

IRISH ASSOCIATION FOR
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MEDICINE



IAEM Clinical Guideline

Emergency Management of Anaphylaxis in Adult Patients

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DISCLAIMER

IAEM recognises that patients, their situations, Emergency Departments and staff all vary. These guidelines cannot cover all clinical scenarios. The ultimate responsibility for the interpretation and application of these guidelines, the use of current information and a patient's overall care and wellbeing resides with the treating clinician.

Revision History

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CONTENTS

GLOSSARY OF TERMS	4
INTRODUCTION	5
PARAMETERS	6
AIM	6
DEFINITION OF ANAPHYLAXIS	6
EPIDEMIOLOGY	7
RECOGNITION OF ANAPHYLAXIS	8
TREATMENT OF ANAPHYLAXIS	9
Figure 1: Resuscitation Council UK anaphylaxis algorithm.....	9
Patient positioning	10
Oxygen	11
Intravenous (IV) fluids	11
Antihistamines	11
Steroids	12
REFRACTORY ANAPHYLAXIS	13
Figure 2: Resuscitation Council UK refractory anaphylaxis algorithm. Reproduced with the kind permission of Resuscitation Council UK.	14
IV adrenaline infusion	15
Figure 3: Peripheral IV adrenaline infusion for refractory anaphylaxis ²	15
ONGOING MANAGEMENT	16
Documentation	16
Investigations – Tryptase levels	16
Period of observation	17
Figure 4: Resuscitation Council UK risk stratification approach to in hospital observation period following anaphylaxis	19
Referral	19
Adrenaline auto-injectors	20
Education	20
SPECIAL CONSIDERATIONS	22
Cardiac arrest during anaphylaxis	22
Anaphylaxis in pregnancy	22
Anaphylaxis in patients taking beta-blockers	22
COMPANION DOCUMENTS	23
REFERENCES	24

GLOSSARY OF TERMS

ABC	Airway, Breathing, Circulation
ACLS	Advanced Cardiac Life Support
CPR	Cardiopulmonary Resuscitation
DAS	Difficult Airway Society
ECG	Electrocardiogram
ED	Emergency Department
EM	Emergency Medicine
IgE	Immunoglobulin E
IM	Intramuscular
IO	Intra-osseous
IV	Intravenous
IVC	Inferior Vena Cava
NICE	National Institute for Health and Care Excellence
UK	United Kingdom
WAO	World Allergy Organization

Emergency Management of Anaphylaxis in Adult Patients

INTRODUCTION

Anaphylaxis is an acute, potentially life-threatening, generalised hypersensitivity reaction.¹ It is the most severe clinical presentation of acute systemic allergic reactions. Anaphylaxis is caused by the sudden release of mast cell and basophil derived mediators into the systemic circulation.³ It most often results from IgE mediated reactions to food, medications and insect stings; however it can also be induced by agents or events that induce sudden, massive mast cell or basophil degranulation in the absence of immunoglobulins.⁴

Acute anaphylaxis is rare; the lifetime prevalence of anaphylaxis in Europe is estimated at 0.3%.⁵ Any compromise in the care of these patients can result in fatality. There are approximately 20 deaths reported each year due to anaphylaxis in the UK, although this may be significantly underestimated.⁶

Evidence suggests that anaphylaxis presentations to EDs continue to rise.⁷ Despite this, there remains confusion over the diagnosis, treatment, investigation and follow up of patients who have anaphylaxis. This life-threatening condition is frequently under-recognised and unfortunately, under-treated.⁸

The Resuscitation Council UK have issued guidelines on the emergency treatment of anaphylaxis² which focus on the life-threatening nature of anaphylaxis, the importance of recognition and the immediate administration of adrenaline. In addition, NICE have issued a quality standard for care after emergency treatment for suspected anaphylaxis, including assessment and referral to specialist allergy services.⁹

PARAMETERS

Target audience: This guideline is intended for all ED staff managing adult patients with acute anaphylaxis

Patient population: The target patient population is adult patients presenting to the ED with acute Anaphylaxis.

AIM

To provide an evidence-based guideline for the assessment and management of adult patients presenting to the ED with acute anaphylaxis.

