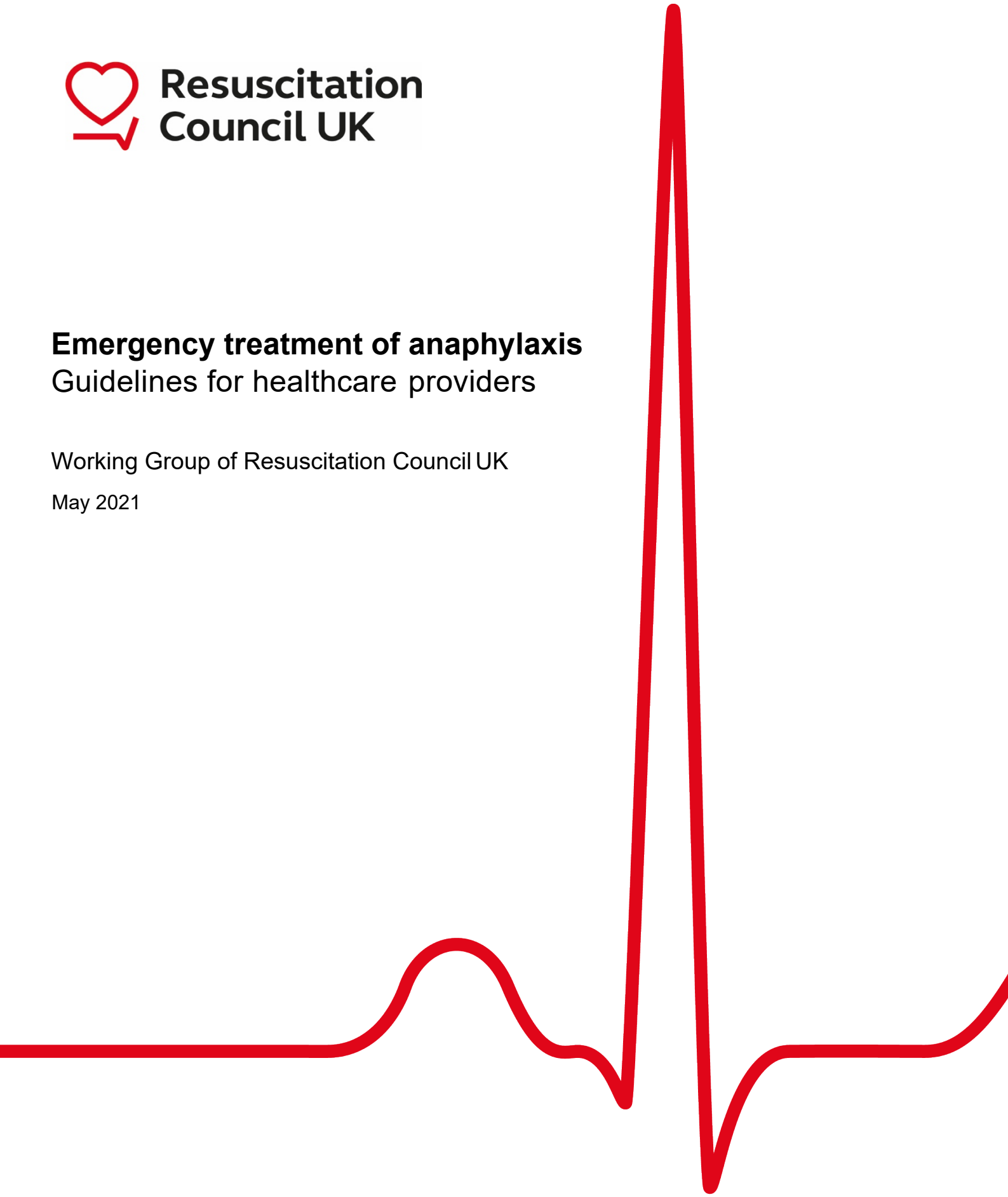
Resuscitation Council UK

Emergency treatment of anaphylaxis

Guidelines for healthcare providers

Working Group of Resuscitation Council UK

May 2021



Resuscitation Council UK

Updated May 2021
Review Date: May 2026

Published by Resuscitation Council UK

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Key recommendations for clinical practice

- Anaphylaxis is a potentially life-threatening allergic reaction.
- Recognise anaphylaxis based on:
    - sudden onset and rapid progression of symptoms
    - **A**irway and/or **B**reathing and/or **C**irculation problems
    - skin and/or mucosal changes (flushing, urticaria, angioedema) – but these may be absent in up to 20% of cases.

  The diagnosis is supported if a patient has been exposed to an allergen known to affect them.
- Treat life-threatening features, using the **A**irway, **B**reathing, **C**irculation, **D**isability, **E**xposure (**ABCDE**) approach.
- Adrenaline is the first-line treatment for anaphylaxis. Give intramuscular (IM) adrenaline early (in the anterolateral thigh) for **A**irway/**B**reathing/**C**irculation problems.
    - A single dose of IM adrenaline is well-tolerated and poses minimal risk to an individual having an allergic reaction. If in doubt, give IM adrenaline.
    - Repeat IM adrenaline after 5 minutes if **A**irway/**B**reathing/**C**irculation problems persist.
- Intravenous (IV) adrenaline must be used only in certain specialist settings, and only by those skilled and experienced in its use.
    - IV adrenaline infusions form the basis of treatment for refractory anaphylaxis: seek expert help early in patients whose respiratory and/or cardiovascular problems persist despite 2 doses of IM adrenaline.
- Follow the National Institute for Health and Care Excellence (NICE) guideline for the assessment and referral of patients suspected to have had anaphylaxis. Specifically:
    - All patients should be referred to a specialist clinic for allergy assessment.
    - Offer patients (or, if appropriate, their parent and/or carer) an appropriate adrenaline injector as an interim measure before the specialist allergy assessment (unless the reaction was drug-induced).
    - Patients prescribed adrenaline auto-injectors (and/or their parents/carers) must receive training in their use, and have an emergency management or action plan
- Further research is needed to better identify and treat patients at greatest

risk of severe anaphylaxis.

- Anaphylaxis reactions should be reported to the UK Anaphylaxis Registry at www.anaphylaxie.net (to register, email anaphylaxis.registry@ic.ac.uk).
- Follow guidance for reporting and debriefing of adverse events.

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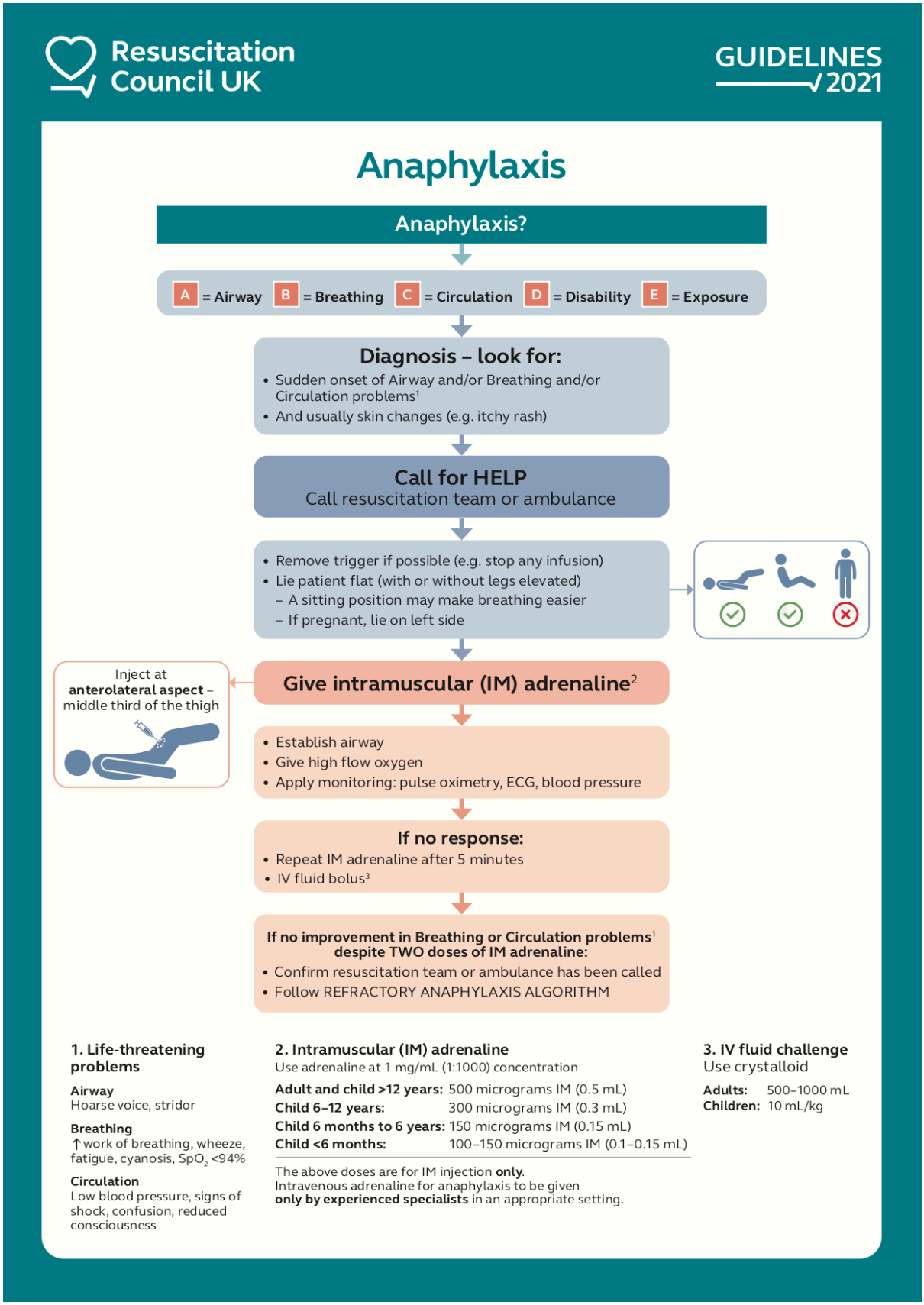
Summary of changes from previous guideline

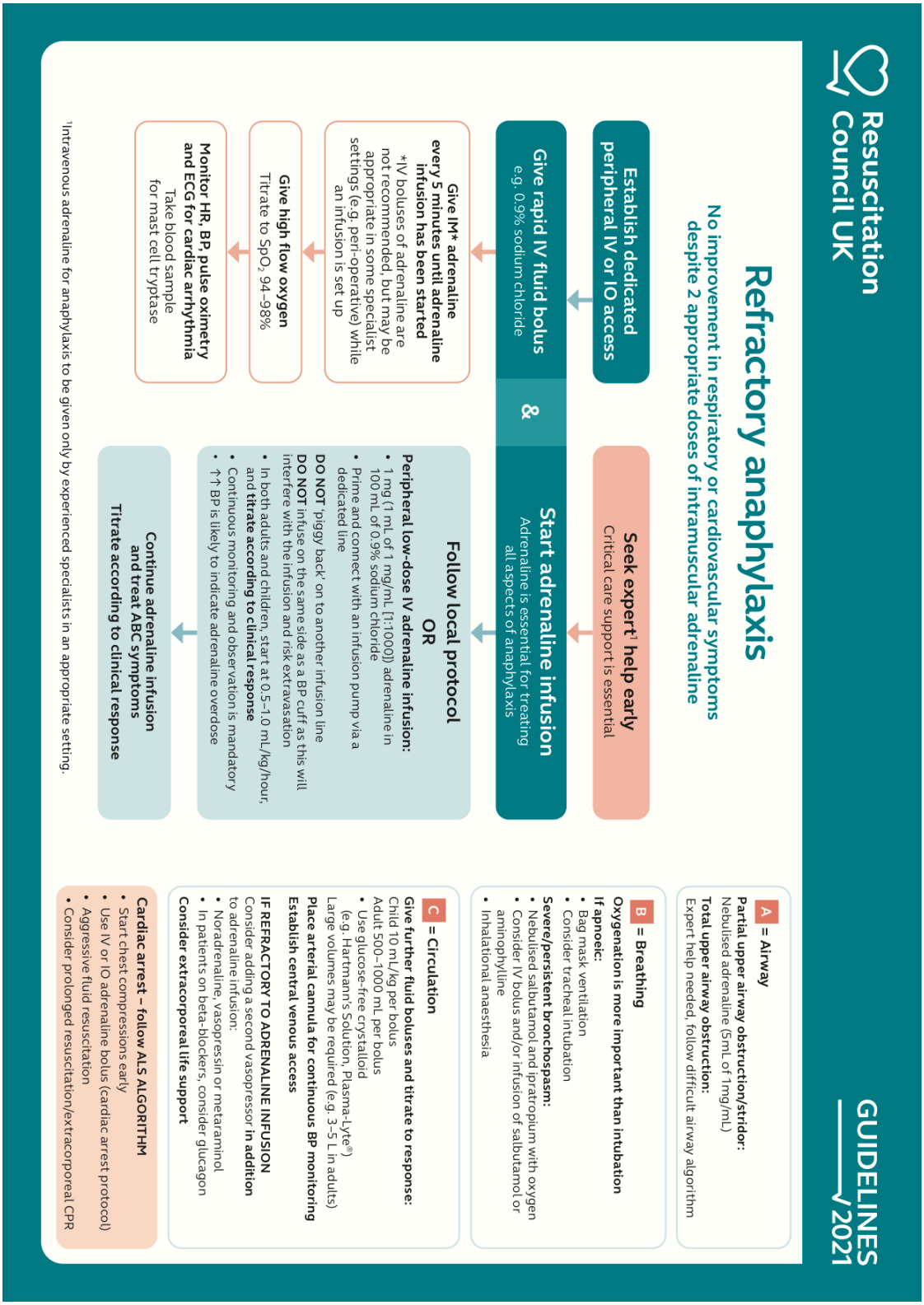
This guideline replaces the previous guideline from Resuscitation Council UK (RCUK): Emergency treatment of anaphylactic reactions – Guidelines for healthcare providers (originally published January 2008, annotated July 2012 with links to NICE guidance).[1]

- Greater emphasis on intramuscular adrenaline to treat anaphylaxis, and repeated after 5 minutes if **A**irway/**B**reathing/**C**irculation problems persist.
- A specific dose of adrenaline is now included for children below 6 months of age.
- Increased emphasis on the importance of avoiding sudden changes in posture and maintaining a supine position (or semi-recumbent position if that makes breathing easier for the patient) during treatment.
- There are 2 algorithms:
    - Initial treatment of **anaphylaxis,** with emphasis on repeating the dose of adrenaline after 5 minutes and giving an IV fluid bolus if **A**irway/**B**reathing/**C**irculation problems persist.
    - Treatment of **refractory anaphylaxis,** defined as anaphylaxis where there is no improvement in respiratory or cardiovascular symptoms despite two appropriate doses of IM adrenaline.
- IV fluids are recommended for refractory anaphylaxis, and must be given early if hypotension or shock is present.
- Antihistamines are considered a third-line intervention and should not be used to treat **A**irway/**B**reathing/**C**irculation problems during initial emergency treatment.
    - Non-sedating oral antihistamines, in preference to chlorphenamine, may be given following initial stabilisation especially in patients with persisting skin symptoms (urticaria and/or angioedema).
- Corticosteroids (e.g. hydrocortisone) are no longer advised for the routine emergency treatment of anaphylaxis.
- New guidance is offered relating to the duration of observation following anaphylaxis, and timing of discharge.

