Emergency management of anaphylaxis in children and young people: new guidance from the Resuscitation Council (UK)

Y Tse, G Rylance

Royal Victoria Infirmary, Newcastle upon Tyne, UK

Correspondence to: Dr George Rylance, Royal Victoria Infirmary, Newcastle upon Tyne NE1 4LP, UK; george.rylance@ncl.ac.uk

Accepted 17 June 2008
Published Online First 1 August 2008

The incidence of anaphylaxis is rising. Confusion can still occur concerning the diagnosis, treatment, investigation and follow-up of children after an anaphylactic reaction. Recently, the Resuscitation Council (UK) published revised consensus guidelines based on the available limited evidence on the recognition and treatment of anaphylactic reactions (http://www.resus.org.uk/pages/reaction.pdf). Significant changes have been made to simplify the emergency management for first responders, especially with regard to the recognition of anaphylaxis and the immediate use of intramuscular adrenaline, which remains the mainstay of treatment.

Anaphylaxis is a severe, life-threatening, generalised or systemic hypersensitivity reaction.[1] Varying multisystem manifestations can result from the rapid release of inflammatory mediators including histamine, IgE, IgG or complements. Previously, clinicians have attempted to differentiate between the different types of hypersensitivity reactions. However, in the emergency management of anaphylaxis this has little practical value as management of the different types is the same and the molecular basis is much more complicated than simply IgE or non-IgE mediated (previously anaphylactoid) reactions.

HOW BIG IS THE PROBLEM?

Published prevalence of anaphylaxis admissions should be interpreted with caution as an unknown number could be miscoded as severe asthma. Several surveys of hospital admission rates for anaphylactic reactions show a three- to sevenfold increase in the UK between 1990 and 2001.[2–4] Boys outnumber girls by 3:2 in preschool children, but from the age of 15 years onwards females predominate. Including adults, deaths from anaphylaxis average 20 per year in the UK.[5] In two thirds of cases, the fatal anaphylaxis was the first ever reaction.

TRIGGERS OF ANAPHYLAXIS

A large proportion of anaphylactic reactions have no discernible trigger.[6] However, for attendance at A&E departments, food is the commonest cause in children, followed by drugs and venom (mostly wasp stings). An international survey of reactions in hospital showed a higher incidence following administration of plasma, streptokinase and antisnake venom, followed by penicillin, dextran, contrast media, blood and pentoxifylline.[7] Fatal iatrogenic reactions were most likely with anaesthetic induction drugs.[5]

When anaphylaxis is fatal, death usually occurs soon after contact with the trigger. The mechanism of death is closely related to the trigger.[5] The majority of fatal food reactions are associated with respiratory arrest following bronchospasm after 30–35 min. Clinical shock predominates as the cause of death following insect stings after 10–15 min and following injected drugs after approximately 5 min. No deaths have been recorded more than 6 h after contact with the trigger.

Fatal reactions to food are more common among those patients who have co-morbid asthma. A disparate group of foodstuffs have been implicated as the cause of fatal anaphylaxis, with the commonest being nuts or milk. Nut allergy is increasing in the UK and affects 1–2% of children with approximately equal numbers of reactions attributed to peanuts, tree nuts and mixed or unidentified nuts.[8]

The incidence of anaphylaxis after vaccination is very low and is estimated to be less than one case per million vaccine doses.[9]

RECOGNITION OF AN ANAPHYLACTIC REACTION

The clinical presentation of anaphylaxis in its extreme or classical form is easily recognised (box 1). However, it is normally far more difficult to identify, with variable target organ involvement and expression of symptoms resulting in over- or under-treatment. Patients usually feel and look unwell. There are often urticarial or angioedematous skin changes, but with shock, children can look pale, cyanosed and mottled. Skin changes are absent in 20% of patients; skin changes without systemic manifestations should not be considered as anaphylaxis.[10 11]