DEFINITION OF ANAPHYLAXIS

The World Allergy Organisation (WAO) Anaphylaxis Committee has proposed the following definition: ¹⁰

*“Anaphylaxis is 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 **A**irway, **B**reathing **and/or** the **C**irculation, and may occur without typical skin features or circulatory shock being present.”*

EPIDEMIOLOGY

Data from the European Academy of Allergy and Clinical Immunology Food Allergy & Anaphylaxis Group estimate the incidence for all-cause anaphylaxis in Europe to be 1.5 to 7.9 per 100 000 person-years.⁵ They estimate that 1 in 300 people will experience anaphylaxis at some point in their life.⁵

There are approximately 20-30 deaths per year in the UK due to anaphylaxis, although this may be an under-estimate.¹¹ Of these deaths, approximately 50% are related to food-induced anaphylaxis; the other 50% are related to peri-operative anaesthesia.¹¹

The most common triggers for anaphylaxis are food, drugs and venom.¹² 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.¹² In contrast, fatal anaphylaxis due to drugs is rare in children, and is highest in older adults.

In patients who have had anaphylaxis, there is an ongoing risk of further anaphylaxis. This emphasises the importance of specialist allergy referral with further investigation and follow up.

RECOGNITION OF ANAPHYLAXIS

Anaphylaxis remains a clinical diagnosis, therefore emphasis must be placed on early recognition. Many patients with anaphylaxis are not given the correct treatment because of failure to recognise anaphylaxis.¹³

Anaphylaxis is likely when ALL the following 3 criteria are met:

1. **Sudden onset and rapid progression of symptoms** – most reactions develop over minutes.
2. **Airway and/or Breathing and/or Circulation (ABC) problems.**
An **ABC** approach should be followed, and any life-threatening problems treated as they arise.
Airway – throat and tongue swelling (pharyngeal / laryngeal oedema), hoarse voice, stridor, patient may complain of their “throat closing up”
Breathing – shortness of breath, wheeze, increased respiratory rate, bronchospasm, respiratory arrest
Circulation – pallor, tachycardia, hypotension, dizziness, collapse, cardiac arrest
3. **Skin and / or mucosal changes** – can be subtle or absent in 20% of anaphylactic reactions.

There may also be gastrointestinal symptoms such as vomiting, abdominal pain and incontinence.

TREATMENT OF ANAPHYLAXIS

Treatment should follow the Resuscitation Council UK anaphylaxis algorithm² in Figure 1.