This updated guideline has been developed according to the GRADE Evidence to Decision (EtD) frameworks for adoption, adaptation, and de novo development of trustworthy recommendations (GRADE-ADOLOPMENT).[2] The evidence tables and conclusions have been peer-reviewed and published.[3]



Download this algorithm:
https://www.resus.org.uk/sites/default/files/2021-04/Anaphylaxis%20algorithm%202021.pdf



Download this algorithm:
https://www.resus.org.uk/sites/default/files/2021-04/Refractory%20anaphylaxis%20algorithm%202021.pdf

Download pages 7-11 (key recommendations, summary of changes, algorithms):
https://www.resus.org.uk/sites/default/files/2021-04/Anaphylaxis%20Summary%20Document.pdf

1. Introduction

1.1 Purpose of this guideline

Increasing numbers of people are presenting to UK hospitals with anaphylaxis.[4,5] Despite previous guidelines, at least 50% of reactions are not treated with IM adrenaline (the first-line treatment of anaphylaxis)[6] and treatment, investigation and follow-up of patients with anaphylaxis is suboptimal.[7-10]

This guideline replaces the previous guideline from Resuscitation Council UK: Emergency treatment of anaphylactic reactions – Guidelines for healthcare providers (originally published January 2008, annotated July 2012 with links to NICE guidance).[1] There are no randomised controlled clinical trials in humans providing unequivocal evidence for the optimal treatment of anaphylaxis; such evidence is unlikely to be forthcoming.[11,12] Nonetheless, the evidence-base for specific management strategies has increased, and international guidelines have been updated.[11,13]

This guideline provides:

- an updated consensus about the recognition and treatment of anaphylaxis in all healthcare settings
- a focus on the treatments that patients with anaphylaxis should receive, that are relevant to all healthcare providers
- recommendations for treatment that are easy to implement, and that will be appropriate for most anaphylaxis reactions
- new guidance on the treatment of refractory anaphylaxis.

This guideline does not cover every possible anaphylaxis scenario, and has been written to be as simple as possible to facilitate teaching, learning and implementation. Improved implementation should reduce harm and deaths from anaphylaxis.

1.2 Scope of this guideline

This guideline is for healthcare providers who are expected to treat anaphylaxis during their usual clinical role (e.g. doctors, nurses, paramedics) working in a hospital or out-of-hospital setting.

There is considerable variation and overlap between the skills and knowledge of different healthcare providers who are expected to treat anaphylaxis. Therefore we have deliberately not developed guidelines for specific groups of healthcare providers.

This guideline does not expect individuals to obtain IV access in an emergency if this is not part of their usual role. Any extra skills specifically for the treatment of a patient with anaphylaxis should be reasonably easy to learn, remember and implement (e.g. IM injection of adrenaline).

The Association of Anaesthetists (anaesthetists.org)[14] and the British Society for Allergy and Clinical Immunology (bsaci.org)[15] have published specific guidance for the treatment of anaphylaxis associated with anaesthesia. Additional resources relating to the treatment and investigation of peri-operative anaphylaxis - including referral pathways - can be found at nationalauditprojects.org.uk/NAP6home. There is also specific guidance from the UK Departments of Health and Social Care for managing anaphylaxis in schools and other educational settings.[16]

The treatment of a patient having anaphylaxis in any setting is broadly the same for children and adults.[11,12] Minor differences are highlighted.

1.3 Key points

Treatment of anaphylaxis should be based on general life-support principles:

- Call for help early.
- Use the **A**irway, **B**reathing, **C**irculation, **D**isability, **E**xposure (**ABCDE**) approach to recognise and treat problems. Treat the greatest threat to life first.
- Give IM adrenaline to treat **A**irway/**B**reathing/**C**irculation problems.
- Initial treatment should not be delayed by a lack of a complete history or definite diagnosis.
- Repeat IM adrenaline after 5 minutes if features of anaphylaxis do not resolve.

Patients having anaphylaxis in any setting should expect the following as a minimum:

- recognition that they are seriously unwell
- an early call for help (resuscitation team or ambulance)
- initial assessment and treatment based on an **ABCDE** approach
- prompt treatment with IM adrenaline
- investigation and specialist follow-up in an allergy clinic.

Both IM and IV routes are recommended for the treatment of anaphylaxis in the peri-operative setting. IV adrenaline should be used for anaphylaxis **only** by experienced specialists in an appropriate setting (e.g. critical care and peri-operative settings). See Section 5.1.2 for more information.

1.4 Methods

The Executive Committee of Resuscitation Council UK appointed two co-chairs who subsequently formed a Working Group to identify key areas that required updating, based on review of the previous guideline, new international evidence-based guidelines and a database of frequently asked questions.

The group met initially in February 2020. The updated guideline was developed according to the GRADE EtD frameworks for adoption, adaptation, and de novo development of trustworthy recommendations (GRADE-ADOLOPMENT).[2] The resulting recommendations and EtD tables have been published in the journal Resuscitation.[3] Feedback from members of a Consultation Panel was incorporated into a draft, which was made available for comment on the Resuscitation Council UK website (www.resus.org.uk) between 23 December 2020 and 24 February 2021. The guideline document was accessed 6057 times, resulting in 130 submissions from individuals and organisations. The feedback was reviewed at a March Working Group meeting and the document updated. The final guideline was made available on the Resuscitation Council UK website in May 2021.

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2. Anaphylaxis

2.1 Definition of anaphylaxis

The World Allergy Organisation Anaphylaxis Committee defines anaphylaxis as:[11]

> *"A serious systemic hypersensitivity reaction that is usually rapid in onset and may cause death.*
> *Severe anaphylaxis is characterized by potentially life-threatening compromise in airway, breathing and/or the circulation, and may occur without typical skin features or circulatory shock being present."*

Anaphylaxis is a clinical diagnosis; a precise definition is not important for treatment.

Anaphylaxis is characterised by:

- Sudden onset and rapid progression of symptoms.
- **A**irway and/or **B**reathing and/or **C**irculation problems.
- Usually, skin and/or mucosal changes (flushing, urticaria, angioedema).

The diagnosis is supported if a patient has been exposed to an allergen known to affect them. However, in up to 30% of cases there may be no obvious trigger.

Remember:

- Skin or mucosal changes ***alone*** are not a sign of anaphylaxis.
- **Skin and mucosal changes can be subtle or absent in 10–20% of reactions** (e.g. some patients present initially with only bronchospasm or hypotension).

Gastrointestinal symptoms (e.g. nausea, abdominal pain, vomiting) in the absence of **A**irway and/or **B**reathing and/or **C**irculation problems do not usually indicate anaphylaxis. Abdominal pain and vomiting can be symptoms of anaphylaxis due to an insect sting or bite.

Anaphylaxis lies along a spectrum of severity in terms of allergic symptoms.[11] (Figure 1).

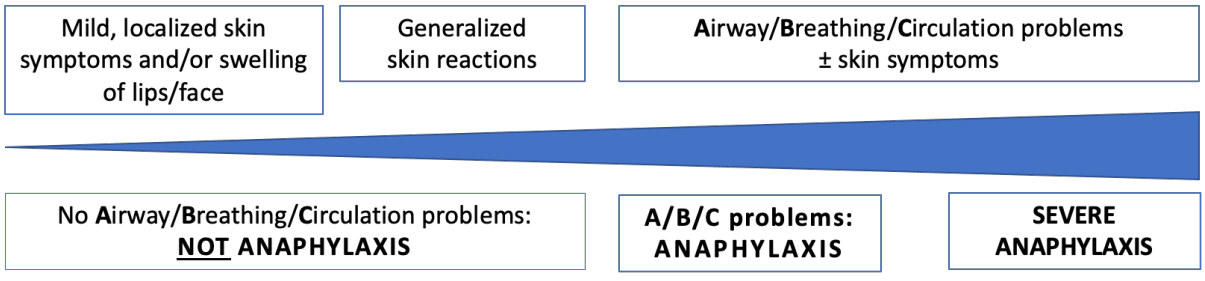


Figure 1: Spectrum of severity of allergy symptoms

2.2 Epidemiology

Incidence and lifetime prevalence
A recent systematic review undertaken by the European Academy of Allergy and Clinical Immunology Food Allergy & Anaphylaxis Group estimated the incidence for all-cause anaphylaxis in Europe to be 1.5 to 7.9 per 100 000 person-years.[17] The same data indicated that an estimated 1 in 300 people will experience anaphylaxis at some point in their lives. These figures are somewhat lower than those reported in the USA; this may reflect differences in criteria for diagnosis of anaphylaxis between Europe and North America.

Mortality
The overall prognosis of anaphylaxis is good, with a case fatality rate of under 1% in those presenting to hospitals in the UK,[4] and a mortality rate within the general population of less than one per million per annum.[18] For food anaphylaxis, the case fatality has halved between 1998 and 2018.[5] The risk of death may be increased in those with pre-existing asthma, particularly if this is poorly controlled or if treatment with adrenaline is delayed.[19]

There are approximately 20–30 deaths reported each year due to anaphylaxis in the UK, but this may be a significant underestimate.[4,5] Around 10 are related to food-induced anaphylaxis; peri-operative anaesthesia also causes around 10 deaths per annum.[20]

Triggers
Anaphylaxis can be caused by a broad range of triggers, but the most common allergens identified include food, drugs and venom.[4] There are clear age distributions for both hospitalisation and fatalities, that vary by trigger. **Food is the most common cause of anaphylaxis in young people**. Pre-school-aged children have the highest rate of hospitalisation due to food anaphylaxis, but a disproportionately low rate of fatal outcomes. **The greatest risk from fatal food allergy appears to be in teenagers and adults up to age 30 years.**[4,5] In contrast, fatal anaphylaxis due to drugs is rare in children, and is highest in the elderly;[4] this may be due to a combination of comorbid factors (e.g. cardiovascular disease, polypharmacy) in this age group, and concomitant use of antihypertensive drugs such as beta blockers and angiotensin-converting-enzyme (ACE) inhibitors (Figure 2).[21]

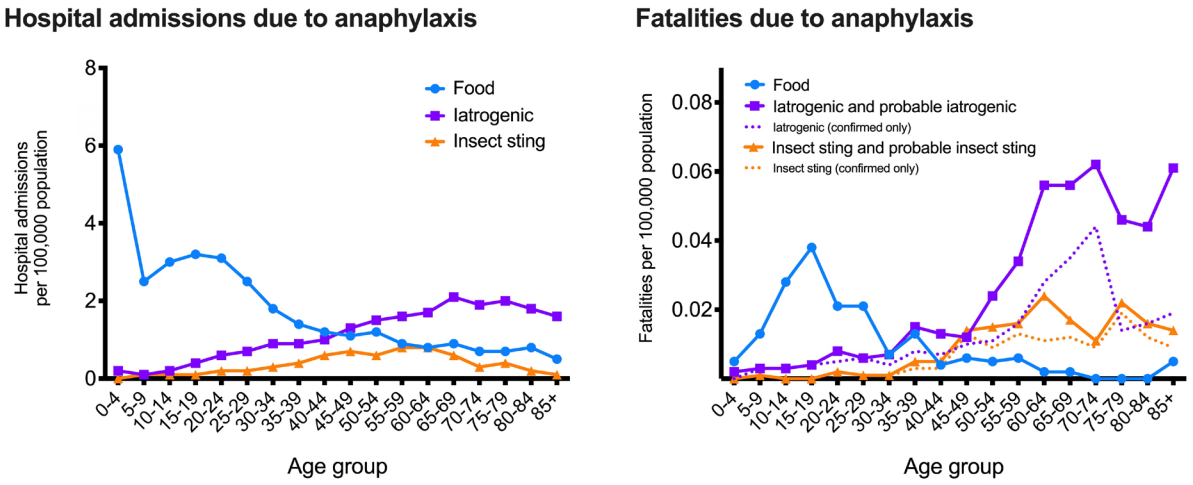


Figure 2: Age distribution for hospital admissions due to anaphylaxis (left) and fatalities (right) in the UK (1992–2012) by trigger (food, iatrogenic, insect stings)[4]

Virtually any food or class of drug can be implicated as a cause of anaphylaxis, although the classes of foods and drugs responsible for the majority of reactions are well-described (see Table 1). In around one third of cases, a specific food or drug trigger may not be evident.[4]

A significant number of cases of anaphylaxis are termed "idiopathic", either because a trigger cannot be identified or a non-immune mechanism is relevant. Nonetheless, the acute treatment of these patients is the same.

