

ANAPHYLAXIS GUIDELINE

Assessment and management of anaphylaxis or suspected anaphylaxis

DOCUMENT CONTROL PAGE

Title:	Anaphylaxis Guideline (adults and children)
Version:	V1; April 2022
Supersedes:	V2; Jan 2016 (Wythenshawe) and V2 Ref MMC-G106 (MRI)
Application:	Trust wide

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Ratified by:	MFT Medicines Management Committee
Date of Ratification:	April 2022

Issue / Circulation Date:	May 2022
Circulated by:	
Dissemination and Implementation:	This guideline will be made available to all staff via the intranet on all sites.
Date placed on the Intranet:	May 2022

Planned Review Date:	April 2025
Responsibility of:	The Clinical Lead of the Allergy Centre, Wythenshawe Hospital

Minor Amendment (If applicable) Notified To:	
Date notified:	

EqlA Registration Number:	2021-206
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Manchester University NHS Foundation Trust

CONSULTATION

Summary of consultation process	<p>The author consulted Consultant colleagues in</p> <ul style="list-style-type: none"> the Allergy Centre, Wythenshawe Hospital: Dr Marina Tsoumani (Consultant Allergist), Dr Jia Li Liau (Consultant Allergist), Dr Iason Thomas (Consultant Allergist) and Professor Angela Simpson, (Professor of Respiratory Medicine) the Immunology and Allergy Service at MRI: Dr Sara Drinkwater (Consultant Immunologist), Dr Tomaz Garcez, Consultant Immunologist The Paediatric Allergy and Immunology Service at RMCH: Dr Vibha Sharma (Consultant in Paediatric Allergy); the Paediatric Allergy Service at Wythenshawe Hospital: Dr Naveen Rao (Consultant Paediatrician with an interest in Allergy; the Paediatric Allergy Service at NMGH: Dr Anita Solanki (Consultant in Paediatric Allergy) Dr Steven Knight (Consultant Anaesthetist/Anaesthesia liaison and Clinical Director of Resuscitation, Wythenshawe Hospital), Dr Andrew Parkes (Consultant Anaesthetist, MRI) and Dr Stephen Hawes (Consultant Emergency Physician and ED Lead for Anaphylaxis, Wythenshawe Hospital)
Control arrangements	<p>The document will be reviewed every three years.</p> <p>The document will be reviewed by the Clinical Lead of the Allergy Service, Wythenshawe Hospital, in consultation with the above colleagues.</p> <p>It is recommended that a HIRS is submitted for all incidents of anaphylaxis.</p> <p>The authors will review all allergy-related HIRS incidents.</p>
Associated documentation and references	<p>References listed in page 20</p> <p>Relevant documentation in appendices in page 22</p>

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1. SUMMARY ON A PAGE

Recognising anaphylaxis (page 8)

- Anaphylaxis is a serious systemic hypersensitivity reaction; sudden onset and rapid progression
- It is a clinical diagnosis – Airway / Breathing / Circulation problems, usually with skin or mucosal changes
- Diagnostic criteria for anaphylaxis on page 8

Treatment (page 10)

- New guidance from the Resuscitation Council UK – 2021
- 2 treatment algorithms: initial management and refractory anaphylaxis
- Main changes: emphasis on use of adrenaline; patient positioning; fluid challenge; antihistamines and corticosteroids *not* recommended as first-line treatment

Investigations (page 15)

- Mast cell tryptase (clotted serum tube – same as for U&Es) → 2 timed samples:
 - As soon as possible after onset (once patient stable)
 - 1 – 2 h after onset

Observation period and discharge (page 15)

- Adults → observe for 6 – 12h (some can be discharged earlier)
- Children → admit to the care of a Paediatric team

Documentation and Integrated Care Pathways (ICPs)

Adults (≥16y)