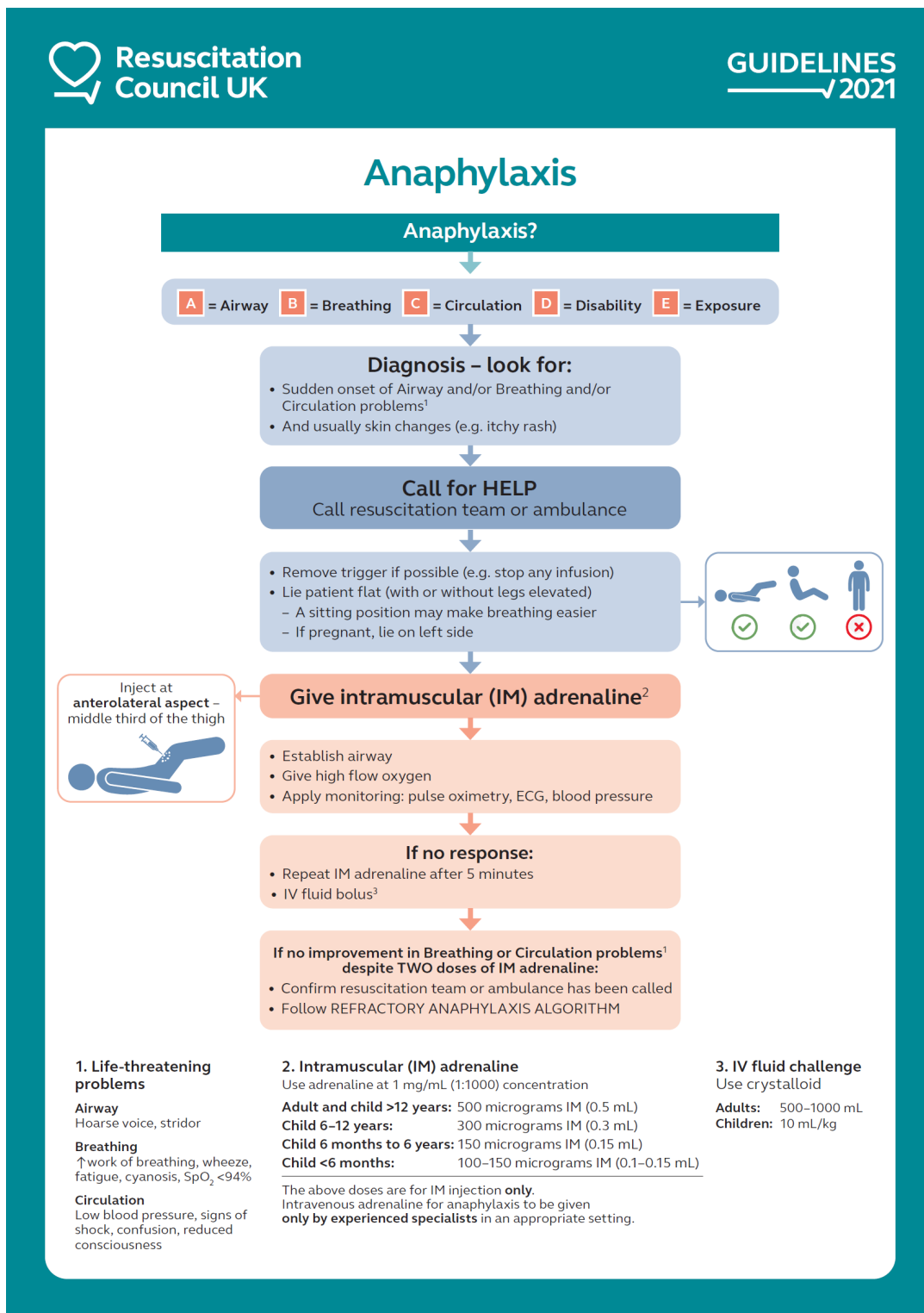


Figure 1: Resuscitation Council UK anaphylaxis algorithm. Reproduced with the kind permission of Resuscitation Council UK.

Patient positioning

Patients should be placed in a comfortable position. Avoid walking or standing during an acute reaction as this can result in fatality within minutes. A semi-recumbent or lying flat position, with or without leg elevation, is appropriate.

Removal of trigger if possible (e.g. stop infusion / remove stinger if bee sting)

Adrenaline – 1st line drug treatment

Adult Adrenaline intramuscular dose

Use 1mg/ml (1:1000) of Adrenaline

500 micrograms IM = 0.5ml of 1mg/ml Adrenaline

IM adrenaline is first line treatment for anaphylaxis (even if IV access is available). If in doubt, seek senior help. Administration of a single dose of IM adrenaline is usually well tolerated and poses minimal risk in the context of an individual having an allergic reaction.¹⁴

The best site for IM injection is the anterolateral aspect of the middle third of the thigh.¹⁵ The needle used for injection must be sufficiently long to ensure that the adrenaline is injected into muscle: use a 21G or 23G needle.

Attach monitoring (pulse, blood pressure, ECG, pulse oximetry) as soon as possible: this will help assess the patient's response to adrenaline. Measure vital signs (respiratory rate, oxygen saturations, pulse, blood pressure, level of consciousness) and auscultate for wheeze to monitor the effect of treatment and assess if further doses of adrenaline are required.

Repeat the IM adrenaline dose if there is no improvement in the patient's condition.

Further doses should be given at about 5-minute intervals, depending on the patient's response. (There can be large inter-individual variability in the response to adrenaline.)

If features of anaphylaxis persist despite 2 doses of IM adrenaline, the patient should be treated for refractory anaphylaxis and an adrenaline infusion should be commenced with expert support. Please refer to [Figure 2](#) for refractory anaphylaxis algorithm.

Oxygen

Initially, give the highest concentration of oxygen possible using a mask with an oxygen reservoir. When feasible, titrate oxygen therapy to maintain oxygen saturations 94-98%. If the patient is at risk of hypercapnic respiratory failure, saturations 88-92% may be appropriate. If intubation is required to secure the airway, or to oxygenate adequately, then it is likely to be a difficult airway and appropriately experienced staff must be available. See DAS guidance at: https://das.uk.com/guidelines/das_intubation_guidelines

Intravenous (IV) fluids

In the presence of hypotension/shock, or poor response to an initial dose of adrenaline, a rapid IV fluid bolus of 500-1000ml of crystalloid should be administered. A non-glucose containing crystalloid e.g. Hartmann's should be used to reduce the risk of hyperchloraemia.¹⁶

IM adrenaline should be administered every 5 minutes 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 causing hypotension and shock.¹⁷ Further fluids should be administered as necessary. A large volume (up to 3-5 litres) may be required.

Antihistamines

Antihistamines are not recommended as part of the initial emergency treatment of anaphylaxis. They have been shown to be of no benefit in treating life-threatening acute anaphylaxis and should not be used until the patient has been stabilised.¹⁸ Many guidelines express concern that administration of antihistamines could delay the administration of adrenaline and thus contribute to morbidity.