	Anaphylaxis (all severities)	Fatal anaphylaxis
Foods	Commonest triggers: • Peanut • Tree nuts • Cow's milk (children) Accounts for 35% of hospital admissions coded as anaphylaxis[5]	Commonest triggers:[5] • Peanut or tree nuts (50%) • Cow's milk (11% of total, 26% in children) 19% of anaphylaxis-related deaths[4]

Medication	Commonest triggers are antibiotics and chemotherapy drugs
	
	Commonest triggers in peri-operative setting:[20]
	• Antibiotics (47%)
	  ○ Co-amoxiclav (23%)
	  ○ Teicoplanin (18%)
	• Neuromuscular blocking agents (NMBAs) (33%)
	• Chlorhexidine (9%)
	
	Accounts for 17% of hospital admissions coded as anaphylaxis[4]
		Commonest triggers:[22]
		• NMBAs (32%)
		• Antibiotics (27%)
		  ○ Penicillins (11%)
		  ○ Cephalosporins (12%)
		• Contrast media (11%)
		• Non-steroidal anti-inflammatory drugs (6%)
		
		39% of anaphylaxis-related deaths[4]

Insect stings	6.5% of hospital admissions coded as anaphylaxis[4]	14% of anaphylaxis-related deaths[4]

Table 1. Common causes of anaphylaxis (non-fatal and fatal) in the UK

Risk of recurrence

In an individual who has had previous anaphylaxis, the risk of another anaphylaxis in the future has been estimated at approximately 1 in 12 per year in the UK.[23] Two studies undertaken in the USA reported a recurrence rate of 2.6–3.6 per 100 person-years.[24,25] Even in children admitted to paediatric ICU with anaphylaxis, there was a recurrence rate of 1.4 per 100 person-years.[26] These data reinforce the importance of specialist allergy investigation and follow-up after anaphylaxis.

Trends over time

An analysis of UK hospitalisation due to anaphylaxis reported a 174% increase in admissions since 1998, from 4.2 to 11.5 admissions per 100 000 population.[5] Around 30% of these are due to food-induced anaphylaxis. Of note, while hospital admissions have increased, irrespective of cause, anaphylaxis fatalities have remained stable over the same time period (Figure 3).

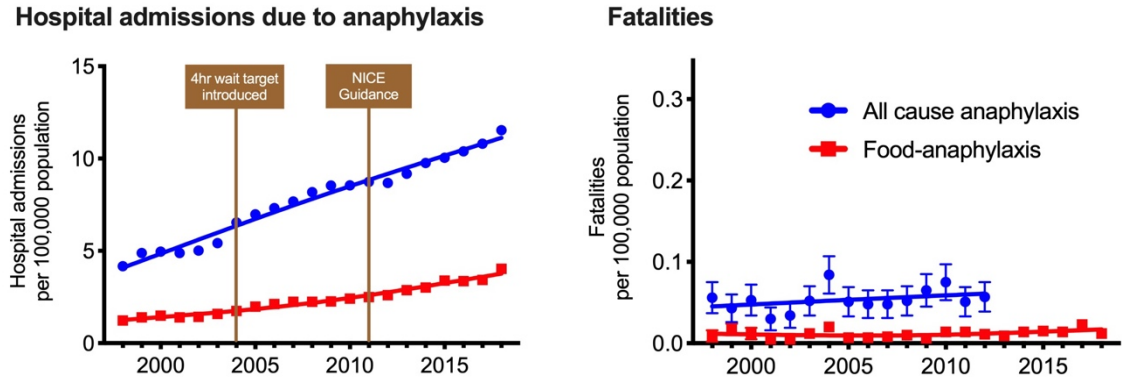


Figure 3: Time trends in UK hospital admissions (left) and fatalities (right) due to anaphylaxis (all cause anaphylaxis and food as the identified trigger), 1998–2018.[5] Vertical bars represent standard error of the mean.

Time course for fatal anaphylaxis

Where anaphylaxis is fatal, death usually occurs very soon after exposure to the trigger. Fatal food reactions typically cause respiratory arrest after approximately 30 minutes; insect stings cause collapse from shock after 10–15 minutes; and deaths caused by IV medication occur most commonly within five minutes. Cardiorespiratory arrest more than 4 h after the initial allergen exposure is rare (Figure 4).[27]

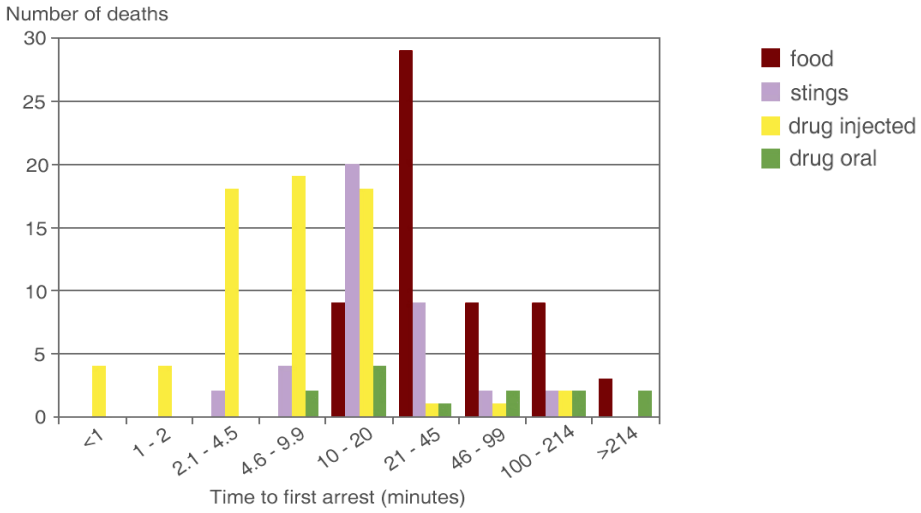


Figure 4: Time to cardiac arrest following exposure to triggering agent[27]

2.3 Pathophysiology of anaphylaxis

In anaphylaxis, the activation of multiple inflammatory pathways causes **A**irway/**B**reathing/ **C**irculation problems:

- Tissue oedema and smooth muscle contraction in the airways (causing bronchospasm and wheeze). This is the most common presentation for food-induced anaphylaxis.
- Fluid extravasation (tissue oedema, hypovolaemia), and a profound reduction in venous tone.[28,29]
    - If severe, this mix of hypovolaemic and distributive shock cannot be overcome by compensatory mechanisms and combine to cause reduced blood flow back to the heart and an underfilled ventricles.[29]
- Depressed myocardial function has also been reported, which can cause cardiogenic shock. Electrocardiographic changes have been noted. Release of mediators may cause arrhythmia such as supraventricular tachycardia; a reduction in coronary perfusion may cause or contribute to ST-segment or T-wave changes.[29]
- Fluid leakage into the bowel and smooth muscle contraction (resulting in abdominal and pelvic cramps).[30]

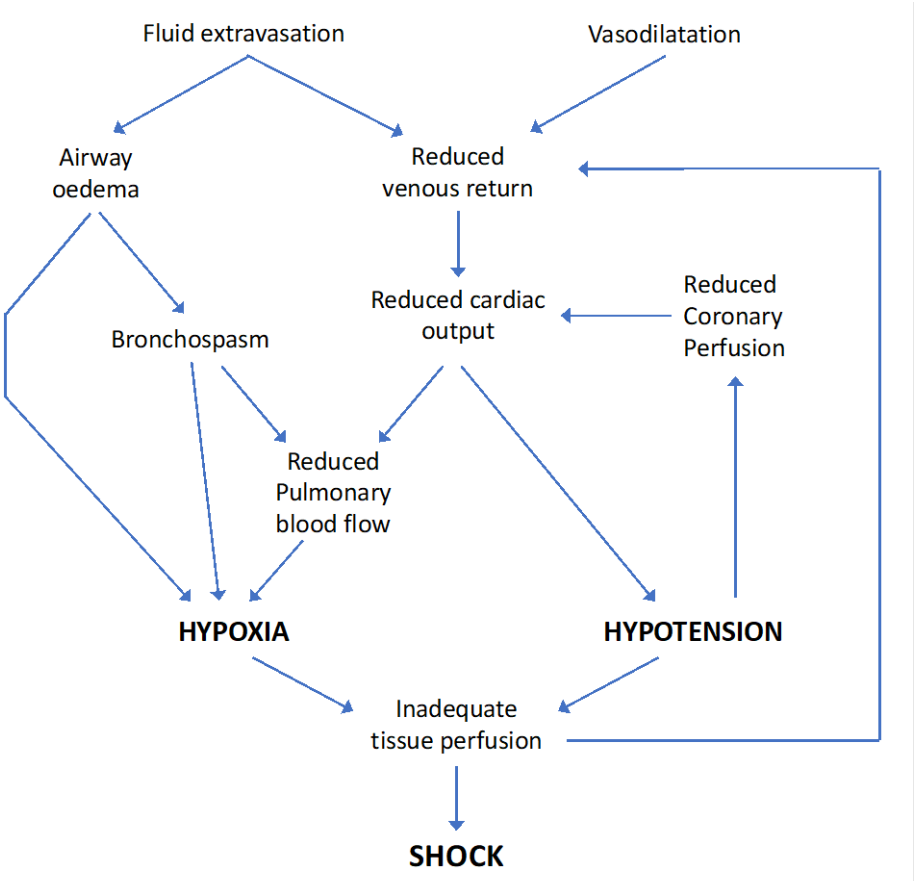


Figure 5: Physiological mechanisms responsible for anaphylactic shock

In a landmark paper, Fisher described 205 adult patients with peri-operative anaphylaxis, many of whom had central venous monitoring in place.[31] He reported:

- low right-heart filling pressures in all patients without cardiac disease; despite having elevated pressures, 9 of 11 patients with cardiac disease appeared to need volume expansion to achieve a stable blood pressure

- increases in haematocrit in 22 patients were indicative of **extravasation of up to 35% of circulating blood volume within 10 minutes of reaction onset**.

These data emphasise the need for aggressive fluid resuscitation in anaphylactic shock.

Changes in posture from supine to standing or sitting upright have been associated with cardiovascular collapse and death during anaphylaxis.[32,33] The change in posture further reduces venous return to the heart; this can lead to a further reduction in cardiac output and can compromise myocardial perfusion.

Keeping a patient with cardiovascular instability flat, with or without the legs raised, will maximise venous return to the heart and is therefore a key component of the initial response to anaphylaxis (see section 4.3). Patients with predominantly respiratory symptoms (and no evidence of cardiovascular instability) may prefer to be in a semi-recumbent position. Pregnant patients should lie on their left side to prevent aortocaval compression, if necessary, with the bed in a head-down position (see Section 4.7).

3. Recognition of anaphylaxis

Anaphylaxis is likely if a patient who is exposed to a trigger (allergen) develops a sudden illness (usually within minutes of exposure) with rapidly progressing skin changes and potentially life-threatening airway and/or breathing and/or circulation problems. The reaction is usually unexpected.

Many patients with anaphylaxis are not given the correct treatment because of failure to recognise anaphylaxis.[8-10,34] Approximately half of anaphylaxis episodes reported in the literature are *not* treated with IM adrenaline, even when reactions occur in a healthcare setting.[6] Conversely, prominent skin features (including facial swelling and generalised urticaria) may be misdiagnosed as anaphylaxis and be treated with adrenaline.[35,36]

A single set of criteria will not identify all anaphylaxis reactions. A range of signs and symptoms may occur, none of which is entirely specific for anaphylaxis; however, certain combinations make the diagnosis more likely.[37] Follow an **ABCDE** approach and treat life-threatening problems as they are recognised.[38] Guidelines must take into account some inevitable diagnostic errors, with an emphasis on the need for safety.

3.1 Diagnosis of anaphylaxis

Look for:

- Sudden onset of **A**irway and/or **B**reathing and/or **C**irculation problems.
- Usually, skin and/or mucosal changes (flushing, urticaria, angioedema).

Skin or mucosal changes alone are not a sign of anaphylaxis and may be absent in up to 20% of reactions.[37]

Confusion may arise because some patients have systemic reactions that are not anaphylaxis. Generalised urticaria, angioedema, and rhinitis are not considered to be anaphylaxis because life-threatening features – an **A**irway and/or **B**reathing and/or **C**irculation problem – are not present. However, **if in doubt, give IM adrenaline and seek expert help**.

Most reactions develop quickly over minutes: the timing is dependent on the trigger (see Table 2 and Figure 4). Allergens given by a parenteral route (e.g. IV drug, intramuscular injection, insect sting) cause a more rapid onset of symptoms than reactions to an ingested food or drug.[27,39]

Different symptoms are often associated with different triggers, as shown in Table 2. Most anaphylaxis in children is due to food, which may explain why respiratory presentations of anaphylaxis are more common in this age group. In around 5 -10% cases, no obvious trigger can be identified.[40,41]

	Food	Medication / iatrogenic	Venom from sting or bite (e.g. insect)
Age distribution: anaphylaxis (all severity)	Most common in preschool children, less common in older adults	Predominantly older ages	All ages
Typical presentation	Breathing problems	Circulation problems (breathing problems less common)	Circulation problems (breathing problems less common)
Onset	Less rapid	Rapid	Rapid
History of asthma/atopy	Common	Uncommon	Uncommon

Table 2. Differences in the presentation of anaphylaxis by trigger[39]

3.2 Airway / Breathing / Circulation problems

Patients can have either an **A** or **B** or **C** problem, or any combination. Use the **ABCDE** approach to recognise these and treat early.

