Recognition and treatment of anaphylaxis
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ABSTRACT
The aim of this paper is to discuss the recognition, treatment and investigation of anaphylaxis. Anaphylaxis is a severe, life-threatening, generalized or systemic hypersensitivity reaction. It is characterized by rapidly developing life-threatening airway and/or breathing and/or circulation problems usually associated with skin and/or mucosal changes. The incidence of anaphylaxis appears to be increasing. A wide range of triggers can cause anaphylaxis. Drugs are the commonest cause of anaphylaxis in hospital and foods in the out-of-hospital setting. Patients having anaphylaxis should be treated using the airway, breathing, circulation, disability, exposure (ABCDE) approach. Early treatment with intramuscular adrenaline is the treatment of choice for patients having anaphylaxis. Intravenous adrenaline must only be used when the patient is monitored and only by those skilled and experienced in its use. A raised serum mast cell tryptase suggests a diagnosis of anaphylaxis. All those who are suspected of having anaphylaxis should be referred to a specialist in allergy. Individuals at high risk of anaphylaxis where the trigger is difficult to avoid should carry an adrenaline auto-injector and receive training and support in its use.

Key words: Anaphylaxis

INTRODUCTION
This paper reviews the recognition, treatment and investigation of anaphylaxis. It is based on Emergency treatment of anaphylactic reactions—Guidelines for health care providers by the working group of the Resuscitation Council, UK (Soar et al., 2008). The European Academy of Allergology and Clinical Immunology Nomenclature Committee use the following broad definition (Johansson et al., 2004).

Anaphylaxis is a severe, life-threatening, generalized or systemic hypersensitivity reaction

This is characterized by rapidly developing life-threatening airway and/or breathing and/or circulation problems usually associated with skin and mucosal changes. Anaphylaxis can be triggered by a broad range of triggers (Pumphrey, 2004) (Table 1). Food is the commonest trigger in children and drugs the commonest in adults.

Anaphylaxis has a good prognosis with a case fatality ratio of less than 1%. When anaphylaxis is fatal, death usually occurs very soon after contact with the trigger. From a case-series, fatal food reactions cause respiratory arrest typically after 30–35 min; insect stings cause collapse from shock after 10–15 min; and deaths caused by intravenous medication occur most commonly within 5 min (Pumphrey, 2000). (Figure 1).

RECOGNITION OF ANAPHYLAXIS
Anaphylaxis is likely when all of the following three criteria are met:

- sudden onset and rapid progression of symptoms;
- life-threatening airway and/or breathing and/or circulation problems;
- skin and/or mucosal changes (flushing, urticaria, angioedema).

The following supports the diagnosis:

- exposure to a known allergen for the patient.

Remember:

- skin or mucosal changes alone are not a sign of anaphylaxis;
- skin or mucosal changes can be subtle or absent in up to 20% of reactions (some patients can have only a decrease in blood pressure, i.e. a circulation problem);
- there can also be gastrointestinal symptoms (e.g. vomiting, abdominal pain, incontinence).
Table 1 Suspected triggers for fatal anaphylactic reaction between 1992 and 2001 in the UK (Reproduced with permission from the Resuscitation Council UK)

<table>
<thead>
<tr>
<th>Trigger</th>
<th>Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stings</td>
<td>47</td>
<td>29 wasp, 4 bee, 14 unknown</td>
</tr>
<tr>
<td>Nuts</td>
<td>32</td>
<td>10 peanut, 6 walnut, 2 almond, 2 brazil, 1 hazel, 11 mixed or unknown</td>
</tr>
<tr>
<td>Food</td>
<td>13</td>
<td>5 milk, 2 fish, 2 chickpea, 2 crustacean, 1 banana, 1 snail</td>
</tr>
<tr>
<td>Food possible cause</td>
<td>17</td>
<td>5 during meal, 3 milk, 3 nut, 1 each – fish, yeast, sherbet, nectarine, grape, strawberry</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>27</td>
<td>11 penicillin, 12 cephalosporin, 2 amphotericin, 1 ciprofloxacin, 1 vancomycin</td>
</tr>
<tr>
<td>Anaesthetic drugs</td>
<td>39</td>
<td>19 suxamethonium, 7 vecuronium, 6 atracurium, 7 at induction</td>
</tr>
<tr>
<td>Other drugs</td>
<td>24</td>
<td>6 NSAID, 3 ACEI, 5 gelatins, 2 protamine, 2 vitamin K, 1 each – etoposide, acetazolamide, pethidine, local anaesthetic, diamorphine, streptokinase</td>
</tr>
<tr>
<td>Contrast media</td>
<td>11</td>
<td>9 iodinated, 1 technetium, 1 fluorescein</td>
</tr>
<tr>
<td>Other</td>
<td>3</td>
<td>1 latex, 1 hair dye, 1 hydatid</td>
</tr>
</tbody>
</table>

NSAID, non-steroidal anti-inflammatory drug; ACEI, angiotensin converting enzyme inhibitor.