H1 antihistamines may be used to help alleviate cutaneous symptoms after patient has been stabilised. A non-sedating oral antihistamine e.g. cetirizine should be used in preference to chlorphenamine which was traditionally used.¹⁸ Antihistamines should be administered via the oral route where possible.

Steroids

Routine administration of corticosteroids is not recommended. There is no strong evidence that corticosteroids help shorten protracted symptoms or prevent biphasic reactions.¹⁹ For anaphylaxis, early administration of steroids is associated with an increased risk of intensive care admission, even after adjusting for severity of initial presenting symptoms.²⁰

Oral steroids may be beneficial where an acute asthma exacerbation may have contributed to the severity of the reaction.

REFRACTORY ANAPHYLAXIS

Refractory anaphylaxis is defined as anaphylaxis requiring ongoing treatment despite two appropriate doses of IM adrenaline. Refractory anaphylaxis is not fully understood but thought to be due to a combination of the following:²¹

- 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), which is uncommon

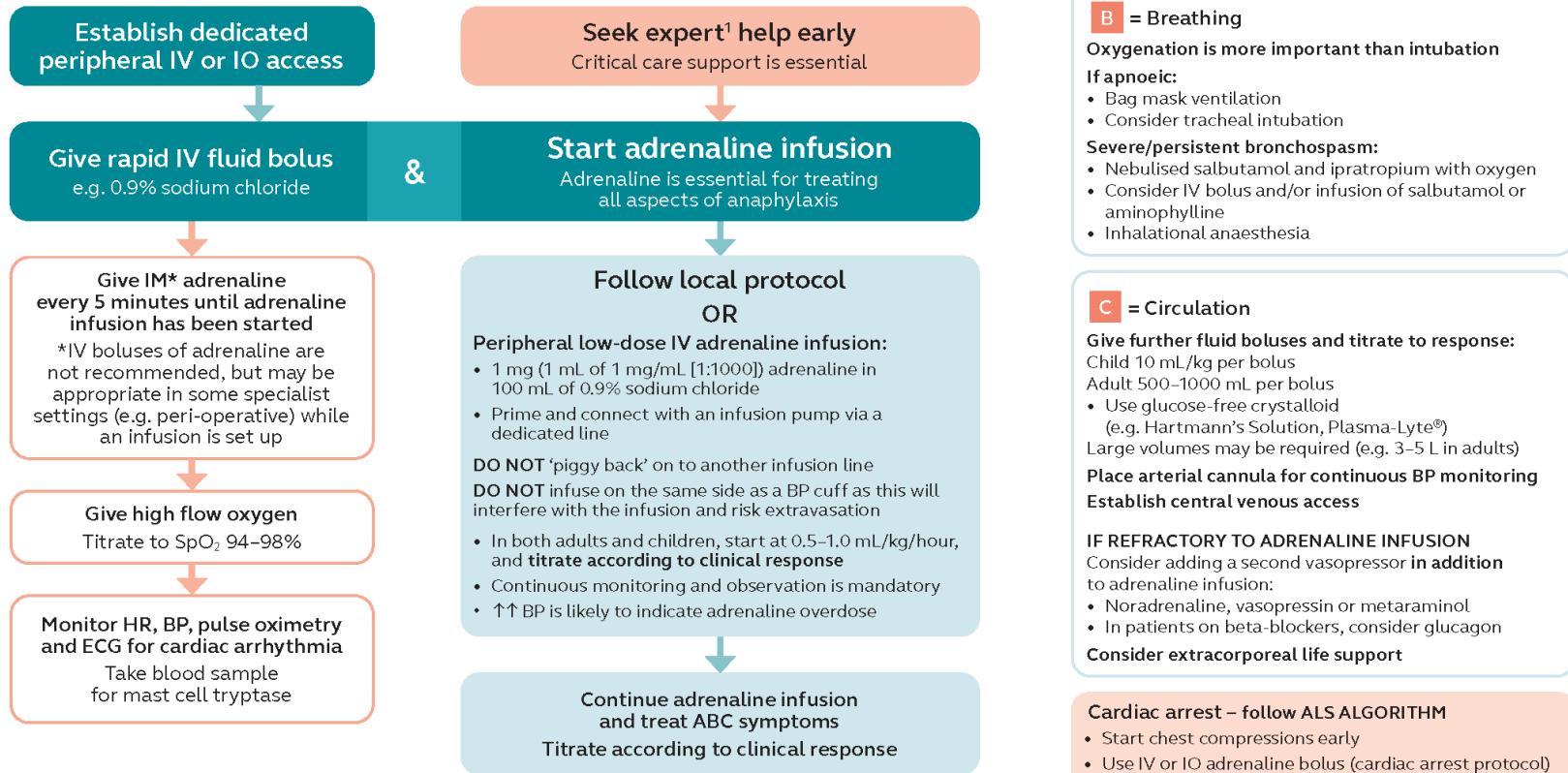
Patients with refractory anaphylaxis require critical care support and should be treated with an IV adrenaline infusion and IV fluid therapy to support delivery of adrenaline at a tissue level.