Airway problems	Breathing problems:	Circulation problems:

• Airway swelling (throat and tongue swelling causing difficulty in breathing/swallowing; patients may feel their throat is closing)
• Hoarse voice
• Stridor (a high-pitched inspiratory noise caused by upper airway obstruction)
	• Increased work of breathing
	• Bronchospasm (wheeze) and/or persistent cough
	• Patient becoming tired with the effort of breathing (fatigue)
	• Hypoxaemia (SpO_2 <94%) which may cause confusion and/or central cyanosis
	• Respiratory arrest
		• Signs of shock:
		  ○ pale, clammy
		  ○ significant tachycardia (increased heart rate)
		  ○ hypotension (low blood pressure)
		• Dizziness, decreased conscious level or loss of consciousness
		• Arrhythmia
		• Cardiac arrest

Breathing problems can vary from mild bronchospasm to life-threatening asthma with no other features to suggest anaphylaxis.[42] Anaphylaxis can present primarily as respiratory arrest.[19,22,27] Consider anaphylaxis in a person with sudden onset breathing difficulties, especially if known to be allergic to a food or insect sting.

Circulation problems (often referred to as anaphylactic shock) can be caused by vasodilation, by capillary leak with loss of fluid from the circulation, and by direct myocardial depression (see Figure 5). Characteristically, these cause a compensatory tachycardia.[20,29] Bradycardia (a slow heart rate) is usually a late feature, often preceding cardiac arrest,[29] but has also been reported in insect/venom anaphylaxis, occurring with the onset of hypotension.[44] Anaphylaxis can also cause myocardial ischaemia and electrocardiogram (ECG) changes,[31] even in individuals with normal coronary arteries.[43]

Anaphylaxis can also affect a patient's neurological status (**D**isability problems) because of decreased brain perfusion or the effect of local allergic mediators in the central nervous

system. There may be confusion, agitation and loss of consciousness. Patients are usually anxious and may experience a "sense of impending doom".[45]

Patients may also have gastrointestinal symptoms (abdominal pain, incontinence, vomiting). These symptoms are more likely to indicate anaphylaxis in the context of reactions due to insect bite or sting, snake bite or parenteral administration of drugs.

3.3 Skin and/or mucosal changes

These are assessed as part of the **E**xposure when using the **ABCDE** approach.

- These are often the first feature of allergic reactions and are present in over 80% of anaphylaxis.[37]
- They can be subtle (e.g. patchy erythema) or dramatic (generalised rash).
- They may involve the skin, the mucosal membranes (e.g. lips), or both.
- There may be urticaria (also called hives, nettle rash, weals or welts), which can appear anywhere on the body. Weals may be pale, pink or red, can be different shapes and sizes, and are often surrounded by a red flare. They are usually itchy.
- Angioedema involves swelling of deeper tissues, most commonly in the eyelids and lips, and sometimes the tongue and in the throat.

Although skin changes can be worrying or distressing for patients and those treating them, skin changes without life-threatening **A**irway/**B**reathing/**C**irculation problems are not anaphylaxis. Reassuringly, most patients who present with skin changes caused by an allergic reaction do not go on to develop anaphylaxis.

3.4 Differential diagnosis

- Following an **ABCDE** approach will help with treating the differential diagnoses.
- In all of the circumstances below, IM adrenaline is unlikely to cause harm and might be clinically useful.

Life-threatening conditions:

- Sometimes anaphylaxis can present with symptoms and signs that are very similar to life-threatening asthma – this is most common in children.
- Hypotension is a late sign in children.
- Seek expert help early if there are any doubts about the diagnosis and treatment.

Other conditions which can mimic anaphylaxis (but do not respond to adrenaline)**:**

- inducible laryngeal obstruction (ILO, formerly known as vocal cord dysfunction)
- ACE inhibitor-induced angioedema, which can be life-threatening and typically does not respond to adrenaline

Non-life-threatening conditions (these usually respond to simple measures):

- faint (vasovagal episode) – this can occur in the context of non-anaphylaxis allergic reactions (see below)
- panic attack
- breath-holding episode in a child
- spontaneous (non-allergic) urticaria or angioedema.

There may be difficulty distinguishing between anaphylaxis and a panic attack. Patients with prior anaphylaxis may be prone to panic attacks if they think they have been re-exposed to the allergen that caused a previous reaction. The sense of impending doom and breathlessness leading to hyperventilation are symptoms that can resemble anaphylaxis. Sometimes, there may be flushing, or blotchy skin associated with anxiety adding to the diagnostic difficulty.

Diagnostic difficulty may also occur with vasovagal attacks after immunisation or other procedures, but the absence of rash, breathing difficulties, and swelling are useful distinguishing features, as is the slow heart rate in a vasovagal attack (whereas anaphylaxis is usually associated with a tachycardia). Symptoms should resolve rapidly on lying flat. **If rapid recovery does not happen, consider anaphylaxis as a cause**.

	Faint	**Anaphylaxis**
Onset	Over seconds	Over minutes to hours
Resolution	Usually rapid on lying flat, without additional treatment	Over minutes to hours
Airway		
-Airway swelling -Hoarseness -Stridor	Absent	May be present
Breathing		
-Respiration	Shallow, not laboured	Increased respiratory rate and/or work of breathing
-Wheeze / persistent cough	Absent	May be present
Circulation		
-Heart rate	Usually slow, rarely normal	Tachycardia common (but alone does not indicate anaphylaxis)
-Pulse	Central pulse usually palpable	Low-volume central pulse
-Blood pressure	Usually transiently low	Persistent hypotension
Disability		
-Consciousness	Dizziness, transient loss of consciousness - improved by lying flat	Dizziness, loss of consciousness persistent despite lying flat
Exposure (skin)	Often pale/clammy	Flushed, itchy, urticaria/hives, angioedema

Table 3: Typical features which may help distinguish between a vasovagal episode and anaphylaxis. Note that patients may not have all of these features.

4. Initial treatment of anaphylaxis

Use an **ABCDE** approach to recognise and treat anaphylaxis. Treat life-threatening problems as you find them. The basic principles of treatment are the same for all age groups.

4.1 The specific treatment of anaphylaxis depends on:

- location
- training and skills of rescuers
- number of responders
- equipment and drugs available.

Location
Treating a patient with anaphylaxis in the community will not be the same as in an acute hospital. If located out of hospital, seek advice by dialling 999 for ambulance support.

Training of rescuers
All clinical staff should be able to call for help and initiate treatment of anaphylaxis. National public health agencies recommend that staff who give immunisations should have annual updates in the treatment of anaphylaxis.[46]

Number of responders
A single responder must always ensure that help is coming. If there are several rescuers, several actions can be undertaken simultaneously.

Equipment and drugs available
In all clinical settings, resuscitation equipment and drugs (at a minimum, access to 1 mg/ml [1:1 000] adrenaline for IM use at the appropriate dose) must be immediately available to help with rapid resuscitation of a patient with anaphylaxis. Clinical staff should be familiar with the equipment and drugs they have available and should check them regularly. It is good practice to keep adrenaline 1 mg in 1 mL ampoule(s) for intramuscular use for the treatment of anaphylaxis in an 'anaphylaxis pack', and adrenaline (usually 1 mg in 10 mL) for the treatment of cardiac arrest in a separate cardiac arrest drug pack. This is to prevent adrenaline route and dosing errors during the treatment of anaphylaxis.

All patients who have anaphylaxis must be monitored (pulse oximetry, non-invasive blood pressure, 3-lead ECG) as soon as possible, although this should not delay initial treatment with adrenaline. Monitoring must be supervised by an individual who is skilled at interpreting and responding to any changes.

4.2 Patients with anaphylaxis in any setting should expect as a minimum:

- recognition that they are seriously unwell
- an early call for help
- initial assessment and treatments based on an ABCDE approach
- prompt treatment with intramuscular adrenaline
- investigation and follow up by an allergy specialist.

4.3 Anaphylaxis algorithm

The key steps for the initial treatment of anaphylaxis are shown in the algorithm (Figure 6) on the next page. This algorithm is applicable to all healthcare settings.

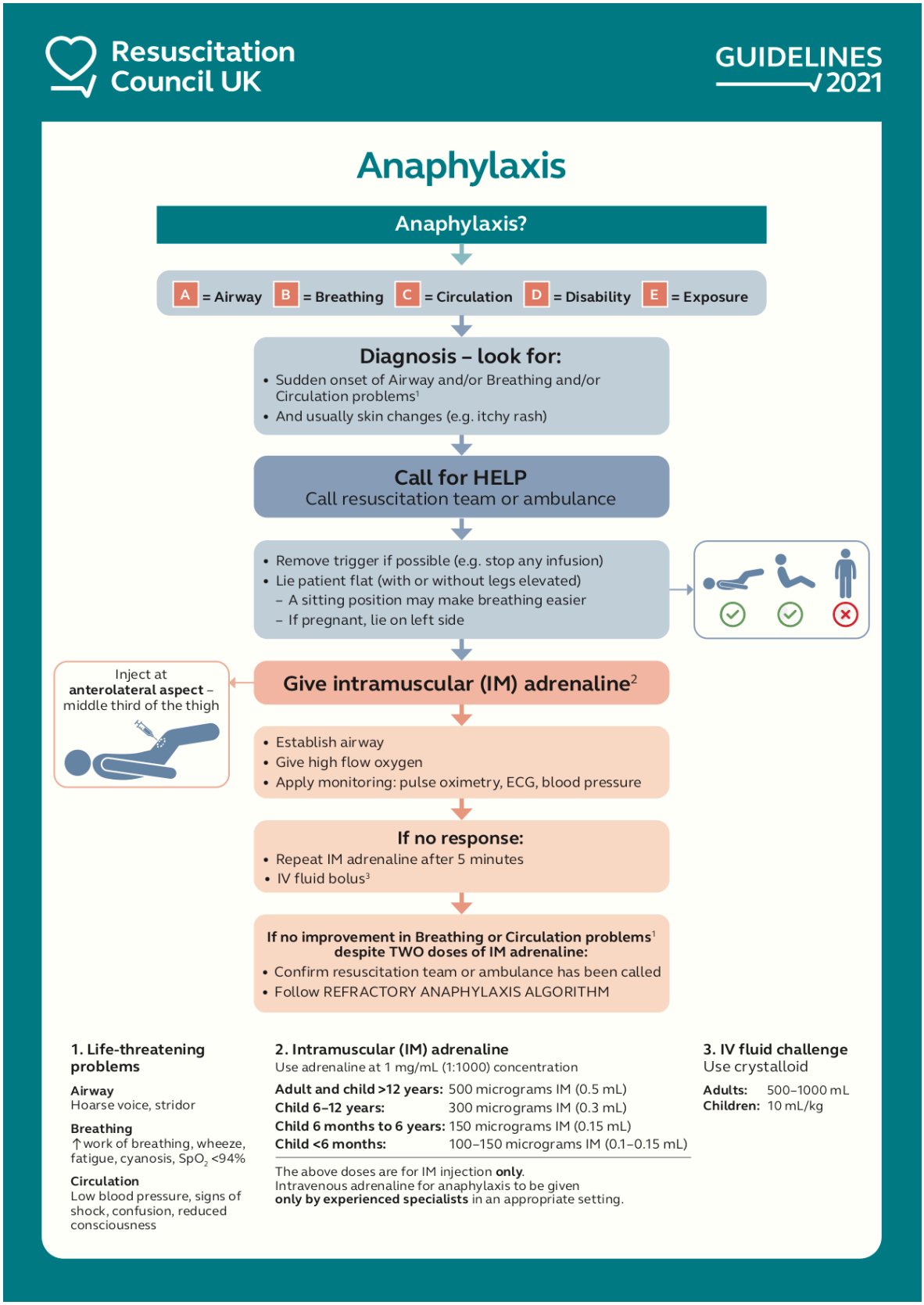


Figure 6. Anaphylaxis algorithm

4.4 Patient positioning

All patients should be placed in a comfortable position. The following factors should be considered:

- Fatality can occur within minutes if a patient stands, walks or sits up suddenly. Patients must **not** walk or stand during acute reactions. Use caution when transferring patients who have been stabilised.

- Patients with **A**irway and **B**reathing problems may prefer to be in a semi-recumbent position, as this will make breathing easier.

- Lying flat, with or without leg elevation, is helpful for patients with low blood pressure (**C**irculation problem).

- Patients who are breathing normally and unconscious should be placed on their side (recovery position). Monitor breathing continuously and prepare to intervene if this changes.

- Pregnant patients should lie on their left side to prevent aortocaval compression.[47] See section 4.7 for further guidance.

4.5 Remove the trigger if possible

- Stop any drug suspected of causing anaphylaxis (e.g. drug infusion, blood products).
- Remove the stinger after a bee sting. Early removal is more important than the method of removal.[48]
- Do **not** try to make a patient vomit.
- Do not delay definitive treatment if removing the trigger is not feasible.

4.6 Cardiorespiratory arrest during anaphylaxis

- Recognise that cardiorespiratory arrest has occurred if the person becomes unresponsive or unconscious, and breathing is absent or abnormal.
- Start cardiopulmonary resuscitation (CPR) immediately and follow current guidelines.[38] High-quality CPR with minimal interruption for other interventions improves the chances of survival from cardiac arrest.
- Rescuers should ensure that help is on its way, as early advanced life support is essential.
- Once cardiac arrest has occurred, absorption of adrenaline given by the intramuscular route will not be reliable and attempts to give it may interrupt or distract from delivery of high-quality CPR. Use IV or intraosseous (IO) adrenaline at doses recommended in advanced life support guidelines.
- Prolonged resuscitation may be successful (as with hypothermia) – see section 6 on ‘Refractory anaphylaxis’.