Confusion arises because some patients have systemic allergic reactions that are less severe. For example, generalized urticaria, angioedema and rhinitis would not be described as anaphylaxis, because the life-threatening features are not present.

Life-threatening features to look for include:

Airway problems:
- airway swelling, e.g. throat and tongue swelling (pharyngeal/laryngeal oedema);
- hoarse voice;
- stridor.

Breathing problems:
- shortness of breath;
- wheeze;
- confusion caused by hypoxia;
- cyanosis is usually a late sign;
- respiratory arrest;
- life-threatening asthma with no features of anaphylaxis can be triggered by food allergy.

Circulation problems:
- signs of shock;
- tachycardia;
- hypotension – patients with anaphylaxis can deteriorate if made to sit up or stand up (Pumphrey, 2003);
- decreased conscious level;
- anaphylaxis can cause myocardial ischaemia and electrocardiograph (ECG) changes;
- cardiac arrest.

Circulation problems (anaphylactic shock) can be caused by direct myocardial depression, vasodilation and capillary leak, and loss of fluid from the circulation.

Airway, breathing and circulation problems also alter the patient’s neurological status (D-disability problems) because of decreased brain perfusion.

Skin and/or mucosal changes (assessed as part of the exposure when using the ABCDE approach):
- often the first feature and present in over 80% of anaphylaxis (Sampson et al., 2006);
- there may be just skin, just mucosal or both skin and mucosal changes;
- erythema – a patchy or generalized, red rash;
- urticaria can appear anywhere on the body;
- angioedema is similar to urticaria but involves swelling of deeper tissues, most commonly in the eyelids and lips, and sometimes in the mouth and throat.

Differential diagnosis

Life-threatening conditions:
- anaphylaxis can present with symptoms and signs very similar to life-threatening asthma – this is commonest in children;
• a low blood pressure with a petechial or purpuric rash can be a sign of septic shock.

Non-life-threatening conditions (usually respond to simple measures):
• faint (vasovagal episode);
• panic attack;
• breath-holding episode in child;
• idiopathic (non-allergic) urticaria or angioedema.

TREATMENT OF ANAPHYLAXIS
The diagnosis of anaphylaxis is not always obvious. The clinical signs of critical illness are generally similar whatever the underlying process because they reflect failing respiratory, cardiovascular and neurological systems. Use an ABCDE approach to recognize and treat anaphylaxis. Treat life-threatening problems as you find them. Patients should be monitored (pulse oximetry, non-invasive blood pressure and 3-lead ECG) as soon as possible.

Patients with airway and breathing problems prefer to sit up as this will make breathing easier. Lying flat with or without leg elevation is helpful for patients with a low blood pressure (circulation problem). Do not make patients sit or stand up if they feel faint—this can cause cardiac arrest. Patients who are breathing and unconscious should be placed on their side (recovery position) as long as their airway is protected.

Stop any drug suspected of causing anaphylaxis (e.g. stop intravenous infusion of a gelatin solution or antibiotic). Do not delay definitive treatment if removing the trigger is not feasible.

If the patient has a cardiac arrest start cardiopulmonary resuscitation (CPR) immediately and follow current guidelines (Biarent et al., 2005; Nolan et al., 2005).

The key steps for the treatment of anaphylaxis are shown in the algorithm (Figure 2).

Adrenaline (epinephrine)
Adrenaline is the most important drug for the treatment of anaphylaxis (Sheikh et al., 2009). Adrenaline seems to work best when given early after the onset of the reaction.

The intramuscular (IM) route is the best for most individuals who have to give adrenaline to treat anaphylaxis as there is a greater margin of safety, intravenous access is not required and it is easier to learn. The best site for IM injection is the anterolateral aspect of the middle third of the thigh (Simons et al., 2001). Further doses can be given at about 5-min intervals according to the patient’s response.

Intravenous (IV) adrenaline (for specialist use only)
Intravenous adrenaline must only be used by those experienced in the use and titration of vasopressors in their normal clinical practice (e.g. anaesthetists, emergency physicians).