Dilute adrenaline can be infused via a peripheral IV cannula or an IO needle until central venous access is obtained. Local policies regarding adrenaline infusions should be followed and the patient should be transferred to the intensive care setting for ongoing management.

IM adrenaline should be administered every 5 minutes until the infusion has been commenced. The key steps for the management of refractory anaphylaxis are outlined in the algorithm below ([Figure 2](#)).²

Refractory anaphylaxis

No improvement in respiratory or cardiovascular symptoms despite 2 appropriate doses of intramuscular adrenaline



¹Intravenous adrenaline for anaphylaxis to be given only by experienced specialists in an appropriate setting.

A = Airway
Partial upper airway obstruction/stridor:
 Nebulised adrenaline (5mL of 1mg/mL)
Total upper airway obstruction:
 Expert help needed, follow difficult airway algorithm

B = Breathing
Oxygenation is more important than intubation
If apnoeic:
 • Bag mask ventilation
 • Consider tracheal intubation
Severe/persistent bronchospasm:
 • Nebulised salbutamol and ipratropium with oxygen
 • Consider IV bolus and/or infusion of salbutamol or aminophylline
 • Inhalational anaesthesia

C = Circulation
Give further fluid boluses and titrate to response:
 Child 10 mL/kg per bolus
 Adult 500-1000 mL per bolus
 • Use glucose-free crystalloid (e.g. Hartmann's Solution, Plasma-Lyte®)
 Large volumes may be required (e.g. 3-5 L in adults)
Place arterial cannula for continuous BP monitoring
Establish central venous access
IF REFRACTORY TO ADRENALINE INFUSION
 Consider adding a second vasopressor in addition to adrenaline infusion:
 • Noradrenaline, vasopressin or metaraminol
 • In patients on beta-blockers, consider glucagon
Consider extracorporeal life support

Cardiac arrest – follow ALS ALGORITHM
 • Start chest compressions early
 • Use IV or IO adrenaline bolus (cardiac arrest protocol)
 • Aggressive fluid resuscitation
 • Consider prolonged resuscitation/extracorporeal CPR

Figure 2: Resuscitation Council UK refractory anaphylaxis algorithm. Reproduced with the kind permission of Resuscitation Council UK.

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. The administration of IV adrenaline should be managed only by a senior EM physician and the patient should be transferred to the intensive care setting for ongoing management.

IV adrenaline boluses are NOT recommended for refractory anaphylaxis unless a patient is in cardiac arrest.

Monitor for adrenaline side effects: tachycardia, arrhythmia, hypertension. If present, reduce the infusion rate (or stop the infusion if side effects are severe). Local policies for adrenaline infusions should be followed. If no local policy available, the Resuscitation Council UK policy for peripheral IV adrenaline infusion for refractory anaphylaxis may be used. ² (Figure 3)

Peripheral IV adrenaline infusion for refractory anaphylaxis⁴⁴

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.

Figure 3: Peripheral IV adrenaline infusion for refractory anaphylaxis².
Reproduced with the kind permission of Resuscitation Council UK.

ONGOING MANAGEMENT

Once stabilised, ongoing ED management of the patient may involve further investigations, decisions regarding admission or discharge and anaphylaxis education.

NICE have issued a clinical guideline for management after emergency treatment for suspected anaphylaxis, including assessment and referral to specialist allergy services.⁹ These guidelines may be incorporated into a local proforma document ([Appendix 1](#)).

Documentation

Documentation of the nature of the reaction, e.g. acute clinical features, is particularly important. Specialist allergy services will use this information to confirm the diagnosis of anaphylaxis. The time of onset of the reaction should be recorded. The circumstances immediately before the onset of symptoms should also be recorded. This can help to identify the possible trigger.

