How to prevent and treat an allergic crisis

Anaphylaxis, the most serious of the allergic conditions, is a sudden, severe, potentially fatal systemic reaction.

M E Levin, MB ChB, FCPaed, Dip Allergy, MMed, PhD

Professor and Head, Allergy Division, Department of Paediatrics and Child Health, University of Cape Town and Red Cross War Memorial Children's Hospital, Cape Town

Professor Levin graduated from UCT medical school in 1994. He has worked with paediatric allergies since 2003, and is currently head of the Division of Allergy in the Department of Paediatrics at UCT. His special interests are anaphylaxis, food allergy, difficult-to-treat asthma, patient education and communication and medical education, both general and allergy related.

Correspondence to: M E Levin (luvuyo@mweb.co.za)

Anaphylaxis, the most serious of the allergic conditions, is a sudden, severe, potentially fatal systemic reaction. It may involve the skin, respiratory tract, gastrointestinal tract or cardiovascular system. Symptoms occur within minutes to two hours after contact with the allergy-causing substance.

Mechanisms of anaphylaxis

Because anaphylaxis is defined clinically, many mechanisms and pathways may result in these manifestations. They include allergic or non-allergic mechanisms. The allergic mechanisms may be IgE or non-IgE mediated. However, regardless of whether the mechanism is triggered via an immunological or non-immunological pathway or whether through an IgE- or non-IgE-mediated mechanism, the final pathway involves mast cells and basophils, resulting in a similar severe allergic-type response being generated. The majority of reactions are IgE-mediated anaphylactic reactions. The term 'anaphylactoid' is no longer recommended. Fig. 1 gives a flow diagram of the pathophysiological classification of anaphylaxis.

Many pre-formed mediators are involved in an anaphylactic reaction, including histamine, tryptase, chymase, mast cell carboxypeptidases, platelet activating factor and others. Newly formed and induced substances include prostaglandins, leukotrienes and cytokines. Although histamine is responsible for many of the milder manifestations of anaphylaxis, including urticaria and itching, platelet activating factor (PAF) is responsible for some of the more severe manifestations such as vascular leakage, bronchoconstriction and circulatory collapse. PAF inhibitors and combined antihistamine/PAF inhibitors are under investigation as second-line treatment for anaphylaxis.

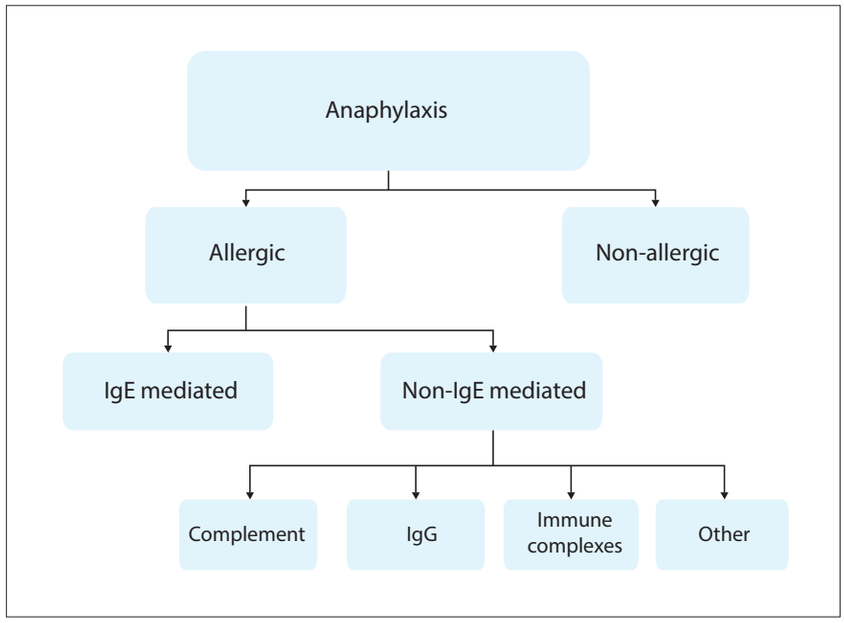

Fig. 1. Pathophysiological classification of anaphylaxis.

Causes of anaphylaxis

Common causes of anaphylaxis include foods (peanut, fish, egg, legumes) and preservatives (metabisulphites), insect venoms (bees, wasps, hornets, fire ants), latex, medications (antibiotics, especially beta lactams, vaccines, muscle relaxants, steroids, insulin) and subcutaneous immunotherapy preparations. The prevalence of anaphylaxis and the substances causing anaphylaxis in South Africa are not known.