There is a continuous spectrum from anaphylaxis, through anaphylaxis with predominantly asthmatic features, to a pure asthma attack with no other features of anaphylaxis. Life threatening asthma with no other features of anaphylaxis may be triggered by food allergy and can present with primary respiratory arrest.[12]

Box 1: Diagnosis of anaphylaxis

Anaphylaxis is likely when all three of the following criteria are met:
- Acute onset of an illness
- Skin and/or mucosal changes (flushing, urticaria, angioedema)
- Life threatening Airway and/or Breathing and/or Circulation problems

The following can help with diagnosis
- Exposure to a known allergen for the patient
- Presence of gastrointestinal symptoms (incontinence, abdominal pain)

Remember
- Skin or mucosal changes alone are not a sign of an anaphylactic reaction

Circulatory compromise can be due to direct myocardial depression, vasodilatation or capillary leak resulting in loss of fluid from the circulation. This causes pallor, clamminess leading to hypotension, and cardiac arrest. Gastro-intestinal symptoms (abdominal pain, incontinence, vomiting) and neurological signs (anxiety, agitation, confusion) can also be present.

The initial evolving non-specific nature of anaphylaxis means a range of differential diagnoses should be considered, such as septic shock, a breath holding attack, a vaso-vagal episode and a panic attack. Patients who have experienced previous anaphylaxis may become particularly anxious if they believe they have been re-exposed to the same trigger. The heart rate in anaphylaxis is usually high, although bradycardia has been reported compared to patients with vaso-vagal syncope in whom it is always low.[13]

TREATMENT OF ANAPHYLAXIS

Because the diagnosis of anaphylaxis is not always obvious, the usual life support systematic ABCDE approach should be taken to treat any life threatening problems as they are found (fig 1). Whether in or out of hospital, help is called immediately and treatment initiated while awaiting advanced equipment and expertise. As soon as the clinical signs support the diagnosis of anaphylaxis, intramuscular adrenaline should be immediately administered.

Intramuscular adrenaline: first line of treatment

Despite a lack of randomised controlled trials, there is sufficient anecdotal evidence advocating the use of adrenaline in respiratory compromise and to restore adequate circulating volume.[13 14] As an α-receptor agonist, it reverses peripheral vasodilatation and reduces oedema. β-Receptor activity dilates the bronchial airways, increases the force of myocardial contraction and suppresses histamine and leukotriene release. Additionally, β-2 adrenergic receptors on mast cells inhibit activation and so early adrenaline attenuates the severity of IgE-mediated allergic reactions. Adrenaline seems to works best when given early.[15 16] Adverse effects are extremely rare when the correct dose is injected intramuscularly (IM). Theoretically, children on regular β-blockers may not respond well to adrenaline and glucagon may be required. Consideration should be given to changing cardiac medication should these children become susceptible to anaphylaxis.[17 18]

Intramuscular injection is the recommended route of adrenaline administration as it requires less training and has a greater margin of safety. The anterolateral aspect of the middle third of the thigh has better absorption than the deltoid muscle.[19] The average time to maximum plasma adrenaline concentration using the intramuscular route is 8 min. The subcutaneous and inhaled routes are not recommended due to their inferior pharmacokinetic profiles.[20] Recommended intramuscular doses are shown in table 1, taking into account the rare safety reports and what it is practical to administer in an emergency. The same dose should be repeated after 5 min if there is inadequate response. Auto-injectors are probably more practical both in and out of hospital as both parents and healthcare workers demonstrated major inaccuracies in drawing up the required small volumes by syringe.[21]

Intravenous adrenaline can be used as second line treatment by clinicians experienced in the use and titration of vasopressors in their usual clinical practice.[22] The intraosseous route is also available for those who require but do not currently have intravenous access[23] and for those patients who fail to respond to intramuscular adrenaline or are so shocked that absorption from intramuscular sites is not expected to be adequate. Constant monitoring is required as rare case reports have associated cardiac arrhythmias or myocardial ischaemia with intravenous adrenaline use, although these reports are confounded by either existing co-morbidities or the life threatening anaphylaxis itself.[14]

In the event of a cardiac arrest following anaphylaxis, cardiopulmonary resuscitation should be commenced with adrenaline given intravenously or intraosseously according to standard Advanced Paediatric Life Support guidelines.

