Appendix 1: Anaphylaxis

Anaphylaxis is a potentially life-threatening systemic allergic reaction. It manifests as a constellation of features but there is disagreement over which are essential. The confusion about definition arises partly because systemic allergic reactions can be mild, moderate or severe. In practice, the term 'anaphylaxis' should be reserved for cases where there is:

- respiratory difficulty (related to laryngeal oedema and/or bronchoconstriction) *or*
- hypotension (presenting as fainting, collapse or loss of consciousness) *or*
- both.[1]

Urticaria, angioedema or rhinitis alone are best not described as anaphylaxis because neither respiratory difficulty nor hypotension is present.[1]

Causes

In anaphylaxis, an allergic reaction results from the interaction of an allergen with specific IgE antibodies bound to mast cells and basophils. This leads to activation of the mast cell with release of chemical mediators stored in granules (including histamine) as well as rapidly synthesised additional mediators. A rapid major systemic release of these mediators causes capillary leakage and mucosal oedema, resulting in shock and respiratory difficulty.[1]

In contrast, anaphylactoid reactions are caused by activation of mast cells and release of the same mediators, but without the involvement of IgE antibodies. For example, certain drugs act directly on mast cells. In terms of management it is not necessary to distinguish anaphylaxis from an anaphylactoid reaction. This difference is relevant only when investigations are being considered.

Common causes of this rare emergency include general anaesthetics, antibiotics, blood products**, aspirin**, another NSAID or **heparin**. Non-drug causes include venom (e.g. wasp sting) and food (e.g. nuts).[2] A possible case has been recorded in a woman with known peanut allergy who received an **arachis** (peanut) **oil** enema.[3] Anaphylaxis is:

- specific to a given drug or chemically-related class of drugs
- more likely after parenteral administration
- more frequent in patients with aspirin-induced asthma or systemic lupus erythematosus.

Clinical features

Clinical manifestations of anaphylaxis typically develop within minutes of taking the causal drug (Box A1.A). Laryngeal oedema and/or bronchoconstriction occurs in only 10% of patients.[4]

Box A1.A Clinical features of anaphylaxis

Essential

Hypotension *and/or* respiratory difficulty (laryngeal oedema, bronchoconstriction)

Possible

Flushing	Tingling of the extremities
Urticaria	Weakness
Angioedema	Agitation

Management

Anaphylaxis requires urgent treatment with **adrenaline** (epinephrine) followed up with an antihistamine and **hydrocortisone** (Box A1.B). However, because their impact is not immediate, corticosteroids are only of secondary value.

Box A1.B Management of anaphylaxis in adults [5-8]

1. Oxygen is of primary importance.
2. Adrenaline (epinephrine) 1 in 1000 (1mg/1ml), 500microgram (0.5ml) IM: [a,b]
   - if the patient is unconscious, double the dose
   - repeat every 5min until blood pressure, pulse and breathing are satisfactory.
3. Chlorphenamine (chlorpheniramine) to counter histamine-induced vasodilation:
   - 10–20mg IM or IV over 1min
   - 4–8mg PO t.d.s. for 24–48h to prevent relapse.
4. Hydrocortisone[c] 100-500mg IM or slowly IV for patients with bronchospasm, and for all severe or recurrent reactions to prevent further deterioration (note: even IV may take 4-6h to act).
5. If still shocked, give 1–2L of IV fluid (a crystalloid may be safer than a colloid)
6. If bronchospasm has not responded to the above, give a nebulised β_2-adrenoceptor stimulant, e.g. salbutamol 5mg.

a. if an adrenaline (epinephrine) auto-injector is used, 300microgram (0.3ml) is generally sufficient.
b. for patients taking a tricyclic antidepressant (e.g. amitriptyline, imipramine), MAOI or a beta-blocker, it is safer to halve the dose of adrenaline (epinephrine).
c. hydrocortisone sodium phosphate or succinate salt should be used. The acetate salt is unsuitable due to delayed absorption and microcrystalline structure preventing IV use.

If the patient deteriorates despite receiving IM **adrenaline** (epinephrine) or there is doubt about the adequacy of the circulation, the initial injection can be given as a dilute IV solution, i.e. *1 in 10 000 (1mg/10ml)*, *500microgram (5ml) over 5min*. However, because too rapid injection of IV **adrenaline** (epinephrine) can cause ventricular arrhythmias, the IV route is generally discouraged unless intensive care facilities are available.[7]

Sometimes emergency tracheotomy and assisted respiration may be necessary.

---

1 Ewan P (1998) ABC of allergies: anaphylaxis. *British Medical Journal.* **316**: 1442–1445.

2 Pumphrey RSH (2000) Lessons for the management of anaphylaxis from a study of fatal reactions. *Clinical and Experimental Allergy*. 30: 1144-50.

3 Pharmax (1998) Data on file.

4 Szczeklik A (1986) Analgesics, allergy and asthma. *Drugs*. **32**: 148-163.

5 Resuscitation Council UK (2002) The Emergency Medical Treatment of Anaphylactic Reactions for Adults by First Medical Responders. www.resus.org.uk

6 Anonymous (2003) *British National Formulary* No. 46. British Medical Association and the Royal Pharmaceutical Society of Great Britain, London, pp.156–158.

7 McLean-Tooke *et al*. (2003) Adrenaline in the treatment of anaphylaxis: what is the evidence? *British Medical Journal.* **327**: 1332–1335.

8 Schierhout G, Roberts I (1998) Fluid resuscitation with colloid or crystalloid solutions in critically ill patients: a systematic review of randomized trials. *British Medical Journal.* **316**: 961–964.