- **Wythenshawe Hospital** → Anaphylaxis and Allergic Reactions ICP
Available on the [Allergy Centre \(Wythenshawe Hospital\) Intranet page](#) and [the ICP page of the Trust's intranet](#) (offers guidance on identification, treatment, investigations, observation, discharge and referral information)
- **ORC** → Pink ED Sheet (MRI)

Children (<16y)

- **Royal Manchester Children's Hospital** → Pink ED Sheet for Paediatric anaphylaxis / Paediatric Anaphylaxis and Allergy pathway (RMCH)
- **Wythenshawe Hospital** → Paediatric Anaphylaxis ICP

Referral Information (page 16)

Adults (≥16y)

- **Allergy Centre, Wythenshawe Hospital** → email Anaphylaxis and Allergic Reactions ICP to allergycentre@mft.nhs.uk or post to Allergy Centre (F10); queries → tel. 0161 291 4055
- **Immunology and Allergy Service, MRI** → email referral to clinical.immunology@mft.nhs.uk; queries → tel. 0161 276 6686

Children (<16y)

- **Paediatric Allergy and Immunology Service, Royal Manchester Children's Hospital** → fax Anaphylaxis pathway + referral form to 0161 7011724
- **Paediatric Allergy Service, Wythenshawe Hospital** → fax Paediatric ED Admission documentation to 0161 291 5307
- **Paediatric Allergy Service, North Manchester General Hospital** → post referral; queries → tel. switch 0161 764 6081

Perioperative anaphylaxis and anaphylaxis during interventional procedures (page 18)

- Follow guidance from the Association of Anaesthetists (AAGBI), [here](#) and [here](#)
- Refer **adults** to:
 - The **Allergy Centre at Wythenshawe Hospital** emailing a referral proforma available on the [Allergy Service intranet page](#) to allergycentre@mft.nhs.uk
 - The **Anaesthetic Reaction Clinic at Manchester Royal Infirmary** emailing a referral form (available on intranet or from <http://bit.ly/ARCref>) to anaesthetic.reaction@mft.nhs.uk
- Refer **children** to the **Peri-anaesthetic Allergy Clinic at RMCH – Paediatric perioperative anaphylaxis**, emailing the referral form on <http://bit.ly/ARCref> to vibha.sharma@mft.nhs.uk or andrew.parkes@mft.nhs.uk

2. INTRODUCTION

ANAPHYLAXIS, EXTENT OF THE PROBLEM

Definition

Anaphylaxis is a clinical emergency and represents the most severe end of the spectrum of allergic reactions, which all healthcare professionals need to be able to recognize and manage.

Over time there have been several different definitions for anaphylaxis, which can have variable presentations, occasionally with no cutaneous involvement, and relatively low prevalence. This has led to confusion on its diagnosis, with the result that many patients do not receive optimal treatment (at least 50% of patients do not receive IM adrenaline, the first-line treatment), and investigations and follow-up of patients is sub-optimal(1–5).

The World Allergy Organisation (WAO) Anaphylaxis Committee defines anaphylaxis as follows(6):

“**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 airway, breathing and/or the circulation, and may occur without typical skin features or circulatory shock being present.”

Anaphylaxis is a clinical emergency so the diagnosis needs to be made rapidly. Research suggests that National Institute of Allergy and Infectious Disease and Food Allergy and Anaphylaxis Network (NIAID/FAAN) clinical criteria(5,7) have high sensitivity(8,9), which are those proposed by the latest update on Anaphylaxis Guidelines by EAACI(5) and in use in this guideline.

The National Institute for Health and Care Excellence (NICE) have published a clinical guideline on ‘Anaphylaxis: assessment to confirm an anaphylactic episode and the decision to refer after emergency treatment for a suspected anaphylactic episode’ - CG 134(10) (Appendix 1), and their recommendations have been incorporated in this guideline; they can be found at <https://www.nice.org.uk/guidance/cg134>. NICE CG 134 care pathway is in Appendix 2. At Wythenshawe Hospital there is an Anaphylaxis and Allergic Reactions Integrated Care Pathway (ICP), designed to aid compliance with the above NICE CG 134 (Appendix 3). The ORC emergency departments use “pink” sheets to guide management of allergic presentations, and these have also been reviewed in line with the NICE CG 134 guidelines. In addition, at ORC there is a rapid access anaphylaxis referral process using the ward order communications system, so any patient experiencing anaphylaxis can be referred easily and in line with the NICE CG 134 guidelines.