Adjunctive medication

Nothing should delay the administration of intramuscular adrenaline as the outcome is superior with early injection.[16] Concurrently, high flow oxygen and rapid fluid resuscitation should be given to restore intravascular volume. If anaphylaxis occurs in hospital, any infusions that may be the trigger (eg, drugs, plasma or blood) should be stopped. After insect stings, a speedy attempt should be made to remove the sting as venom continues to be secreted from the sac increasing dose response.[24] Inducing vomiting after food reactions is not recommended.

Bronchospasms should be treated in the same way as life-threatening asthma with inhaled, and if necessary, intravenous bronchodilators (salbutamol, aminophylline, ipratropium and magnesium). Intravenous magnesium can cause vasodilatation and exaggerate any hypotension.

Antihistamines may help counteract components of anaphylaxis due to histamine mediated vasodilatation and bronchospasm. No recommendations can be made due to the lack of controlled

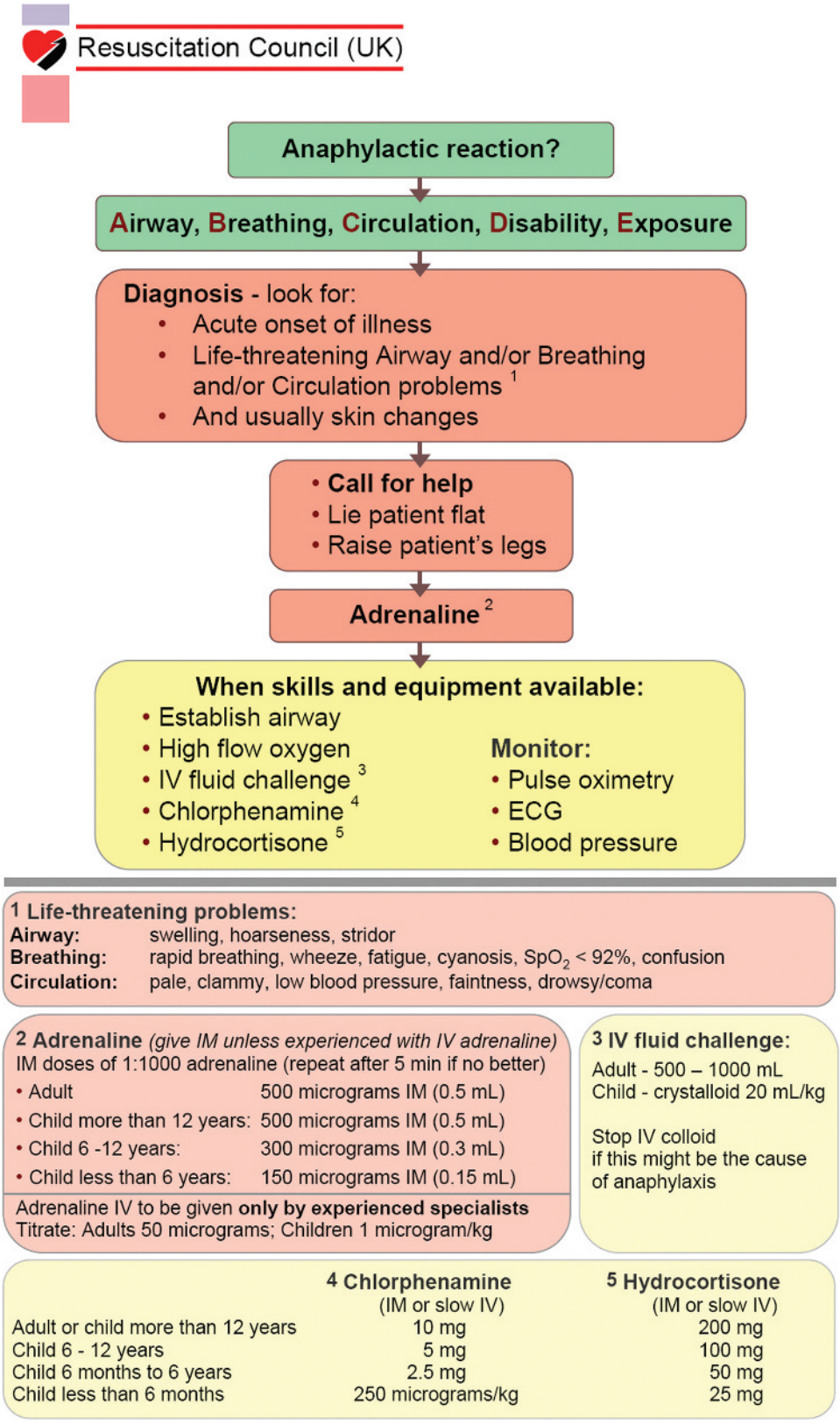

Figure 1 Algorithm for acute management of anaphylaxis. Reproduced with permission from the Resuscitation Council (UK).

studies.[25] Antihistamines can be administered intravenously or intramuscularly but is it unlikely that their use would be life saving.

Corticosteroids may help in an acute attack, in preventing or shortening protracted reactions and in the treatment of recurrent idiopathic anaphylaxis. Early corticosteroid treatment is beneficial in asthma.[26] Higher doses of hydrocortisone do not appear to offer any benefit over smaller doses in asthma and there are no studies on the optimal dose in anaphylaxis. Steroids do not prevent biphasic reactions (see below).

Table 1 Adrenaline doses

Intramuscular*	
>12 years	500 μg IM (0.5 ml), ie, same as adult dose
	300 μg IM (0.3 ml) if child is small or prepubertal
