wise, the overriding concern is that hypoxia or poor tissue perfusion will lead to ischaemia of critical organs (or harm the fetus).
2. False. This is how lethal errors are made. Even the "correct" dose can cause severe side effects. A controlled infusion is much safer, better tolerated and more efficacious, as a sustained therapeutic concentration is obtained.
3. True. Adrenaline given into the lateral thigh can result in useful serum levels of adrenaline within 3–5 minutes — the time that may be required to get intravenous access and start an infusion. In many cases, intramuscular adrenaline is effective on its own. ◆

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Competing interests

None identified.

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