Triggers

Anaphylaxis may be an allergic response that is immunologically mediated, or a non-immunologically mediated response, or idiopathic. Certain foods, insect venoms, some drugs and latex are common precipitants of immunoglobulin E (IgE)-mediated allergic anaphylaxis. Many drugs can also act through non-allergic mechanisms. A significant proportion of anaphylaxis is classified as idiopathic, in which there are significant clinical effects but no readily identifiable cause. The relative likelihood of the reaction being allergic, non-allergic or idiopathic varies considerably with age (see Appendix 4: Anaphylaxis - mechanisms and triggers)(6,11).

Incidence and lifetime prevalence

Increasing numbers of patients are presenting to UK hospitals with anaphylaxis(1,12,13). The UK incidence of anaphylaxis (based on hospital admission data extracted from national databases in England and Wales for a 20 year period) has risen steadily and significantly (7-fold) from 1992 but appears to have reached a plateau since 2008(12). There is no overall figure for the frequency of anaphylaxis from all causes in the UK. 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(14). The same data indicated that an estimated 1 in 300 people will experience anaphylaxis at some point in their lives.

Mortality

There are approximately 20-30 deaths from anaphylaxis reported each year in the UK, although this may be a considerable underestimate(1,12,13). Around half the deaths are due to drug hypersensitivity (with perioperative anaphylaxis causing ~10 deaths per year (15), and 10 being food-induced(12,13). Admission and fatality rates for drug- and insect sting-induced anaphylaxis are highest in patients aged 60 years and older; admissions because of food-triggered anaphylaxis appear to be most common in young people, with a marked peak in the incidence of fatal food reactions during the second and third decades of life. In contrast to the increase in hospital admissions for anaphylaxis, recent UK data demonstrate that the annual fatality rate from all-cause anaphylaxis remained stable at 0.047 cases per 100,000 population. The overall prognosis of anaphylaxis is good, with a case fatality rate of under 1% in those presenting to hospitals in the UK(12), and a mortality rate within the general population of less than one per million per annum(16).

3. PURPOSE OF THE DOCUMENT

This guideline is aimed at healthcare providers who are expected to deal with patients presenting with an anaphylactic reaction during their usual clinical role (e.g., doctors, nurses, paramedics) in a hospital setting and at MFT's community services.

The aim of this guideline is:

- to provide guidance on the recognition/diagnosis, investigation and emergency treatment of patients presenting with 'suspected anaphylaxis' to any of MFT's Emergency Departments, hospital wards or at MFT community services;
- to provide guidance on the care of adults, young people and children following emergency treatment for 'suspected anaphylaxis', including discharge information and referral pathways at MFT: to the Allergy Centre at Wythenshawe Hospital or to the Immunology and Allergy Service at Manchester Royal Infirmary for adults, and to the Paediatric Allergy and Immunology Service at RMCH, Paediatric Allergy Service at Wythenshawe Hospital or at North Manchester General Hospital, for children.

This guideline incorporates the recommendations from NICE Clinical Guidance 134(10).

The Association of Anaesthetists of Great Britain & Ireland and the British Society for Allergy and Clinical Immunology have published specific guidance for the treatment of anaphylactic reactions associated with anaesthesia (www.aagbi.org and www.bsaci.org). This guidance is also covered within this document.

The treatment of a patient having an anaphylactic reaction in any setting is the same for children and adults. Any differences will be highlighted.

This document facilitates adherence to national guidance within Manchester University NHS Foundation Trust (MFT).