6–12 years	300 μg IM (0.3 ml) Epipen auto-injector
<6 years	150 μg IM (0.15 ml) Epipen Junior auto-injector
Intravenous bolus dose	
It is recommended that adrenaline is administered intravenously only in specialist paediatric settings by those familiar with its use. The dose is titrated according to response. The pre-filled 10 ml syringe of 1:10 000 adrenaline contains 100 μg/ml. A dose of 50 μg represents 0.5 ml which is the smallest dose that can be given accurately. A child may respond to a dose as little as 1 μg/kg. The dose therefore requires very careful dilution and checking to prevent dose errors. Continuous haemodynamic monitoring should be instituted.	
Intravenous bolus dose	
Dose should be titrated according to response. Local guidelines for the preparation and infusion of adrenaline should be followed.	

*IM, intramuscular. The equivalent volume of 1:1000 adrenaline is shown in brackets.

INVESTIGATIONS AFTER AN ANAPHYLACTIC REACTION

Patients should be investigated as clinically indicated for their life threatening presentations. Additionally, tryptase released from massive mast cell degranulation during anaphylaxis can be helpful in cases of diagnostic uncertainty.[27 28] Blood tryptase concentrations increase significantly from 30 min after the onset of symptoms, peak at 1–2 h and revert to baseline within 6–8 h. Some patients have high baseline levels and it is recommended that serial samples be obtained to improve specificity and sensitivity. Tryptase levels may not always rise in food induced anaphylaxis.[29] This may be due to the timing of sampling as this trigger has a slower onset of reaction or it may be due to other mechanisms such as mast cell degranulation being limited within the gut lumen. Conversely, tryptase can be non-specifically increased by severe illnesses such as trauma, so tryptase levels must be interpreted within the clinical context.[30]