4.7 Anaphylaxis during pregnancy

The treatment of anaphylaxis during pregnancy is similar to that for the non-pregnant patient. If the mother is supine, manoeuvres are required from around 20 weeks gestation (when the uterus is palpable at or above the umbilicus) to reduce compression of the inferior vena cava and abdominal aorta by the pregnant uterus.[47]

- Pregnant patients should lie on their left side to prevent aortocaval compression
- If the mother is breathing normally and has a cardiac output maximal venous return is achieved in the full lateral (recovery) position. She can be then be placed in a head-down position instead of lifting the legs.
- If she is placed supine in order to treat the airway or perform CPR then the uterus must be displaced manually to the left with one or two hands. A head-down tilt can be performed if she is on a firm surface (e.g. operating table).
- If anaphylaxis is severe and refractory to treatment, consideration should be given to early peri-arrest caesarean section.[49]

4.8 Refractory anaphylaxis

Most of the anaphylaxis reactions occurring in a community setting will respond to initial treatment with IM adrenaline, although currently around 10% receive a second dose and 2.2% (95% confidence interval, 1.1- 4.1%) receive more than two doses.[6]

All healthcare professionals should be able to identify patients with **B**reathing and/or **C**irculation problems of anaphylaxis which do not respond to initial treatment with IM adrenaline, and to escalate care quickly by calling for support from the resuscitation team or from the ambulance service for urgent transfer to hospital.

More details on the treatment of refractory anaphylaxis are in Section 6.

5. Drugs used in the initial treatment of anaphylaxis

5.1 Adrenaline (Epinephrine)

- Intramuscular adrenaline is the first-line treatment for anaphylaxis (even if intravenous access is available).
- A single dose of IM adrenaline is well-tolerated and poses minimal risk to an individual having an allergic reaction.
- If features of anaphylaxis persist despite two doses of IM adrenaline, follow the refractory anaphylaxis algorithm (see section 6) and call for expert support to allow an intravenous adrenaline infusion to be started.

Adrenaline is the most important drug for the treatment of anaphylaxis.[11,12] Although there are no randomised controlled trials, evidence from observational data, clinical experience and animal models support its use to reduce bronchoconstriction and restore adequate tissue oxygenation.

As an alpha-receptor agonist, adrenaline reverses peripheral vasodilation and reduces tissue oedema. Its beta-receptor activity dilates the bronchial airways, increases the force of myocardial contraction, and suppresses histamine and leukotriene release. Adrenaline also acts directly on beta-2 adrenergic receptors on mast cells to inhibit activation,[50-52] so early adrenaline may attenuate the severity of IgE-mediated allergic reactions.

Adrenaline seems to work best when given early after the onset of anaphylaxis symptoms.[53] Delayed administration is associated with protracted reactions, hypotension and fatal outcomes.[48,49] However, adrenaline – particularly via the intravenous route – is not without risk.[13,54] Adverse effects are extremely rare with correct doses injected by the IM route.[56] Rarely, complications (e.g. myocardial ischaemia) have been reported, but there is uncertainty about whether these were due to the allergic reaction itself, the adrenaline used to treat it or a combination of both.

Difficulties can arise if the clinical picture is evolving when the patient is first assessed. Adrenaline should be given to all patients with life-threatening features (i.e. evidence of **A**irway/**B**reathing/**C**irculatory involvement). If these features are absent but there are other features of a systemic allergic reaction, the patient needs careful observation and appropriate symptomatic treatment using the **ABCDE** approach.

Adrenaline must be readily available in clinical areas where anaphylaxis could occur. This includes out-of-hospital settings, e.g. where immunisations may be administered.[46]

5.1.1 IM adrenaline (give as soon as possible)

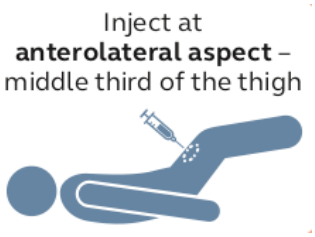
- **IM adrenaline is the first-line treatment for anaphylaxis in all healthcare settings.**

The IM route has several benefits:

- It is safer than the IV route.
- It does not require IV access.
- The IM route is easier to learn.

Attach monitoring (pulse oximetry, blood pressure, ECG) as soon as possible: this will help assess the patient's response to adrenaline.

The best site for IM injection is the anterolateral aspect of the middle third of the thigh.[57] The needle used for injection must be sufficiently long to ensure that the adrenaline is injected into muscle: use a green (21G) or blue (23G) needle (see Appendix 2 for further guidance regarding needle length and IM injection technique).[1]



The subcutaneous or inhaled routes for adrenaline are not recommended for the treatment of anaphylaxis because they are less effective.[13,57-59]

Adrenaline IM dose	Use 1 mg/mL [1:1000] adrenaline	
Adult and child* > 12 years:	500 micrograms IM	(0.5 mL of 1 mg/ml adrenaline)
6 – 12 years:	300 micrograms IM	(0.3 mL)
6 months – 6 years:	150 micrograms IM	(0.15 mL)
< 6 months:	100 – 150 micrograms IM	(0.1 to 0.15 mL)

*Give 300 micrograms IM (0.3 mL) in a child who is small or prepubertal

The scientific evidence for the recommended doses is weak. The recommended doses are based on what is considered to be safe and practical to draw up and inject in an emergency,[60] and have been used for many decades, as per international guidelines.

Repeat the IM adrenaline dose after 5 minutes if there is no improvement in the patient's condition. Some guidelines recommend further doses are given in the contralateral thigh to aid absorption, although the evidence for this is uncertain.

There is large inter-individual variability in the response to adrenaline, with peak absorption occurring around 5–10 min after IM injection. If there is no improvement in **B**reathing or **C**irculation problems despite two doses of adrenaline, follow the algorithm for refractory anaphylaxis (Section 6).

Pallor can occur following adrenaline, due to vasoconstriction. This might be misinterpreted as ongoing cardiovascular compromise or anaphylaxis and thereby can increase the risk of adrenaline overdose. **This is a particular concern in small children, who may remain pale following 2–3 doses of adrenaline**.[61] A significantly raised BP is a key indicator of adrenaline overdose.[62]

Measure vital signs (respiratory rate, oxygen saturations, heart rate, BP, level of consciousness) **and auscultate for wheeze to monitor the effect of treatment and assess if further doses of adrenaline are required.**

5.1.2 IV adrenaline (for specialist use only)

The IM route for adrenaline is the route of choice for the vast majority of healthcare providers. IV adrenaline should only be given by experienced specialists in an appropriate setting.

When using IV adrenaline, there is a much greater risk of causing harmful side effects due to dilution errors or incorrect dosing.[35,36,55-57] Excessive doses of adrenaline, particularly by the IV route, can cause tachyarrhythmias, severe hypertension, myocardial infarction and stroke. Fatalities have occurred in the UK due to the inappropriate use of IV adrenaline to treat non-anaphylaxis allergic reactions.[36] Adverse events are more common after IV adrenaline, particularly with IV bolus administration and dosing errors (e.g. using 1 mg/mL (1:1 000) solution (appropriate for IM injection) instead of more dilute solutions (e.g. 0.1 mg/mL (1:10 000) for IV injections).[63]

Healthcare providers with experience in the use and titration of vasopressors in their normal clinical practice (e.g. anaesthetists, critical care practitioners) may choose to administer adrenaline by the IV route. Both IM and IV routes are recommended for use in treating peri-operative anaphylaxis,[14] although **international guidelines recommend IM adrenaline for first-line treatment of anaphylaxis in all settings.**

Many healthcare providers will have given IV adrenaline as part of resuscitating a patient in cardiac arrest. **This alone is insufficient experience to justify them using IV adrenaline for the treatment of anaphylaxis.** In patients with a spontaneous circulation, IV adrenaline can cause life-threatening hypertension, tachycardia, arrhythmias, and myocardial infarction.

More information about the use of IV low-dose adrenaline infusions can be found in Section 6 (refractory anaphylaxis).

5.1.3 Nebulised adrenaline

Nebulised adrenaline may be effective as an adjunct to treat upper airways obstruction caused by laryngeal oedema, but only after treatment with IM (or IV) adrenaline and not as an alternative.[12] Recommended doses are 5 mL of 1 mg/mL (1:1 000) adrenaline.

5.1.4 Adrenaline in special populations

Dose adjustments are no longer recommended in specific patient groups, for example in patients taking tricyclic antidepressants.

5.1.5 Adrenaline auto-injector devices

Auto-injectors are often prescribed to patients at risk of anaphylaxis for early self-administration or injection by a carer or family member in the event of an anaphylactic reaction. Depending on the brand, they are available in three doses of adrenaline: 150 micrograms (0.15 mg), 300 micrograms (0.3 mg) and 500 micrograms (0.5 mg). Healthcare professionals should be familiar with their use.

In all healthcare settings, giving adrenaline from an ampoule by syringe and needle is preferred in an emergency, since auto-injectors will not allow delivery of an age/weight-appropriate dose in most patients. In addition, concerns have been raised as to whether auto-injectors will deliver an IM dose in some patients.[64]

If the only available adrenaline preparation is an auto-injector, this can be used in the first instance. Some settings (e.g. allergy challenge clinics) may recommend a patient to self-administer adrenaline using an auto-injector under supervision, to train them in its use, which is associated with significant patient benefit.[65]

Auto-injectors are not recommended in healthcare settings for administration of adrenaline in patients needing more than one dose of adrenaline. If further doses of adrenaline are needed, give these from an ampoule by syringe and needle (see Appendix 2).

5.2 Oxygen (give as soon as available)

Initially, give the highest concentration of oxygen possible, using a mask with an oxygen reservoir. As soon as is feasible, adjust the inspired oxygen concentration to achieve an oxygen saturation of 94 – 98% (in patients at risk of hypercapnic respiratory failure, consider a target range of 88 – 92%).[66] If the patient's trachea has been intubated, ventilate the lungs with an appropriate inspired concentration of oxygen. Use blood gas measurements to guide further oxygen and ventilation therapy.

5.3 Intravenous fluids

In the presence of hypotension/shock, or poor response to an initial dose of adrenaline:

- Secure IV access and give a rapid IV fluid bolus (10 mL/kg in a child or 500 – 1 000 mL in an adult) and monitor the response.
    - Use non-glucose-containing crystalloids that contain sodium in the range 130 – 154 mmol/L (e.g. 0.9% sodium chloride, Hartmann's) for initial resuscitation.[67]
- Give further fluids as necessary. A large volume (up to 3 – 5 litres in adults) may be needed for severe anaphylactic shock (see section 6). Use a non-glucose-containing crystalloid (e.g. Hartmann's or Plasma-Lyte®) rather than 0.9% sodium chloride to reduce the risk of causing hyperchloraemia.
- Give fluids via the IO route if IV access is delayed.

Ensure a further dose of IM adrenaline is administered after 5 minutes if breathing or circulation symptoms persist and while attempting to secure IV or IO access.

Up to one third of the circulating volume may be lost through extravasation and fluid redistribution during anaphylaxis,[31] causing hypotension and shock.[29] Anaphylaxis causes vasodilation, which can mask features of poor tissue perfusion, which would normally be a presenting sign of circulatory shock. Venous return is reduced in anaphylaxis, even in the absence of apparent cardiovascular compromise.[28]

Colloid solutions are not recommended for treatment of anaphylaxis and are a recognised cause of anaphylaxis. Stop a colloid infusion in any patient presenting with possible anaphylaxis.[68]

5.4 Antihistamines

- **Antihistamines are *not* recommended as part of the initial emergency treatment for anaphylaxis.[3]**
  - Antihistamines have no role in treating respiratory or cardiovascular symptoms of anaphylaxis
- **Antihistamines can be used to treat skin symptoms that often occur as part of allergic reactions including anaphylaxis.[3]**
  - Their use must not delay treatment of respiratory or cardiovascular symptoms of anaphylaxis (using adrenaline and IV fluids).

The role of antihistamines in anaphylaxis is debated but there is consensus across all guidelines that they are not a first-line treatment.[11,12,61,63,69] They are of no benefit in treating life-threatening features of anaphylaxis. Most guidelines express concern that their use often delays administration of initial and subsequent doses of adrenaline, thereby increasing morbidity.[3]

Antihistamines can be helpful in alleviating cutaneous symptoms (whether these are due to anaphylaxis or non-anaphylaxis allergic reactions), but must not be given in preference to adrenaline to treat anaphylaxis. In the presence of ongoing **A**irway/**B**reathing/ **C**irculation problems of anaphylaxis, give further IM adrenaline and seek expert advice.

Once a patient has been stabilised, use a **non-sedating oral antihistamine** (e.g. cetirizine) in preference to chlorphenamine which causes sedation.[11,69] Recommended doses are shown in Table 4. If the oral route is not possible, chlorphenamine can be given by intravenous or intramuscular injection, but note that such H1-receptor antihistamines can cause hypotension when given as a rapid IV bolus.[70]

Age	Dose of oral cetirizine
< 2 years	250 micrograms/kg
2–6 years	2.5–5 mg
6–11 years	5–10 mg
12+ years	10–20 mg
Adults	10–20 mg

Table 4. Recommended doses for oral cetirizine for an allergic reaction

There is no evidence to support the routine use of an H2-receptor antihistamine (e.g. ranitidine) to treat anaphylaxis.[11,12]

5.5 Steroids

- **The routine use of corticosteroids to treat anaphylaxis is not advised.**
- **Consider giving steroids after initial resuscitation for refractory reactions or ongoing asthma/shock. Steroids must not be given preferentially to adrenaline.**

The primary action of corticosteroids is the downregulation of the late-phase (rather than early-phase) inflammatory response. However, **there is little evidence that corticosteroids help shorten protracted symptoms or prevent biphasic reactions** (see section 8.2).[3,71] Moreover, there are emerging data suggesting that early use of steroids is associated with an increased risk of intensive care admission, even after adjusting for severity of presenting symptoms.[41,72] These recommendations regarding steroid use are based on very low-certainty evidence.[3]

In asthma, early corticosteroid treatment may be beneficial in adults and children.[73,74] Corticosteroids may be indicated where an acute asthma exacerbation may have contributed to the severity of anaphylaxis. Steroids should be given by the oral route where possible. Refer to the BNF for Children to find information on appropriate dosing.