4. DEFINITIONS OF KEY TERMS USED

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 airway, breathing and/or the circulation, and may occur without typical skin features or circulatory shock being present(1,6).

Biphasic anaphylaxis. After complete recovery of anaphylaxis, a recurrence of symptoms several hours later with no further exposure to the allergen. It is managed in the same way as anaphylaxis. This occurs in ~5% of patients and the median time to biphasic symptoms (i.e., the time by which 50% of biphasic reactions have occurred) is ~12h (17–19).

Idiopathic anaphylaxis. Denotes a form of anaphylaxis where no identifiable cause can be found. All known causes of anaphylaxis must be excluded before this diagnosis can be reached.

Suspected anaphylaxis. The diagnosis, prior to assessment by a specialist allergist/immunologist, for people who present with symptoms of anaphylaxis.

In emergency departments (ED), a person who presents with the signs and symptoms of anaphylaxis may be classified as having a 'severe allergic' reaction, or an 'anaphylactoid' reaction (a term that should be abandoned), rather than an 'anaphylactic' reaction. Throughout this guideline, anyone who presents with such signs and symptoms is classed as experiencing a 'suspected anaphylactic reaction' and should be diagnosed as having 'suspected anaphylaxis'.

5. RECOGNITION OF AN ANAPHYLACTIC REACTION

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

See Figure 1, below, with diagnostic criteria (NIAID/FAAN and EAACI 2021 Anaphylaxis criteria)(5,7).