Investigations – Tryptase levels

The specific test to help confirm a diagnosis of anaphylaxis is measurement of mast cell tryptase. Tryptase is the major protein component of mast cell secretory granules. During anaphylaxis, mast cell degranulation leads to an increase in blood tryptase concentrations.²⁶

Tryptase levels are not required for the initial recognition and emergency treatment of anaphylaxis. **Measuring tryptase levels must not delay resuscitation.** Tryptase levels can be helpful however for the specialist allergy service for their follow-up management of suspected anaphylaxis. Tryptase levels may confirm the diagnosis of anaphylaxis and ensure appropriate ongoing care.

The timing of tryptase levels is important. Tryptase concentrations in the blood may not increase significantly until 30 minutes or more after the onset of symptoms, and peak 1-2

hours after onset.²⁷ The half-life of tryptase is short (approximately 2 hours), and concentrations may return to normal within 6-8 hours.

NICE guidelines⁹ recommend that a sample for tryptase level should be taken as soon as possible after emergency treatment has started and a second sample ideally within 1 to 2 hours (but no later than 4 hours) from the onset of symptoms. It is again emphasized that resuscitation should not be delayed to take samples. At a minimum, one sample for tryptase level should be taken. However serial measurements are most beneficial.

The patient should be informed that a follow up third sample is usually taken by the specialist allergy services. This is important as it provides a baseline tryptase level – some individuals have an elevated baseline level and may be at greater risk of anaphylaxis.

Tryptase levels should be taken in a “serum” tube and a separate sample is required in most laboratories i.e. not “added on” to baseline electrolytes. It is particularly important that the timing of the sample and the timing of onset of symptoms is recorded.

Period of observation

The optimal duration of observation after anaphylaxis is unknown. NICE guidelines⁹ (2011) for anaphylaxis management recommend that adults and young people aged 16 years or older who have had emergency treatment for suspected anaphylaxis should be observed for 6 to 12 hours from the onset of symptoms, depending on their response to treatment.

In people with reactions that are controlled promptly and easily, a shorter observation period may be considered provided that they receive appropriate post-reaction care prior to discharge.

All patients should be reviewed by a senior clinician and a decision made about the need for further treatment and duration of observation.

Patients are observed during this time period for **biphasic reactions**. Biphasic reactions refer to the phenomenon that anaphylaxis can appear to resolve but then a recurrence of symptoms can occur several hours later in the absence of further allergen exposure. It is estimated to occur in 5% of patients.²⁸ Published studies report the median time to biphasic symptoms (i.e. time by which 50% of biphasic reactions have occurred) to be approximately 12 hours.²⁸ Patients who have a biphasic reaction or those who are at particular risk of a biphasic reaction should be admitted to hospital for observation.

Risk factors for biphasic reactions following anaphylaxis include:

- a more severe initial presentation of anaphylaxis,
- initial reaction needing more than one dose of adrenaline,
- delay in adrenaline administration (>30-60 minutes from symptom onset).²⁹

Patients with a history of prior biphasic reaction may also be at an increased risk. Resuscitation Council UK guidelines ² have proposed a risk stratification approach to the duration of the observation period following anaphylaxis. ([Figure 4](#))

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:
<ul style="list-style-type: none"> • Good response (within 5–10 minutes) to a single dose of adrenaline given within 30 minutes of onset of reaction <p>and</p> <ul style="list-style-type: none"> • Complete resolution of symptoms <p>and</p> <ul style="list-style-type: none"> • The patient already has unused adrenaline auto-injectors and has been trained how to use them <p>and</p> <ul style="list-style-type: none"> • There is adequate supervision following discharge 	<ul style="list-style-type: none"> • 2 doses of IM adrenaline needed to treat reaction* <p>or</p> <ul style="list-style-type: none"> • Previous biphasic reaction 	<ul style="list-style-type: none"> • 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.

Figure 4: Resuscitation Council UK risk stratification approach to in hospital observation period following anaphylaxis ².

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Referral

All patients presenting to the ED with anaphylaxis should be referred to a specialist allergy service on discharge. Input from specialist allergy service can help to identify the cause, and thereby reduce the risk of future reactions and prepare the patient to manage future episodes themselves.

Adrenaline auto-injectors

EDs should liaise with their nearest specialist allergy service to devise a local guideline regarding the prescription of adrenaline auto-injectors on discharge for patients treated for anaphylaxis e.g.

“Jext” adrenaline autoinjector 500mcg IM x 2 pens

NICE guidelines⁹ recommend that patients should be provided with appropriate adrenaline injector as an interim measure before the specialist allergy service appointment. They also recommend that patients with adrenaline auto-injectors should have TWO devices available at all times.