In patients with a spontaneous circulation, intravenous adrenaline can cause life-threatening hypertension, tachycardia, arrhythmias and myocardial ischaemia. Patients who require repeated IM doses of adrenaline may benefit from IV adrenaline. It is essential that these patients receive expert help early. If the patient requires repeated IV bolus doses of adrenaline, start an adrenaline infusion.

Oxygen and fluids (give as soon as available)
Initially, give the highest concentration of oxygen possible. If there is intravenous access, infuse intravenous fluids immediately. Give a rapid IV fluid challenge (20 mL/kg in a child or 500–1000 mL in an adult) and monitor the response; give further doses as necessary.

Other drugs
Antihistamines are a second line treatment for anaphylaxis. The evidence to support their use is weak. Antihistamines (H1-antihistamine) may help counter histamine-mediated vasodilation and bronchoconstriction. Corticosteroids can help prevent or shorten protracted reactions.

INVESTIGATION OF ANAPHYLAXIS
Mast cell tryptase released from mast cell is the specific test to confirm a diagnosis of anaphylaxis. Tryptase concentrations in the blood may not increase significantly until 30 min or more after the onset of symptoms, and peak 1–2 h after onset (Schwartz, 2006). The half-life of tryptase is short (approximately 2 h), and concentrations may be back to normal within 6–8 h, so timing of any blood samples is very important.

(a) Minimum: one sample at 1–2 h after the start of symptoms.
(b) Ideally: Three timed samples:
• initial sample as soon as feasible after resuscitation has started—do not delay resuscitation to take sample;
• second sample at 1–2 h after the start of symptoms;
• third sample either at 24 h or in convalescence and this provides baseline tryptase levels—some individuals have an elevated baseline level.
DISCHARGE AND FOLLOW-UP

Patients with suspected anaphylaxis should be treated and then observed for at least 6 h. Patients requiring respiratory support (tracheal intubation and ventilation) or continuing resuscitation with fluids or an adrenaline infusion should be admitted to a critical care setting. Some patients require adrenaline infusions for over 24 h.

In most patients with anaphylaxis, there is a rapid improvement with early recognition and treatment with adrenaline. Patients should be observed for up to 24 h if:

- slow onset idiopathic anaphylaxis;
- they have severe asthma;
- they have a history of prolonged (biphasic) reactions;
- access to emergency care is difficult.

Before hospital discharge patients must be:

- reviewed by a senior clinician;
- given clear instructions to return to hospital if symptoms return;
- considered for antihistamines and oral steroids therapy for up to 3 days. This is helpful for urticaria and may decrease the chance of further reaction;
- considered for an adrenaline auto-injector, or given a replacement;
- have follow-up arranged.
An auto-injector is an appropriate treatment for patients at increased risk of an idiopathic anaphylaxis, or for anyone at continued high risk of reaction, e.g. to triggers such as venom stings and food-induced reactions (unless easy to avoid).

All patients presenting with anaphylaxis should be referred to an allergy clinic to identify the cause, and thereby reduce the risk of future reactions and prepare the patient to manage future episodes themselves. Patients need to know the allergen responsible and how to avoid it. Patients need to be able to recognize the early symptoms of anaphylaxis, so that they can summon help quickly and prepare to use their emergency medication.

CONCLUSION
The UK incidence of anaphylactic reactions seems to be increasing. The guidelines for emergency treatment of anaphylactic reactions have recently been revised. The emphasis is on recognizing and treating patients using the ABCDE approach. The exact treatment depends on the patient’s location, the equipment and drugs available and the skills of those providing treatment. All patients having an anaphylactic reaction should have early treatment with IM adrenaline. All patients suspected of having an anaphylactic reaction should be referred to an allergy specialist and advised in future recognition and management.

KEY LEARNING POINTS
- The UK incidence of anaphylactic reactions is increasing.
- Patients who have an anaphylactic reaction have life-threatening airway and/or breathing and/or circulation problems usually associated with skin and mucosal changes.
- Despite previous guidelines, there is still a confusion about the indications, dose and route of adrenaline.
- Patients having an anaphylactic reaction should be recognized and treated using the airway, breathing, circulation, disability, exposure (ABCDE) approach.
- Early treatment with IM adrenaline is the treatment of choice for patients having an anaphylactic reaction.

RECOMMENDED TEXTS FOR FURTHER READING
- This is a review is based on Emergency treatment of anaphylactic reactions - Guidelines for healthcare providers by the working group of the Resuscitation Council UK. The complete document is available at on the Resuscitation Council UK website (www.resus.org.uk)
- Consider two points of learning that have occurred as a result of reading the revision note. Consider two points of action you will do as a consequence of this learning.

REFERENCES