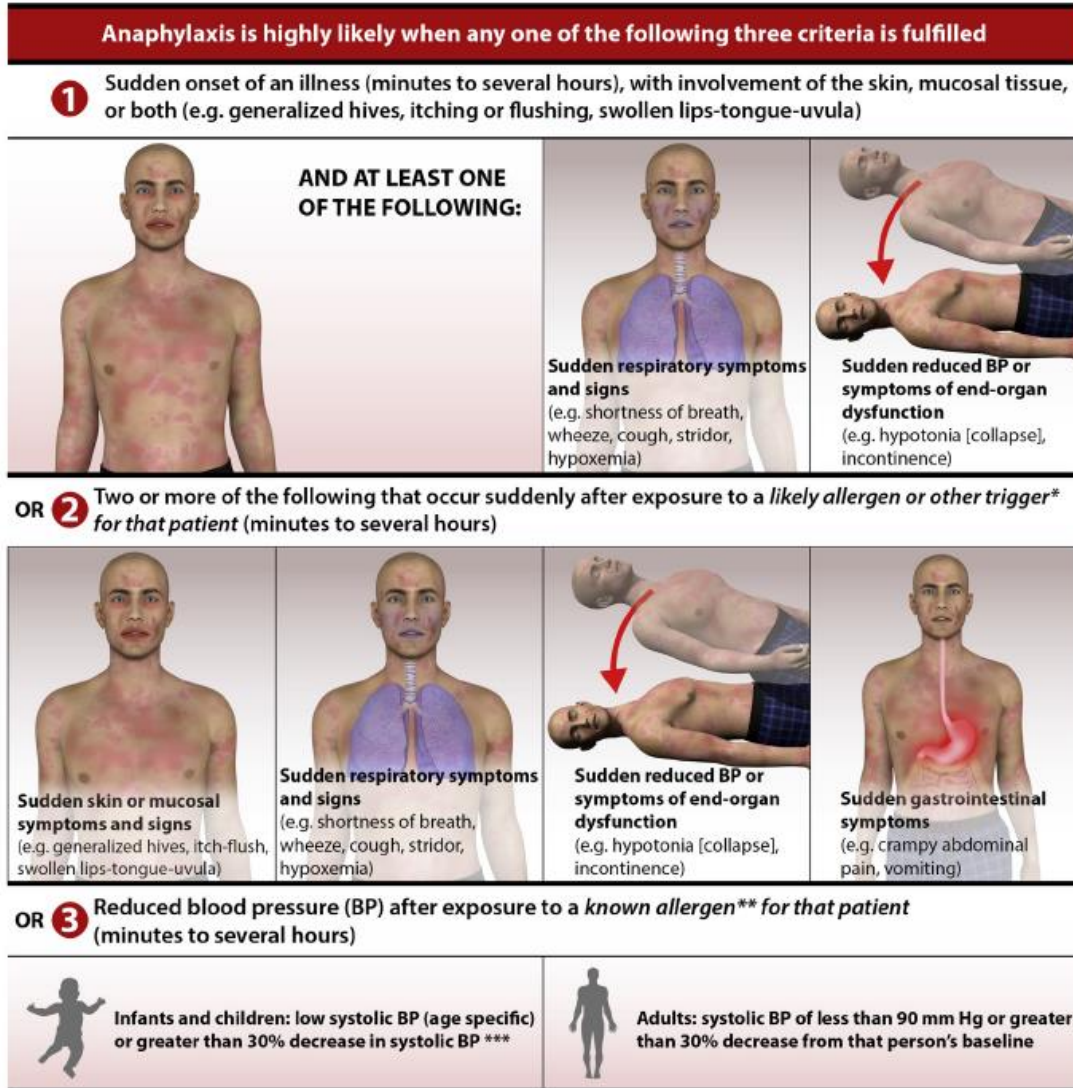


Figure 1 – Anaphylaxis diagnostic criteria (NIAID/FAAN and EAACI 2021); from Shaker M et al. (7)

Other points to 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** (for example, some patients present initially with only bronchospasm and/or hypotension).
- **Gastrointestinal symptoms** (e.g., nausea, abdominal pain, vomiting, diarrhoea) in the absence of **Airway and/or Breathing and/or Circulation** problems do not usually indicate anaphylaxis.

A diagnosis of anaphylactic reaction 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 life-threatening airway and/or breathing and/or circulation problems. The reaction is usually unexpected.

A single set of criteria will not identify all anaphylactic reactions. There is a range of signs and symptoms, none of which are entirely specific for an anaphylactic reaction; however, certain combinations of signs make the diagnosis of an anaphylactic reaction more likely. Specific criteria have been proposed by international allergy organisations and scientific societies, the latest from EAACI 2021, shown in Figure 1, above.

Anaphylaxis lies along a **spectrum of severity** in terms of allergic symptoms(1,6), Figure 2:

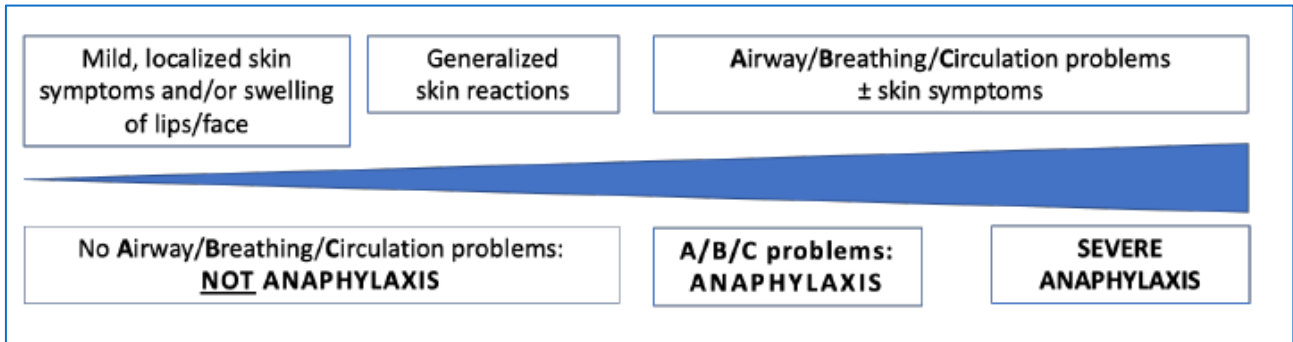


Figure 2 – Spectrum of severity of allergy symptoms; from(1)

Confusion arises because some patients have systemic allergic reactions that are less severe. For example, generalised urticaria, angioedema (not affecting the airway), and rhinitis would not be described as an anaphylactic reaction, because the life-threatening features – an airway problem, respiratory difficulty (breathing problem) and hypotension (circulation problem) – are not present.