Education

Anaphylaxis education must be provided to all patients who are treated for anaphylaxis in the ED. This should include:

1. Information about anaphylaxis including the signs and symptoms of an anaphylactic reaction
2. Information about the risk of a biphasic reaction
3. Information on what to do if an anaphylactic reaction occurs (use the adrenaline injector and call emergency services)
4. A demonstration of the correct use of the adrenaline injector and when to use it
5. Advice about how to avoid the suspected trigger (if known)
6. Information about the need for referral to a specialist allergy service and the referral process
7. Information about patient support groups.

Patients should be provided with an anaphylaxis patient information leaflet ([Appendix 2](#)) as well as an Emergency Management or Action Plan ([Appendix 3](#)) on discharge. These may be

downloaded (at www.anaphylaxis.org.uk) or developed locally to facilitate recognition of the early symptoms of anaphylaxis, early request for help and appropriate use of emergency medication. An example of an anaphylaxis care pathway proforma is provided in [Appendix 1](#) which may be adopted locally in Irish EDs.

SPECIAL CONSIDERATIONS

Cardiac arrest during anaphylaxis

Chest compressions should be started early for the peri-arrest patient in the context of anaphylaxis.²² Once cardiac arrest has occurred, IV or IO adrenaline should be used as absorption of IM adrenaline will not be reliable and attempts to give it may interrupt or distract from delivery of high-quality CPR. Cardiac arrest following anaphylaxis is a situation when prolonged CPR should be considered (including extra-corporeal CPR). This is because the patients have usually arrested rapidly from a previously well state and a potentially reversible cause.

Anaphylaxis in pregnancy

The medical management of anaphylaxis during pregnancy is similar to the non-pregnant patient. After 20 weeks gestation (when the uterus is palpable at or above the umbilicus), pregnant patients should be placed in the left lateral position to reduce compression of the IVC and abdominal aorta by the pregnant uterus. Pregnant patients may be placed in a head-down position instead of lifting the legs.

If anaphylaxis is severe and refractory to treatment, consideration should be given to an early peri-arrest caesarean section.²³

Anaphylaxis in patients taking beta-blockers

Adrenaline may be less effective in patients treated with beta-blockers.²⁴ Administration of glucagon should be considered if symptoms remain refractory to adrenaline infusion and adequate fluid resuscitation.²⁵

COMPANION DOCUMENTS

1. [Appendix 1: Local proforma](#)
2. [Appendix 2: Anaphylaxis patient information Leaflet](#)
3. [Appendix 3: Emergency Management or Action Plan](#)

REFERENCES

1. Yu JE, Lin RY. The Epidemiology of Anaphylaxis. *Clin Rev Allergy Immunol.* 2018;54(3):366.
2. Resuscitation Council UK Emergency Treatment of Anaphylaxis Guidelines for healthcare providers, Working Group of Resuscitation Council UK, May 2021 2021 Resuscitation Guidelines | Resuscitation Council UK
3. Sampson HA, Muñoz-Furlong A, Campbell RL, et al; Second symposium on the definition and management of anaphylaxis: summary report--Second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network symposium. *J Allergy Clin Immunol.* 2006;117(2):391.
4. Johansson SG, Bieber T, Dahl R et al; Revised nomenclature for allergy for global use: Report of the Nomenclature Review Committee of the World Allergy Organization, October 2003. *J Allergy Clin Immunol.* 2004;113(5):832.
5. Panesar SS, Javad S, de Silva D, et al; EAACI Food Allergy and Anaphylaxis Group. The epidemiology of anaphylaxis in Europe: a systematic review. *Allergy.* 2013;68(11):1353-61.
6. Pumphrey R, Anaphylaxis: can we tell who is at risk of a fatal reaction? *Curr Opin Allergy C 2)lin Immunol.* 2004;4(4):285.
7. Baseggio Conrado A, Lerodiakonou D, Gowland MH, Boyle RJ, Turner PJ. Food Anaphylaxis in the United Kingdom: an analysis of national data, 1998- 2018. *BMJ* (under review)
8. Lindor RA, McMahon EM, Wood JP, Sadosty AT, Boie ET, Campbell RL. Anaphylaxis-related Malpractice Lawsuits. *West J Emerg Med.* 2018 Jul;19(4):693-700.
9. Anaphylaxis: assessment and referral after emergency treatment Clinical guideline [CG134]; December 2011 <https://www.nice.org.uk/guidance/cg134>