5.6 Other drugs

Bronchodilators

The presenting symptoms and signs of severe anaphylaxis and life-threatening asthma can be the same. Individuals presenting with asthma in the context of possible exposure to a known allergen (so that anaphylaxis is a differential diagnosis) should receive treatment with intramuscular adrenaline.

In addition to the drugs listed above, consider further inhaled bronchodilator therapy with salbutamol and/or ipratropium. There are no data to support the choice of one bronchodilator above another in the treatment of anaphylaxis.[12] However, **bronchodilators should not be used as an alternative to further parenteral treatment with adrenaline** in the presence of persisting respiratory problems.

Further guidance on treatment of bronchospasm in severe asthma can be found in the asthma guidelines published by the British Thoracic Society and Scottish Intercollegiate Guideline Network (SIGN) (www.brit-thoracic.org.uk).

Cardiac drugs

Adrenaline remains the first-line vasopressor for the treatment of anaphylaxis. Refer to Section 6 for details of alternative vasopressors and inotropes when initial resuscitation with adrenaline and fluids has not been successful.

Resuscitation Council UK

6. Refractory anaphylaxis

6.1 Key points

Refractory anaphylaxis is defined as anaphylaxis requiring ongoing treatment (due to persisting respiratory or cardiovascular symptoms) despite two appropriate doses of IM adrenaline.

- When treating refractory anaphylaxis, a rapid **ABCDE** assessment should be undertaken, and priority given to treating the greatest threat to life.
- Critical care support should be sought early (in hospital, call for the resuscitation team according to local protocol; dial 999 for the ambulance service in a community setting).
- The algorithm below is designed to support clinicians, and not to replace the expertise of experienced critical care clinicians.
- **Maintenance adrenaline therapy is critical**, using a low-dose IV adrenaline infusion. If an IV infusion cannot be administered safely (e.g. due to a patient being outside a hospital environment), continue to give IM adrenaline after every 5 minutes while life-threatening cardiovascular and respiratory features persist.
    - Adrenaline therapy should be supported with an initial rapid fluid bolus and maintenance fluid therapy.
    - IV adrenaline infusions are important in the management of all aspects of refractory anaphylaxis – not just cardiovascular shock.
- Prolonged resuscitation and critical care support (hours to days) may be required.
- In settings where it is available, consider extra-corporeal life support.

6.2 Introduction

The majority of anaphylaxis episodes occurring in a community setting will respond to initial treatment with IM adrenaline, although currently around 10% receive more than one dose.[6] This may sometimes be due to the use of auto-injectors which cannot deliver an age/weight-appropriate dose in most patients.

Less than 1% of reactions are refractory to initial adrenaline treatment, and intensive care admissions for anaphylaxis are uncommon.[75]

Data from the UK Fatal Anaphylaxis Registry shows that one third of deaths from food anaphylaxis occur despite timely administration of a first dose of adrenaline.[76] These data are consistent with case reports and coronial inquests, where inability to deliver sufficient adrenaline and other resuscitation measures (rather than an avoidable delay in giving initial adrenaline) may have contributed to a fatal outcome. This is the rationale for emphasising the need to recognise refractory anaphylaxis and escalate early to ensure appropriate management.[77]

6.3 Definition

We have used the following definition:

Refractory anaphylaxis is defined as anaphylaxis requiring ongoing treatment (due to persisting respiratory or cardiovascular symptoms) despite two appropriate doses of IM adrenaline.

6.4 Pathophysiology of refractory anaphylaxis

Refractory anaphylaxis is poorly studied; however, evidence from case series[44,78] and animal models[53,79] of severe anaphylaxis suggest that refractory reactions may be due to a combination of the following:[29]

- delayed or insufficient delivery of adrenaline (**common**)
- progression of reaction due to ongoing release of inflammatory mediators (**common**)
- diminished response to repeated adrenaline doses administered during reactions (tachyphylaxis) (**uncommon**).

The treatment of refractory anaphylaxis should therefore include the following strategies:

- Patients with refractory anaphylaxis require **critical care support** to ensure effective airway management, tissue oxygenation and circulatory support.

- **Optimising delivery of adrenaline**: adrenaline is important in the treatment of all aspects of anaphylaxis and not only cardiovascular shock. A single dose of adrenaline (by any route) is unlikely to be sufficient in severe reactions.[30] Refractory reactions should therefore be treated with an adrenaline infusion and fluid therapy to support delivery of adrenaline at a tissue level.[77]

  Data from case series in severe human anaphylaxis[44,78] and animal models[80] suggest that low-dose IV adrenaline infusions may be more efficient in the treatment of anaphylaxis than use of other routes of administration and/or IV bolus therapy.

- The response to an adrenaline infusion may sometimes be suboptimal, particularly if cardiovascular shock is fully established. Seek urgent expert advice to guide the use of other vasopressors to treat shock.

  There are no data from human studies to support recommending a specific vasopressor strategy in anaphylaxis refractory to adrenaline infusion. Data from animal models of anaphylaxis suggest that adrenaline infusion followed by an alternative vasopressor (e.g. vasopressin) is superior to vasopressin alone in the treatment of refractory anaphylactic shock.[79,81] Follow local protocols for treatment of refractory shock, including the choice of noradrenaline, metaraminol and/or vasopressin.

6.5 Refractory anaphylaxis algorithm

The key steps for the treatment of refractory anaphylaxis are shown in the algorithm (Figure 7) on the next page.

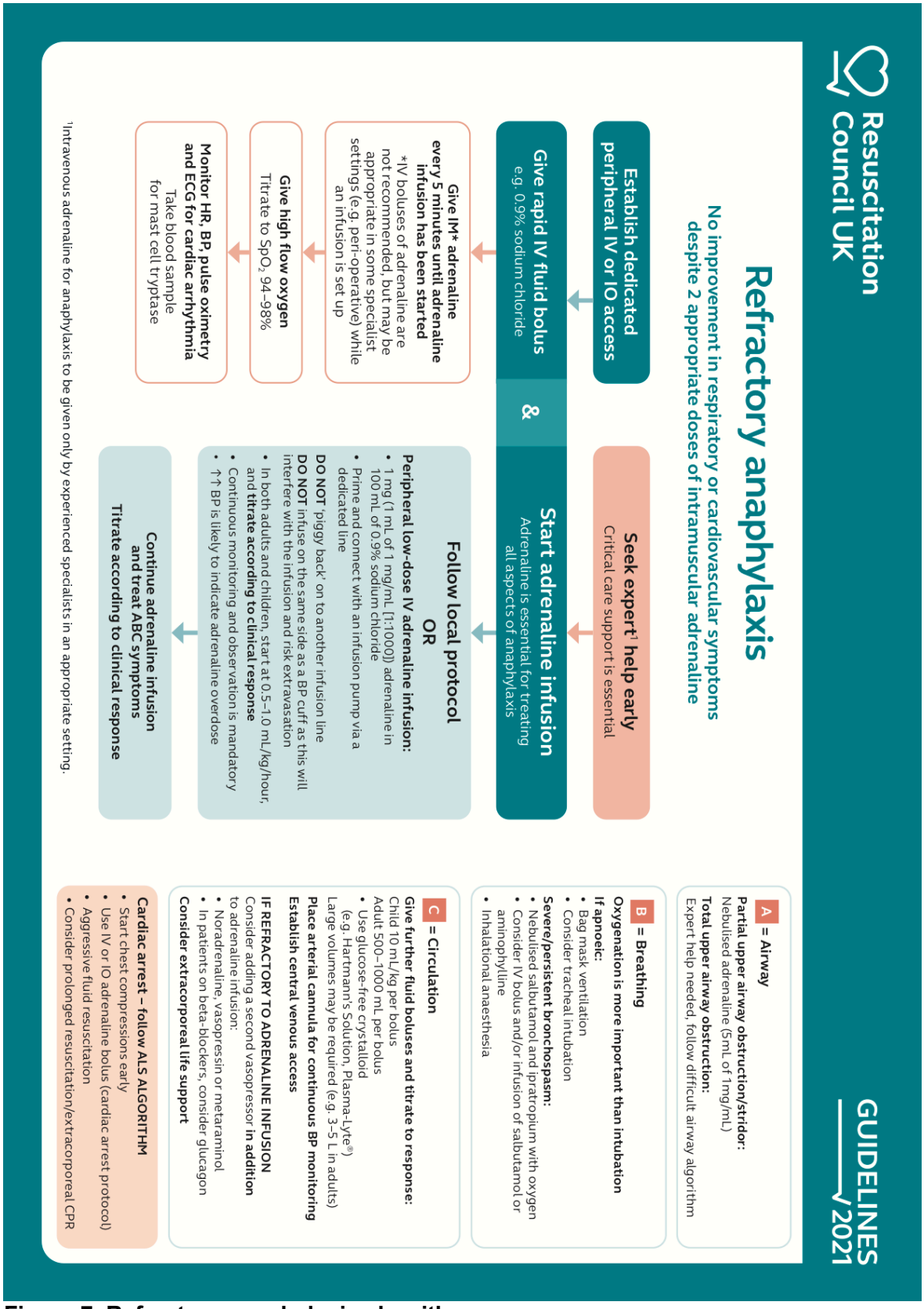


Figure 7. Refractory anaphylaxis algorithm

6.6 IV adrenaline infusion

Patients with no improvement in respiratory and/or cardiovascular symptoms due to anaphylaxis, despite two appropriate doses of adrenaline, should be started on an adrenaline infusion.

- Seek urgent expert help to establish a low-dose, IV adrenaline infusion. IV adrenaline should be given only by experienced specialists in an appropriate setting.

Dilute adrenaline can be infused via a peripheral IV cannula or IO needle until central venous access is obtained.[44,82] Where a local protocol is not available, the protocol[44] below (used in other guidelines[61,83]) can be followed.

Continue to repeat IM adrenaline after 5 minutes until the infusion has been started. If an IV infusion cannot be administered safely (e.g. due to a patient being outside a hospital setting), continue to repeat IM adrenaline after every 5 minutes while life-threatening respiratory or cardiovascular features persist, and seek urgent ambulance support/expert help.

IV adrenaline boluses are NOT recommended for refractory anaphylaxis unless a patient is in cardiac arrest (but they may be used by those experienced in the use and titration of vasopressors in their normal clinical practice, while an adrenaline infusion is set up).

Monitor for adrenaline side effects: tachycardia, arrhythmia, hypertension. If present, reduce the infusion rate (or stop the infusion if side effects are severe).

Peripheral IV adrenaline infusion for refractory anaphylaxis[44]

Follow local protocol or:

Preparation

- **Continuous monitoring and observation are mandatory**:
  - ECG, pulse oximetry, non-invasive BP at least every 5 minutes
- Mix 1 mg (1 mL of 1 mg/ml [1:1 000]) adrenaline in **100 mL** of 0.9% sodium chloride and connect using an infusion pump via a dedicated line.
  - **Do not "piggy-back" on to another line** unless using an anti-reflux valve.
- **Do not** infuse on the same side as a BP cuff, as BP measurements will interfere with the infusion and risk extravasation injury.

Initiation and adjustment

- **In children and adults, start at 0.5 – 1.0 mL/kg/h** depending on severity:
  - Moderate severity 0.5 mL/kg/h (~0.1 micrograms/kg/min)
  - Severe (hypotensive or hypoxic) 1 mL/kg/h
- **Titrate** up or down according to response, aiming for the lowest effective rate.
  - Steady state is reached 5 – 10 min after a change in infusion rate.
  - Monitor infusion site regularly to ensure patency of cannula
- **Tachycardia, tremor, pallor with a normal or raised BP** may indicate excessive adrenaline treatment: reduce the infusion rate (or stop infusion if severe).
- If refractory to adrenaline infusion, seek urgent further expert help. Patients will require central venous access for prolonged infusions; follow local protocols.

WEANING

- **As symptoms improve, reduce the infusion**, aiming for 50% of the starting rate.
- One hour after resolution of all symptoms and signs, reduce the infusion rate progressively over 30 min and then stop; monitor closely for recurrence, and restart if necessary.

6.7 Other supportive measures

See appendix 3 for recommended drug doses to treat refractory anaphylaxis.

6.7.1 Airway

Severe upper-airway obstruction is uncommon in refractory anaphylaxis. Evidence from autopsy shows significant laryngeal oedema in under 10% of cases.[84] This may be due to laryngeal oedema being responsive to adrenaline treatment.

Tissue oxygenation is more important than tracheal intubation.

If tracheal intubation is indicated, it should be performed by the most experienced clinician available, following a difficult airway protocol (das.uk.com/guidelines).

Nebulised adrenaline can be used to treat upper airway obstruction due to anaphylaxis[12] but should not be prioritised over an adrenaline infusion or delay tracheal intubation in cases of critical upper airway obstruction.

6.7.2 Breathing

Severe bronchospasm is common in food-induced anaphylaxis,[85] and in children; in these cases, cardiac arrest is usually secondary to hypoxia. **Treat severe respiratory symptoms that are refractory to IM adrenaline with an adrenaline infusion** in addition to nebulised and intravenous bronchodilator therapy.

Magnesium sulfate is not recommended as a first-line intravenous bronchodilator in anaphylaxis as it can cause significant vasodilation and worsen hypotension.

6.7.3 Circulation

Reduced venous return is common in anaphylaxis, even in the absence of obvious circulatory compromise (e.g. in those with severe bronchospasm). An adrenaline infusion should be the first-line treatment alongside a fluid bolus.

Give further fluids as necessary. There is a tendency to underuse fluids to treat hypotension during anaphylaxis.[20] A large volume (up to 3 – 5 litres in adults) may be needed for severe anaphylactic shock.[29] When giving large volumes of fluid, use a non-glucose-containing crystalloid (e.g. Hartmann's or Plasma-Lyte®) rather than 0.9% sodium chloride to reduce the risk of causing hyperchloraemia.