Signs and symptoms of anaphylaxis

The presence of any of the below signs and symptoms (Figure 3) *in isolation* does not constitute anaphylaxis and diagnosis is based on the criteria in Figure 1, above.

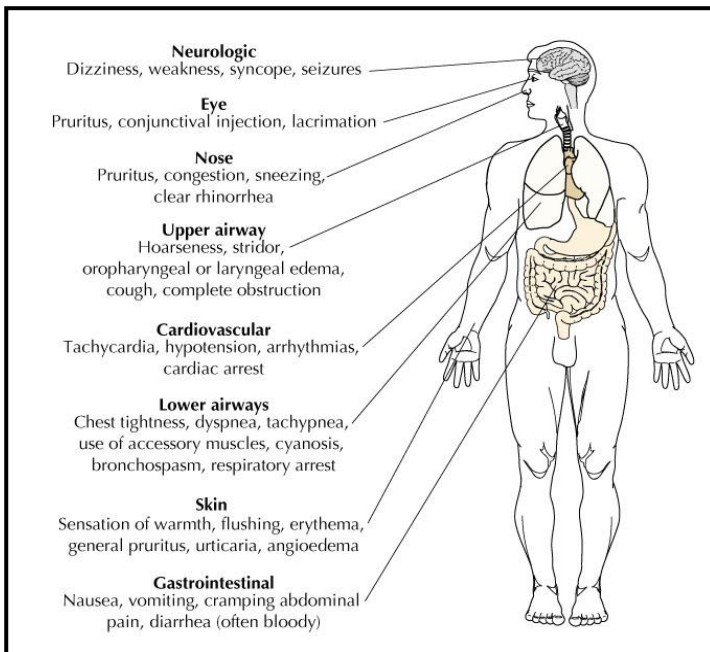


Figure 3 – Signs and symptoms of anaphylaxis

Skin and/or mucosal changes

- Are often the first feature and present in over 80% of anaphylactic reactions
- Can be subtle or dramatic
- There may be just skin, just mucosal, or both skin and mucosal changes
- There may be erythema – a patchy, or generalised, red rash
- There may be urticaria (also called hives, nettle rash, wheals or welts), which can appear anywhere on the body. The wheals may be pale, pink or red, and may look like nettle stings. They can be different shapes and sizes, and are often surrounded by a red flare. They are usually itchy.
- Angioedema is similar to urticaria but involves swelling of deeper tissues, most commonly in the eyelids and lips, and sometimes in the mouth and throat

6. TREATMENT OF AN ANAPHYLACTIC REACTION

Anaphylaxis algorithm for adults and children

(applicable in all healthcare settings)

See [Error! Reference source not found.](#), below.

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.

Key recommendations

- Treat life-threatening features, using the **Airway, Breathing, Circulation, Disability, Exposure (ABCDE)** approach.
- Adrenaline is the first-line treatment for anaphylaxis. Give intramuscular (IM) adrenaline early (in the anterolateral thigh) for **Airway/Breathing/Circulation** 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 **Airway/Breathing/Circulation** 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.

Important changes from previous guideline

- Greater emphasis on intramuscular adrenaline to treat anaphylaxis, and repeated after 5 minutes if **Airway/Breathing/Circulation** 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 **Airway/Breathing/Circulation** problems persist (**Error! Reference source not found.**).
 - Treatment of **refractory anaphylaxis**, defined as anaphylaxis where there is no improvement in respiratory or cardiovascular symptoms despite two appropriate doses of IM adrenaline (**Figure 5**).
- **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 **Airway/Breathing/Circulation** 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.