10. Cardona V, Ansotegui I, Ebisawa M, et al, on behalf of the World Allergy Organisation Anaphylaxis Committee. Anaphylaxis Guidance 2020. World Allergy Organization Journal 2020; doi:10.1016/j.waojou.2020.100472.
11. Turner PJ, Jerschow E, Umasunthar T, Lin R, Campbell DE, Boyle RJ. Fatal Anaphylaxis: Mortality Rate and Risk Factors. J Allergy Clin Immunol Pract. 2017;5(5):1169–1178
12. Turner PJ, Gowland MH, Sharma V, et al. Increase in anaphylaxis-related hospitalizations but no increase in fatalities: an analysis of United Kingdom national anaphylaxis data, 1992–2012. J Allergy Clin Immunol. 2015; 135(4):956–63.e1.
13. Haymore BR, Carr WW, Frank WT. Anaphylaxis and epinephrine prescribing patterns in a military hospital: underutilization of the intramuscular route. Allergy Asthma Proc 2005;26(5):361-5.
14. Cardona V, Ferré-Ybarz L, Guilarte M, et al. Safety of Adrenaline Use in Anaphylaxis: A Multicentre Register. Int Arch Allergy Immunol. 2017; 173(3):171-177.
15. Simons FE, Gu X, Simons KJ. Epinephrine absorption in adults: intramuscular versus subcutaneous injection. J Allergy Clin Immunol 2001;108(5):871–3.
16. National Institute for Health and Care Excellence. Intravenous fluid therapy for adults in hospital. (Clinical guideline 174.) 2013. www.nice.org.uk/CG174.
17. Brown SG. Cardiovascular aspects of anaphylaxis: implications for treatment and diagnosis. Curr Opin Allergy Clin Immunol 2005;5(4):359-64.
18. Sheikh A, Ten Broek V, Brown SG, Simons FE. H(1)-antihistamines for the treatment of anaphylaxis: Cochrane systematic review. Allergy 2007;62(8):830-7.
19. Lee S, Bellolio MF, Hess EP, Erwin P, Murad MH, Campbell RL. Time of Onset and Predictors of Biphasic Anaphylactic Reactions: A Systematic Review and Meta-analysis. J Allergy Clin Immunol Pract. 2015;3(3):408- 16.e162. doi:10.1016/j.jaip.2014.12.010).

20. Gabrielli S, Clarke A, Morris J, et al. Evaluation of Prehospital Management in a Canadian Emergency Department Anaphylaxis Cohort. *J Allergy Clin Immunol Pract.* 2019;7(7):2232-2238.e3. doi:10.1016/j.jaip.2019.04.018)
21. Brown SG. The pathophysiology of shock in anaphylaxis. *Immunol Allergy Clin North Am.* 2007;27(2):165–175.
22. Harper NJN, Nolan JP, Soar J, Cook TM. Why chest compressions should start when systolic arterial blood pressure is below 50 mm Hg in the anaesthetised patient. *Br J Anaesth.* 2020;124(3):234–238
23. Chu, J, Johnston, TA, Geoghegan, J, on behalf of the Royal College of Obstetricians and Gynaecologists. Maternal Collapse in Pregnancy and the Puerperium. *BJOG* 2020;127:e14–52
24. Thomas M, Crawford I. Best evidence topic report. Glucagon infusion in refractory anaphylactic shock in patients on beta-blockers. *Emerg Med J* 2005;22(4):272–3.
25. Muraro A, Roberts G, Clark A, et al, on behalf of EAACI Food Allergy and Anaphylaxis Guidelines Group. Anaphylaxis: Guidelines from the European Academy of Allergy and Clinical Immunology. *Allergy* 2014;69(8):1026-45
26. Francis A, Fatovich DM, Arendts G, et al. Serum mast cell tryptase measurements: Sensitivity and specificity for a diagnosis of anaphylaxis in emergency department patients with shock or hypoxaemia. *Emerg Med Australas.* 2018;30(3):366-374.
27. Schwartz LB. Diagnostic value of tryptase in anaphylaxis and mastocytosis. *Immunol Allergy Clin North Am* 2006;26(3):451-63
28. Kraft M, Scherer Hofmeier K, Ruëff F, et al. Risk Factors and Characteristics of Biphasic Anaphylaxis. *J Allergy Clin Immunol Pract.* 2020:S2213- 2198(20)30794-7.
29. Liu X, Lee S, Lohse CM, Hardy CT, Campbell RL. Biphasic Reactions in Emergency Department Anaphylaxis Patients: A Prospective Cohort Study. *J Allergy Clin Immunol Pract.* 2020;8(4):12301238.