Recognising anaphylaxis

The clinical diagnosis of anaphylaxis relies upon satisfying one of three possible clinical scenarios:

- The first scenario is the most common, requiring the acute onset of illness (minutes to 2 hours) with involvement of the skin, mucosal tissue, or both, AND either respiratory compromise or reduced blood pressure (BP) (or major systemic symptoms of end-organ dysfunction due to reduced BP). However, because some anaphylactic responses manifest in atypical ways, there are additional criteria for patients who are known to be at high risk for anaphylaxis or sensitised to a particular allergen.
- The second scenario concerns a known allergic patient who is exposed to a likely allergen and who experiences two or more of the following occurring rapidly after exposure:
  - involvement of the skin-mucosal tissue
  - respiratory compromise
  - reduced BP or associated symptoms
  - persistent gastrointestinal symptoms.

- The third scenario concerns a patient known to be sensitised to a specific allergen who experiences (isolated) reduced BP rapidly after exposure. Although anaphylaxis is predominantly a clinical diagnosis, a serum tryptase level, taken 30 minutes after the reaction occurs (immediately on presentation to a facility if occurring in the ambulatory setting), 1 - 2 hours later and 12 - 24 hours later, may show a characteristic rise and then fall to baseline levels due to mast cell degranulation. The other cause of a raised tryptase is mastocytosis, in which the baseline level may be high and the alpha tryptase is >20x higher than the beta tryptase.

Treatment of anaphylaxis

The treatment of anaphylaxis requires close adherence to basic life support principles (airway, breathing and circulation) and rapid administration of intramuscular adrenaline. Healthcare practitioners and other staff at facilities where anaphylaxis may be treated should be skilled in the prompt recognition and treatment of anaphylaxis, as delay in administration of adrenaline is associated with adverse outcomes, including death. The provision and implementation of protocols has been shown to improve the rate of administration of adrenaline, the rate of admission and the duration of subsequent observation of the patients.

Symptoms occur within minutes to two hours after contact with the allergy-causing substance.

The dose of adrenaline is 0.01 mg/kg (0.01 ml/kg of 'neat' adrenaline) (maximum 0.5 mg/0.5 ml) given intramuscularly into the large vastus muscle of the thigh. It has a rapid onset of action, and symptoms often perceived as side-effects (such as tremor) are useful signals of its onset of therapeutic activity. Second-line therapy includes antihistamines and nebulisation or metered-dose inhalation of short-acting beta-2 agonists with ipratropium bromide for wheezing, or nebulisation of adrenaline for stridor. After 5 minutes of observation, adrenaline should be repeated if there has been no resolution and repeat nebulisation or MDI should also be considered. For refractory cases, fluid therapy may be necessary and an adrenaline infusion may be considered. Adjunctive therapy may include corticosteroids, H_2 receptor antagonists and glucagon. There is absolutely no place for the treatment of anaphylaxis with steroids alone or as first-line therapy.

Admit patients

Patients with anaphylaxis should be admitted to a healthcare facility even if there has been a swift resolution. Although most anaphylaxis is uniphasic, subsiding within 1 - 2 hours after onset of symptoms either with or without therapy, up to 20% may be biphasic, in which symptoms resolve after treatment but return between 30 minutes and 72 hours later. While in hospital, patients should be reviewed by an allergy specialist or someone with a special interest in anaphylaxis in order to assess progress, assess future risk and address risk management including the provision of appropriate discharge medications, instructions and follow-up.

Before discharge the following strategies for the prevention and treatment of anaphylaxis should be implemented:

- Medical care.
- Provision of self-injectable adrenaline from an auto-injector is a preferable option to self-injectable adrenaline from an ampoule and syringe or a prefilled syringe.
- A personalised written anaphylaxis emergency action plan.
- Medic Alert bracelet or necklace.
- Medical record identification on front cover as anaphylaxis.
- Training in anaphylaxis recognition and management to patient and family.
- Assessment of sensitisation to allergen(s)
- Before discharge, allergen-specific IgE levels in serum may assess for sensitisation to possible allergens from the history of the anaphylactic episode. These are useful if positive; however, if they are negative further tests for allergen sensitisation (skin and/or specific IgE tests) should be repeated at least 3 - 4 weeks after the episode, as such tests may be negative in the period immediately following a reaction.
- A medically supervised challenge/provocation test, for example with food or drugs, might also be needed to assess the risk of future anaphylactic episodes.
- Long-term risk reduction: avoidance and/or immune modulation.
- Patients with food-triggered anaphylaxis should strictly avoid the relevant food(s).
- Patients with stinging insect-triggered anaphylaxis should avoid stinging insects and be assessed for subcutaneous venom immunotherapy (protects up to 90% of adults and 98% of children against anaphylaxis from future stings).
- Patients with medication-triggered anaphylaxis should avoid relevant medications and use safe substitutes. If medications are critically needed and no substitutes are available patients may be desensitised using a published protocol conducted in a healthcare setting.