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 **Airway** and **Breathing** problems may prefer to sit up as this will make breathing easier.
- Lying flat, with or without leg elevation is helpful for patients with a low blood pressure (**Circulation** problem); *if the patient feels faint, do not sit or stand them up - this can cause cardiac arrest.*
- Patients who are breathing and unconscious should be placed on their side (recovery position)
- Pregnant patients should lie on their left side to prevent aortocaval compression.

Remove the trigger if possible

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

Other treatment

- **Glucagon**, 1mg IV every 5 minutes, may be used for patients on β -blockers who do not respond to standard therapy.
- Severe, resistant bronchospasm should be treated with nebulised **salbutamol** (5mg/dose or continuous); a continuous infusion of salbutamol may also be given if required. Intravenous magnesium sulphate and aminophylline may be considered for resistant bronchospasm.

Monitoring

Continuous monitoring required - respiratory rate, SpO₂, pulse, and BP - until clinical risk re-assessment at 6-12 hours (or earlier if clear signs of improvement/deterioration).

*BP frequency – every 15 minutes in first hour; every 30 minutes in second hour and then hourly if patient stable

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(20) – ALS or APLS protocol. 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.
- Prolonged resuscitation may be successful (as with hypothermia).

Adrenaline use

- Use doses of adrenaline recommended in the ALS/APLS guidelines.
- 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(20).
- Peripheral low-dose IV adrenaline infusion: 1 mg (1 mL of 1 mg/mL [1:1000]) adrenaline in 100 mL of 0.9% sodium chloride. Prime and connect with an infusion pump via a dedicated line. In both adults and children, start at 0.5–1.0 mL/kg/hour, and **titrate according to clinical response**.
- Nebulized adrenaline (5ml of 1mg/ml – 1:1000) can be used in addition to intramuscular adrenaline for partial upper airway obstruction (stridor) from laryngeal oedema. The injection can be used nebulised off-label.

Anaphylaxis

Anaphylaxis?

A = Airway **B** = Breathing **C** = Circulation **D** = Disability **E** = Exposure

Remove the trigger if possible:

- Stop any drug suspected of causing an anaphylactic reaction (e.g. stop IV antibiotics, gelatine solution)
- Remove the stinger after bee sting (early removal more important than the method)
- After food-induced anaphylaxis, attempts to induce vomiting are not recommended
- Do not delay treatment if removal of trigger not feasible

Diagnosis – look for:

- Sudden onset of Airway and/or Breathing and/or Circulation problems¹
- And usually skin changes (e.g. itchy rash)

Call for HELP

Call resuscitation team or ambulance

- Remove trigger if possible (e.g. stop any infusion)
- Lie patient flat (with or without legs elevated)
 - A sitting position may make breathing easier
 - If pregnant, lie on left side



Give intramuscular (IM) adrenaline²

Inject at anterolateral aspect – middle third of the thigh



- Establish airway
- Give high flow oxygen
- Apply monitoring: pulse oximetry, ECG, blood pressure

If no response:

- Repeat IM adrenaline after 5 minutes
- IV fluid bolus³

If no improvement in Breathing or Circulation problems¹ despite TWO doses of IM adrenaline:

- Confirm resuscitation team or ambulance has been called
- Follow REFRACTORY ANAPHYLAXIS ALGORITHM

1. Life-threatening problems

- Airway**
 Hoarse voice, stridor
- Breathing**
 ↑work of breathing, wheeze, fatigue, cyanosis, SpO₂ <94%
- Circulation**
 Low blood pressure, signs of shock, confusion, reduced consciousness

2. Intramuscular (IM) adrenaline

- Use adrenaline at 1 mg/mL (1:1000) concentration
- Adult and child >12 years:** 500 micrograms IM (0.5 mL)
Child 6–12 years: 300 micrograms IM (0.3 mL)
Child 6 months to 6 years: 150 micrograms IM (0.15 mL)
Child <6 months: 100–150 micrograms IM (0.1–0.15 mL)

The above doses are for IM injection **only**.
 Intravenous adrenaline for anaphylaxis to be given **only by experienced specialists** in an appropriate setting.