DISCHARGE FROM HOSPITAL

After treatment and resolution of their symptoms, patients should be observed until a recurrence is unlikely. Special attention should be given to those with severe reactions with slow onset, a severe asthmatic component, the possibility of continuing absorption of the allergen or previous biphasic reactions. Biphasic reactions are defined as the recurrence of symptoms requiring treatment following complete resolution, usually occurring within 4 h.[31] In the only paediatric study of biphasic reactions, they occurred in six out of 105 anaphylactic patients with a symptom free interval of 1.3–28 h between reactions.[32] Steroids had been administered in five out of six of these patients.

All patients must be instructed before discharge to return to hospital if their symptoms recur, should be considered for an adrenaline auto-injector, and need to be followed up in a specialist allergy clinic. If there is urticaria, oral antihistamines and steroids for 3 days have been shown to be helpful for symptom relief.[33] With meticulous record keeping including reports from first responders and a detailed search for the trigger, the chance of future events occurring may be reduced. All anaphylactic drug reactions should be reported to the Medicines and Healthcare products Regulatory Agency (MHRA) using the Yellow Card scheme.

WHEN TO PRESCRIBE AN ADRENALINE AUTO-INJECTOR?

For children at increased risk of anaphylaxis, an auto-injector can save their lives but should be seen as one part of an overall individualised management plan which includes education, allergen avoidance, knowledge of first aid and optimal management of co-morbidities, especially asthma. Controversy exists as to what level of risk warrants an auto-injector since there is a perception that they are being over prescribed in the UK.[34] In general, after appropriate training and counselling, auto-injectors should be given to those at a continuing high risk of a future anaphylactic reaction, for example idiopathic reactions, venom stings and most food induced reactions (unless the food is easily avoidable). Adrenaline auto-injectors and carers who are trained to diagnosis anaphylaxis and willing to use the auto-injector need to be available at all times, including when the child is at school or staying with relatives. Some advocates suggest that two auto-injectors should be available at every location in the event of faulty technique or defective equipment.[35]

Surveys on children already prescribed auto-injectors prove disappointing. One showed that only 71% of children were in possession of their auto-injector at the allergy clinic, 10% of these had passed the expiry date and only 32% of families could correctly demonstrate its use.[36] A retrospective analysis showed that only 29% of children with recurrent anaphylaxis were actually treated with their own adrenaline auto-injector.[37]

PATIENT AND FAMILY EDUCATION

It is recommended that all patients who have had an anaphylactic reaction should be referred to a specialist clinic providing comprehensive assessment of risk and management as this may help to reduce future reactions and improve parental knowledge.[38] The patient needs to be able to identify the allergen responsible for the anaphylactic reaction and know how to avoid it. If the allergen is a food, they need to know what products are likely to contain it, and all the names which can be used to describe it. Where possible they also need to avoid situations where they are likely to come into contact with the allergen. At follow-up clinics patients should rehearse their emergency action plan and practice their auto-injector technique, and arrangements should be made to ensure all their carers are competent with

their training, for example via the school or community nurses.[39] A Medic-alert bracelet is a useful adjunct to aid first responders in the event of a future attack.

SUMMARY

These new guidelines on the emergency treatment of anaphylactic reactions update those originally published in 1999. They serve to clarify the diagnostic and treatment approach for all health professions and first responders and merge it with the ABCDE procedure used in the familiar UK life support algorithms. Although no new treatments have been advocated due to lack of efficacy data, the use of existing drugs and dosages have been simplified, especially for children, to reduce recognition-to-needle time. Other national guidelines all agree on the use of prompt intramuscular adrenaline[40 41] but differ marginally as regards its dose and the use of adjunctive drugs. This reflects the weak evidence base and the perspectives of differing guideline writers.

Competing interests: Dr George Rylance was the RCPCH representative on the Working Group of the Resuscitation Council (UK) in producing these new guidelines.

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