In considering second-line vasopressor treatment, there is insufficient evidence to recommend any particular vasopressor; expert advice and local protocols should be followed. Doses should be titrated to clinical response, and administered only where there is sufficient expertise and monitoring available to minimise the risk of potential side effects (e.g. hypertensive crises and pulmonary oedema).

Cardiac Arrest

Recognise that cardiac arrest has occurred if the person becomes unresponsive or unconscious, and breathing is absent or abnormal. Other signs of cardiac arrest in a person with advanced monitoring include falling end-tidal CO_2 and absent arterial waveform. In adults, start chest compressions early in the peri-arrest patient.[38] Recommendations for the treatment of peri-operative anaphylaxis are to start chest compressions if the non-invasive (i.e. measured with a blood pressure cuff) systolic BP remains below 50 mmHg, especially in the presence of bradycardia.[86]

Cardiac arrest following anaphylaxis is a situation when prolonged CPR should be considered (including extra-corporeal CPR). This is because these patients have usually arrested from a sudden and potentially reversible cause, having been previously well.

6.7.4 Other medications

Steroids

The routine administration of corticosteroids to treat anaphylaxis is **not** recommended (see Section 5.5).

However, there is no evidence for or against their use for refractory anaphylaxis. It is reasonable to consider corticosteroids (such as hydrocortisone) for refractory reactions after initial resuscitation.[3] Corticosteroids should not be prioritised over adrenaline infusion and fluid resuscitation.

Glucagon

Adrenaline may be less effective in patients treated with a beta blocker.[12,87] In these cases, consider giving glucagon when symptoms remain refractory to adrenaline infusion and adequate fluid resuscitation.[12,61,87] Monitor for adverse events, including hyperglycaemia, vomiting, hypokalaemia and hypocalcaemia.

7. Investigations

Undertake investigations appropriate for a medical emergency, e.g.12-lead ECG, chest X-ray, urea and electrolytes, arterial blood gases.

7.1 Mast cell tryptase

There are several differential diagnoses for anaphylaxis, and an elevated serum tryptase can be very useful to confirm anaphylaxis where the diagnosis is uncertain. **Mast cell tryptase should be measured in all patients with suspected anaphylaxis where the diagnosis is uncertain.**

Tryptase is the major protein component of mast cell secretory granules. During anaphylaxis, mast cell degranulation can lead to an increase in blood tryptase concentrations (Figure 4), although this may not be obvious in food-induced anaphylaxis.[88] Tryptase levels can be useful in the follow-up of suspected anaphylaxis, but not in the initial recognition and treatment.[89] Measuring tryptase levels must not delay initial treatment and resuscitation. 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.[90] The half-life of tryptase is short (approximately 2 h), and concentrations may return to normal within 6 – 8 h, so timing of any blood samples is very important. A normal mast cell tryptase level does not exclude anaphylaxis.

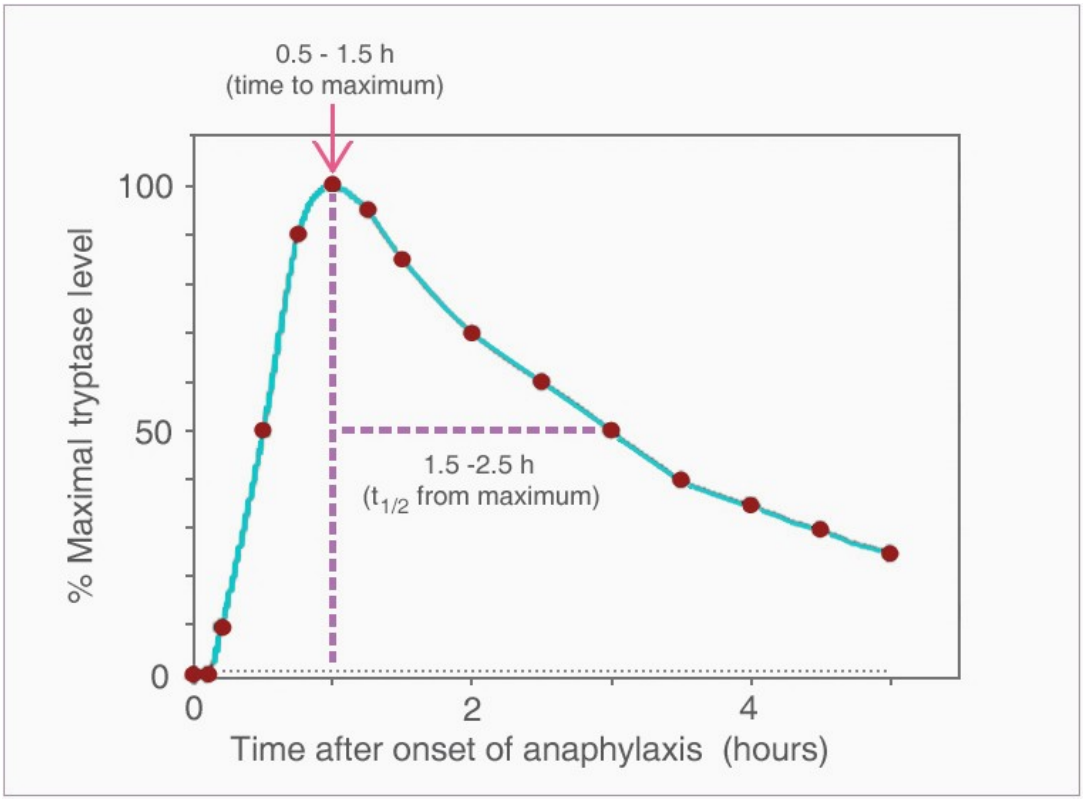


Figure 7. Suggested time course for the appearance of tryptase in serum or plasma during systemic anaphylaxis.[90] (Reproduced with permission).

7.2 Sample timing

The time of onset of anaphylaxis is the time when symptoms were first noticed. It is important that this time is recorded accurately.

a) Minimum: one sample, ideally within 2 h (when peak tryptase levels generally occur) and **no later than 4 h after onset of symptoms.**
b) Ideally: take three **timed** samples:
   1) An initial sample as soon as feasible – but do not delay treatment to take sample.
   2) A second sample 1 – 2 h (but no later than 4 h) **after onset of symptoms.**
   3) A third sample at least 24 h after complete resolution, or in convalescence (for example, at a follow-up allergy clinic). This sample is important as it provides a baseline tryptase value – some individuals have an elevated baseline level and may be at greater risk of anaphylaxis in response to some triggers.

Serial samples have better specificity and sensitivity than a single measurement in confirming a diagnosis of anaphylaxis.[89,91]

7.3 Sample requirements

- Either serum ('liver function test' tube) or plasma samples are acceptable in most laboratories.
- Sample volumes as little as 0.5 mL are usually sufficient, but >2 mL is preferred.
- Record the timing of each sample accurately on the request form, on the sample tube and in the clinical records. State on the request form (and in the clinical records) how many minutes/hours after the onset of symptoms the sample was taken. This will enable tracking of changes in tryptase levels over time, which is essential for interpretation.
- Specimens are stable for up to two days at room temperature, up to seven days refrigerated at 2 – 8°C, and for longer if frozen at – 20°C.[92] Note that samples stored for longer than these times may still provide useful information and should therefore be submitted for analysis.
- Consult your local laboratory if you have any queries.

7.4 Normal range for mast cell tryptase

Three separate definitions for a raised mast cell tryptase concentration are used:

1. Values exceeding 11.4 or 14 micrograms/L (95/99% upper limits of normal values)
2. Values exceeding [convalescent sample tryptase x1.2] + 2 micrograms/L
3. Increase from pre-reaction level (but pre-reaction tryptase not usually available)

A normal tryptase level does not exclude anaphylaxis. Note that mast cell tryptase increases post-mortem and in severe asthma. Seek advice from a specialist in allergy/immunology for advice on interpretation. Laboratory processing times mean that mast cell tryptase levels are not available to inform patient care in the acute setting.

8. Discharge and follow-up

8.1 Recovery from anaphylaxis

Patients who have had suspected anaphylaxis should be treated and then observed in a clinical area with facilities for treating life-threatening ABC problems.

- **Some patients experience further symptoms following resolution** of the initial reaction. This may be a true biphasic reaction (see Section 8.2) but can also represent further allergen absorption (e.g. if there is residual food allergen present in the gut, eating may cause further intestinal absorption of the allergen, resulting in further symptoms).[93]
    - It may be advisable for patients to eat some food at least one hour prior to discharge to mitigate against the risk of subsequent symptoms after leaving hospital.
- **In some patients, postural hypotension** has been reported after both anaphylaxis and milder allergic reactions.[93]
    - Before discharge, patients should be asked to stand up and be assessed for dizziness. Measure blood pressure if appropriate. If the patient is unable to stand due to an existing disability – sit upright if possible, and assess.

8.2 Biphasic reactions

Anaphylaxis can appear to resolve but then cause a recurrence of symptoms several hours later in the absence of further allergen exposure. This is known as a biphasic reaction and occurs in around 5% of patients.[40,94] Biphasic reactions can be difficult to distinguish from sustained anaphylaxis with a transient response to adrenaline, or progression due to further allergen absorption from residual food in the gastrointestinal tract. Published studies report the median time to biphasic symptoms (i.e. time by which 50% of biphasic reactions have occurred) to be around 12 h.[40,84,94,95]

The optimal duration of observation to monitor for biphasic reactions after anaphylaxis is unknown. The previous RCUK guideline referred to the NICE 2011 recommendation that patients over 16 years of age should be observed for 6–12 h from the onset of symptoms.[96] However, recent evidence suggests that this strategy may miss over 50% of biphasic reactions in the 5% of patients who experience them.[40,84,94,95]

Biphasic reactions can also occur following milder (non-anaphylactic) allergic reactions, with a similar incidence to biphasic reactions after anaphylaxis.[97]

Risk factors for biphasic reactions following anaphylaxis include:[71]

- more severe initial presentation of anaphylaxis
- initial reaction requiring more than one dose of adrenaline
- delay in adrenaline administration (> 30 – 60 min from symptom onset).[98]

Patients with a history of a previous biphasic reaction may also be at an increased risk.

Fatal outcomes due to biphasic reactions are very rare: over 9 000 cases of anaphylaxis (including 28 fatalities) were reported to the European Anaphylaxis Registry between 2011 and 2019: there were 435 cases with biphasic reactions, but no patients with a biphasic reaction died.[40]

On the basis of a review of the available evidence, the Working Group recommends a risk-stratified approach to the length of in-hospital observation following anaphylaxis:

Consider fast-track discharge (after 2 hours observation from resolution of anaphylaxis) if:	**Minimum 6 hours observation after resolution of symptoms recommended if:**	**Observation for at least 12 hours following resolution of symptoms if any one of the following:**
• Good response (within 5–10 minutes) to a single dose of adrenaline given within 30 minutes of onset of reaction **and** • Complete resolution of symptoms **and** • The patient already has unused adrenaline auto-injectors and has been trained how to use them **and** • There is adequate supervision following discharge	• 2 doses of IM adrenaline needed to treat reaction* **or** • Previous biphasic reaction	• Severe reaction requiring >2 doses of adrenaline. • Patient has severe asthma or reaction involved severe respiratory compromise. • Possibility of continuing absorption of allergen, e.g. slow-release medicines. • Patient presents late at night, or may not be able to respond to any deterioration. • Patients in areas where access to emergency care is difficult.
In all cases, discharge must comply with NICE Clinical Guidance CG134.[96]		

*It may be reasonable for some patients to be discharged after 2 hours despite needing two doses of IM adrenaline, e.g. following a supervised allergy challenge in a specialist setting.

8.3 Discharge from hospital

All patients should be reviewed by a senior clinician and a decision should be made about the need for further treatment and duration of observation. There is no reliable way of predicting who will have a biphasic reaction,[71] so decisions about discharge must be made for each patient by an experienced clinician.

Patients should be warned of the possibility of a biphasic reaction causing recurrence of symptoms, and advised how they should respond.

NICE recommends that prior to discharge, a healthcare professional with the appropriate skills and competencies should offer patients (or their parent/carer) the following:

- information about anaphylaxis, including the signs and symptoms of anaphylaxis
- information about the risk of a biphasic reaction (and clear instructions to return to hospital if symptoms return)
- information on what to do if anaphylaxis occurs (use the adrenaline injector and call emergency services), (e.g. Allergy Action Plans which can be downloaded at bsaci.org or sparepensinschools.uk)
- prescription of adrenaline auto-injectors (see Section 8.6 for more detail) or provision of replacement(s) if they have been used
- demonstration of the correct use of the adrenaline injector and when to use it
- advice about how to avoid the suspected trigger (if known)
- information about the need for referral to a specialist allergy service and the referral process
- information about patient support groups (e.g. Anaphylaxis Campaign, Allergy UK).

Patients should be provided with an **emergency management or action plan**. For children, these are available at bsaci.org or sparepensinschools.uk.

8.4 Record keeping

To help confirm the diagnosis of anaphylaxis and identify the most likely trigger, it is useful for the allergy clinic to have:

- a detailed description of the reaction with circumstances and timings to help identify potential triggers, including all administered treatments and the times they were given
- copies of relevant patient records (e.g. ambulance charts, emergency department records, observation charts, anaesthetic charts)
- results of any investigations already completed, including the timings of mast cell tryptase samples.

The Association of Anaesthetists recommends that anaesthetists follow a referral pathway outlined in the Sixth National Audit Project (NAP6) for patients who have experienced peri-operative anaphylaxis.[14] The pathway includes a list of relevant patient records which are required for the referral, and can be found at nationalauditprojects.org.uk/NAP6home.

A list of clinics with a specific interest in peri-operative anaphylaxis is available at the British Society for Allergy and Clinical Immunology (BSACI) and Association of Anaesthetists websites (bsaci.org and anaesthetists.org).