- Patients with unknown or idiopathic anaphylaxis require specialist investigation and may benefit from prophylactic therapy.
- Optimal management of asthma and other concomitant diseases.

Risk for anaphylaxis

Eight large studies have been done on fatal and near-fatal anaphylaxis, four in the UK, two in the USA and two in Australia. These epidemiological studies have helped to identify high-risk groups for fatal anaphylaxis, including known food allergy (particularly peanut allergy in patients aged >5 years), patients with food allergy and concomitant asthma (both in the history as well as current symptoms), delayed (or non-) administration of adrenaline, adolescents and young adults, accidental (unexpected) food ingestion and lack of advice related to their food allergy. These patients are particular 'high-risk groups' for severe anaphylaxis and should have all the interventions above.

Unmet needs

Information

There is a paucity of local knowledge about anaphylaxis epidemiology and treatment in South Africa. Studies should urgently be performed to assess the prevalence of food and other allergies, and a patient register of subjects with anaphylaxis and severe allergies should be established to assess their demographics, allergen profiles and the nature of treatment received.

Treatment

Despite guidelines, adrenaline is currently under-utilised and often dosed suboptimally to treat anaphylaxis and is under-prescribed for potential future self-administration. In South Africa all the medication required for treatment of anaphylaxis is available, but cost constraints mean that access to vital precautionary adrenaline auto-injector therapy is not widely available.

Substantial advocacy regarding the availability of adrenaline auto-injectors and public awareness of anaphylaxis and its treatment, particularly at schools, is necessary if we are to appropriately manage the burgeoning food allergy epidemic. This should include legislation from the department of education that makes it necessary for all teachers to be trained in the management of anaphylaxis and that schools be mandated to keep all appropriate emergency medication for named children at risk for anaphylaxis. Allergy clinics at state institutions should motivate to drug and therapeutic committees to have auto-injectors available to subjects at high risk of food or venom anaphylaxis.

Patients with anaphylaxis should be admitted to a healthcare facility even if there has been a swift resolution.

Risk reduction

Appropriate protocols and training should be provided for healthcare practitioners to assess and manage anaphylaxis in the acute setting as well as to provide holistic risk-reduction treatment. Subjects with previous anaphylaxis or at high risk for anaphylaxis should preferably be assessed and managed (at least initially) by an allergy specialist or someone with a special interest in anaphylaxis. Care of such patients must go beyond medical care and include assessment of sensitisation to allergens, long-term risk reduction and optimal management of asthma and other concomitant diseases. Access to prevention and treatment of severe allergic reactions in ambulatory settings is an additional area that requires strong public participation and pressure. Patients with food allergy, severe allergies or anaphylaxis should be encouraged to join local and international patient advocacy groups. A list of such organisations is available online at www.allergysa.org.

As the prevalence of food allergies increases, more schools will have at least one learner with severe food allergies. These patients have the right to be safely accommodated at school without discrimination, to be able to participate in all educational activities, to have access to medication and to trained personnel who can deal with an acute allergic reaction. It is highly recommended that schools enquire about allergies as part of admission screening and that parents or guardians inform schools of any new allergy diagnosis. Patients with allergies should provide the school with a copy of their written, personalised action plan, that should contain a photo ID. The Allergy Society of South Africa has such an action plan available online at www.allergysa.org. Educators at schools with allergic subjects should be educated about allergen avoidance and the recognition and management of severe reactions. Medication should be available in schools at all times and staff indemnified against prosecution for the consequences of administering emergency medication. Facilities should be provided to allow patients with severe allergies to avoid their triggers, predominantly food allergens. This might entail the culture of avoiding sharing of food between children, the provision of food from home and strict attention to avoiding cross-contamination of food before and during meals.

In a nutshell

- Anaphylaxis is a tremendously important, possibly fatal, allergic condition.
- Information about the triggers and management of anaphylaxis in South Africa is lacking.
- It is a clinical diagnosis, but further investigations to ascertain a cause are necessary.
- Anaphylaxis is often under-recognised, under-diagnosed and inappropriately managed.
- Treatment of anaphylaxis comprises intramuscular adrenaline 0.01 mg/kg (max 0.5 mg) as soon as signs or symptoms are observed, as delay in administration of adrenaline may be fatal.
- All patients should be admitted and reviewed by an allergy specialist to reduce future risk by providing appropriate discharge medications, instructions and follow-up.
- Adrenaline auto-injectors, Medic Alert bracelets and individualised action plans are the cornerstones of effective risk reduction.
- Public awareness of anaphylaxis and its treatment, particularly at schools, is necessary if we are to appropriately manage the burgeoning food allergy epidemic.