8.5 Reporting of reaction

An Anaphylaxis Registry has been established in the UK. Healthcare professionals are encouraged to report all anaphylaxis events anaphylaxie.net (to register, healthcare professionals should email anaphylaxis.registry@ic.ac.uk). All cases of fatal anaphylaxis must be reported to the coroner (or equivalent).

Adverse drug reactions that involve anaphylaxis should be reported to the Medicines and Healthcare products Regulatory Agency (MHRA) using the yellow card scheme (https://www.gov.uk/report-problem-medicine-medical-device)

8.6 When to prescribe an adrenaline auto-injector

Prescription of adrenaline auto-injectors is appropriate for **all** patients who have had anaphylaxis, with the exception of those with a drug-induced reaction (unless it is difficult to avoid future exposure to the trigger drug).

Individuals provided with adrenaline auto-injectors on discharge from hospital must be given instructions and training, and have appropriate follow-up, including contact with the patient's general practitioner. Following advice from MHRA, NICE guidelines currently recommend that patients prescribed adrenaline auto-injectors should have **two** devices available at all times. Patients (and those close to them, such as immediate family members, friends, carers) should receive training in their use, and practise regularly using a suitable training device so that they will know what to do in an emergency.

8.7 Specialist referral

All patients presenting with anaphylaxis should be referred to an allergy clinic to investigate the cause, thereby reduce the risk of future reactions, and prepare the patient to manage future episodes themselves. A list of specialist clinics is available on the BSACI website.

8.8 Patient education

Patients at risk of anaphylaxis should be referred to an appropriate allergy clinic. Patients need to know the allergen responsible and how to avoid it. For food allergens, patients need information on dietary avoidance (including what products may contain a relevant allergen and alternative names for the allergen).

Patients should be provided with an emergency management or action plan (these can be downloaded at bsaci.org or sparepensinschools.uk), to facilitate recognition of the early symptoms of anaphylaxis, request help early, and use the appropriate emergency medication.

Patients must always seek urgent medical help when experiencing anaphylaxis and after using an adrenaline auto-injector. Information about managing severe allergies can be obtained from their allergy specialist, general practitioner, other healthcare professional, or patient helplines/websites (the Anaphylaxis Campaign, Allergy UK).

Specific guidance and training is available for schools with children at risk of allergic reactions (sparepensinschools.uk).

Individuals at high risk of anaphylaxis should consider wearing a warning device (e.g. MedicAlert band) that provides information about their history of reaction. A number of "In case of emergency" (ICE) apps are also available for free download to mobile phones, which have a similar function.

Any person who has a ReSPECT form (Recommended Summary Plan for Emergency Care and Treatment) [99,100] or similar emergency treatment plan should have recorded on it details of serious allergies and how to treat them.

Resuscitation Council UK

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Acknowledgements

RCUK thanks all the individuals and organisations who took part in the open consultation.

RCUK thanks the following individuals who contributed to the 2008 version of this guideline as Working Group members:

Richard Pumphrey (Royal College of Pathologists)
Andrew Cant (Royal College of Paediatrics and Child Health)
Sue Clarke (Anaphylaxis Campaign)
Allison Corbett (British National Formulary)
Peter Dawson (Royal College of Radiologists)
Pamela Ewan (British Society for Allergy and Clinical Immunology)
Bernard Foëx (College of Emergency Medicine)
David Gabbott (Resuscitation Council UK)
Matt Griffiths (Royal College of Nursing)
Judith Hall (Royal College of Anaesthetists)
Nigel Harper (Association of Anaesthetists of Great Britain & Ireland)
Fiona Jewkes – (Royal College of General Practitioners, Joint Royal College Ambulance Liaison Committee)
Ian Maconochie (Resuscitation Council UK)
Sarah Mitchell (Resuscitation Council UK)
Shuaib Nasser (British Society for Allergy and Clinical Immunology)
Jerry Nolan (Resuscitation Council UK)
George Rylance (Royal College of Paediatrics and Child Health)
Aziz Sheikh (Resuscitation Council UK)
David Joseph Unsworth
David Warrell (Royal College of Physicians)

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Appendices

Appendix 1 Legal aspects of administering adrenaline for anaphylaxis in an emergency

There is no legal problem in a healthcare professional treating anaphylaxis by administering an adrenaline injection that:

- either has been prescribed to a specific person (e.g. an adrenaline auto-injector)
- or is from an emergency drug supply, for example, a dedicated emergency trolley or bag.

Adrenaline is a prescription-only medicine (POM). Under Regulation 214 of The Human Medicines Regulations 2012 (which can be found at www.legislation.gov.uk), "a person may not parenterally administer (otherwise than to himself or herself) a prescription-only medicine unless the person is "an appropriate practitioner" (e.g. doctor, dentist, nurse prescriber) or acting in accordance with the directions of such a practitioner.

However, a number of medicines are exempt from this restriction, where "this is for the purpose of saving life in an emergency" (Regulation 238). This includes adrenaline.

Where adrenaline is held as an emergency drug (and not specifically provided on a named-patient basis), any person competent to do so may administer adrenaline (using 1 mg/mL strength) at the doses recommended in this guideline, without the need for it to be prescribed first. However, the individual must be working within the standards of the relevant regulator (e.g. Nursing & Midwifery Council; Health & Care Professionals Council) or other supervisory body and competent in being able to recognise anaphylaxis and administer adrenaline, either from an ampoule by syringe and needle or an auto-injector device that has not been prescribed on an individual-patient basis.

In addition, under Schedule 17 of the Human Medicines Regulation (as amended in 2017), "generic" adrenaline auto-injectors can now be supplied to schools without being issued against a prescription. The legislation allows for any person who is "carrying on the business of a school" and who is suitably trained to do so, to administer such an auto-injector for the emergency treatment of anaphylaxis. Further information can be found at sparepensinschools.uk.

Where the adrenaline has been prescribed for a named person (e.g. as an auto-injector), the auto-injector can be administered by any person competent to do so, but only to the person for whom the auto-injector has been prescribed. Currently, the law does not allow a non-prescriber to administer an adrenaline auto-injector, which has been specifically prescribed to a named person, to another individual.

Appendix 2. Choice of needle and technique for IM injection

There is no specific evidence for using any particular technique of IM injection when treating anaphylaxis. This guidance is based on the recommendations for IM injections for vaccination (Immunisation against infectious disease. Department of Health UK, 2006). For IM injections, the needle must be long enough to ensure that the drug is injected into the muscle.

A 25mm needle is best and is suitable for all ages. In pre-term or very small infants, a 16mm needle is suitable for IM injection. In some adults, a longer needle (38 mm) may be needed.

Standard UK needle gauges and lengths		
Brown	26 G	10 mm
Orange	25 G	16 mm or 25 mm
Blue	23 G	25 mm
Green	21 G	38 mm

The best site for IM injection is the anterolateral aspect of the middle third of the thigh (Figure 8).

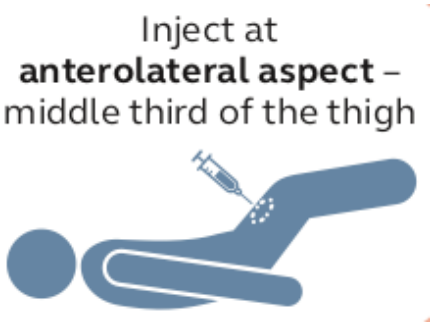

Figure 8: Site for injecting IM adrenaline

Appendix 3. Suggested drug doses for refractory anaphylaxis

	Adult	Paediatric
Adrenaline infusion	Where a local protocol is not available, the following can be used: Mix 1 mg (1 mL of 1 mg/mL (1:1 000)) adrenaline in 100 mL of 0.9% sodium chloride. Start at 0.5 mL/kg/h (~0.1 microgram/kg/min) and titrate according to response. This dilution can be given via peripheral venous cannula. Continuous monitoring mandatory: ECG, Pulse oximetry, non-invasive BP at least every 5 min	
Adrenaline (IV bolus, until infusion is ready) **To be given only by experienced specialists.**	50 micrograms, if repeated, start an IV adrenaline infusion. Prefilled syringes of **1:10 000** adrenaline contain 100 micrograms/mL. 0.5 mL is equivalent to 50 micrograms and is the smallest dose that can be given accurately. **Do not use 1:1 000 adrenaline undiluted**	There is no evidence on which to base a dose recommendation – a child may respond to a dose as small as 1 microgram/kg. **This requires very careful dilution and checking to prevent dosing errors**.
Aminophylline	Loading dose: • 5 mg/kg (max 500 mg) IV over 20 min (omit if on theophylline) IV infusion: • < 12 years 1 mg / kg /h • > 12 years: 0.5 – 0.7 mg/kg/h (0.3 mg/kg/h in elderly)	
Atropine	Consider if severe persistent bradycardia despite adequate fluid resuscitation: 0.5 mg IV, repeat if necessary	Consider if severe persistent bradycardia: < 12 years: 10 – 20 micrograms/kg (IV) > 12 years: 300 – 600 micrograms (IV)
Glucagon	1 mg IV [11] Can be repeated or followed by an infusion of 1 – 2 mg/h	20 – 30 micrograms/kg (max 1 mg) can be repeated every 5 min
Hydrocortisone	200 mg IV as initial dose	4 mg/kg IV (maximum 200 mg)
Ipratropium	Nebulised: 500 micrograms	Nebulised: < 2 years: 125 micrograms; 2 -12 years: 250 micrograms; > 12 years: 500 micrograms
Metaraminol	IV bolus: 0.5 mg, repeat as required Infusion: seek local expert advice	IV bolus: 10 micrograms/kg, repeat as required and titrate to response
Noradrenaline	Seek local expert advice. IV infusion: 0.05 – |0.5 micrograms/kg/min	Seek expert advice. Commence at 0.1 micrograms/kg/min
Salbutamol	Nebulised: 5 mg IV bolus (give over 5 min): 250 micrograms	Nebulised: < 5 years 2.5 mg > 5 years 5 mg IV bolus (give over 5 min): < 2 y: 5 micrograms/kg over 5 min 2 – 18y: 15 micrograms /kg (max 250 micrograms)
Vasopressin	IV bolus: 2 units [11] (repeat as needed, consider infusion)	Infusion: 0.02 – 0.06 units/kg/h [77] Mix 1 unit/kg in 50 mL Give 2 mL bolus, then 1 – 3 mL/h

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Appendix 4. Useful websites

https://www.resus.org.uk/
Resuscitation Council UK

https://www.bsaci.org/
British Society of Allergy & Clinical Immunology

https://www.anaphylaxis.org.uk/
The Anaphylaxis Campaign

https://www.allergyuk.org/
Allergy UK

https://www.eaaci.org/
The European Academy of Allergology and Clinical Immunology

https://erc.edu/
European Resuscitation Council

https://anaesthetists.org/
Association of Anaesthetists

https://www.cochrane.org/
The Cochrane collaboration

https://www.sparepensinschools.uk/
Website to support the use of adrenaline auto-injectors (including “generic” devices”) in schools and other educational settings.

https://www.nice.org.uk/
National Institute for Health and Care Excellence

Appendix 5. Glossary of terms and abbreviations

- **ABCDE**: **A**irway, **B**reathing, **C**irculation, **D**isability, **E**xposure
- **ACE:** Angiotensin converting enzyme
- **anaphylactic shock:** poor perfusion of the body's vital organs caused by anaphylaxis
- **BNF:** British National Formulary
- **BP:** blood pressure
- **BSACI:** British Society for Allergy and Clinical Immunology
- **CO_2:** carbon dioxide
- **CPR:** cardiopulmonary resuscitation (which refers to chest compressions and ventilations)
- **ECG:** electrocardiogram
- **GRADE: G**rading of **R**ecommendations, **A**ssessment, **D**evelopment and **E**valuations
- **h:** hour(s)
- **IgE:** immunoglobulin E
- **ILO:** inducible laryngeal obstruction
- **IM:** intramuscular
- **IO:** intraosseous
- **IV:** intravenous
- **kg:** kilogram(s)
- **L:** litre(s)
- **min:** minute(s)
- **mg:** milligram(s)
- **MHRA: M**edicines & **H**ealthcare products **R**egulatory **A**gency
- **mL:** millilitre(s)
- **mmHg:** millimetres of mercury

- **mmol:** millimole(s)
- **NICE:** National Institute for Health and Care Excellence
- **patient:** The term ‘patient’ is used to describe an individual person suffering from anaphylaxis in any setting, rather than alternative terms (e.g. victim, casualty)
- **RCUK:** Resuscitation Council UK
- **ReSPECT: Re**commended **S**ummary **P**lan for **E**mergency **T**reatment and **C**are
- **SpO_2:** Oxygen saturation

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Appendix 6. Equality impact assessment

RCUK is committed to promoting equality, eliminating unlawful discrimination and actively considering the implications of its guidance for human rights. It aims to comply fully with the Equality Act (2010).

		Yes/No	Comments
1.	**Does the guidance affect one group less or more favourably than another on the basis of:**		
	• Race	No	
	• Ethnic origins (including gypsies and travellers)	No	
	• Nationality	No	
	• Gender	No	
	• Culture	No	
	• Religion or belief	No	
	• Sexual orientation including lesbian, gay and bisexual people	No	
	• Age	No	Guidance covers all age groups
	• Disability – learning disabilities, physical disability, sensory impairment and mental health problems	No	
2.	**Is there any evidence that some groups are affected differently?**	Yes	Causes of anaphylaxis vary with age. This is addressed in the guidelines
3.	**If you have identified potential discrimination, are any exceptions valid, legal and/or justifiable?**	No	
4.	**Is the impact of the policy/ guidance likely to be negative?**	No	
5.	**If so, can the impact be avoided?**	N/A	
6.	**What alternatives are there to achieving the policy/guidance without the impact?**	N/A	
7.	**Can we reduce the impact by taking different action?**	N/A	