3. IV fluid challenge

- Use crystalloid
- Adults:** 500–1000 mL
Children: 10 mL/kg

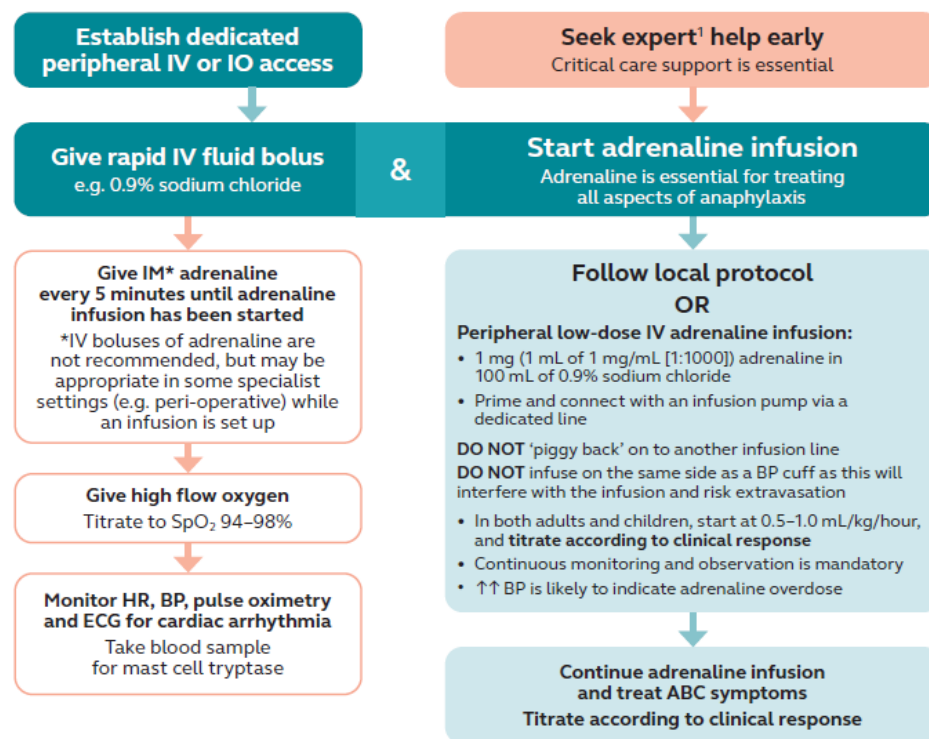
Call for help if life-threatening features - 2222

If profound shock or cardiac arrest → follow ALS or APLS algorithm

Figure 4 - Resuscitation Council UK Anaphylaxis Algorithm (2021)(1)

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 5 – Management of refractory anaphylaxis(1)

7. INVESTIGATION OF AN ANAPHYLACTIC REACTION FOLLOWING INITIAL RESUSCITATION

Notes

- **For Wythenshawe Hospital only:** Use the appropriate '[Anaphylaxis and Allergic Reactions Integrated Care Pathway \(ICP\)](#)'- adults (similar ICP for children under development).
- **For Royal Manchester Children's Hospital:** use the '[Pink](#)' developed specifically for Anaphylaxis in ED, available on MFT's intranet.

Documentation of reaction details (as per NICE CG134)(10)

- Document the **acute clinical features** of the suspected anaphylactic reaction
- Record the **time of onset** of the reaction
- Record the **circumstances immediately before** the onset of symptoms to help to identify the possible trigger

The above should be documented in the electronic systems or notes and Anaphylaxis ICP, as appropriate.

All anaphylactic reactions occurring in the Trust (i.e., admitted patients, day cases and outpatients, including those where patients present to the Emergency Departments and anaphylaxis occurring after allergy challenge procedures/other investigations or treatments, such as allergen immunotherapy, as well as cases occurring at MFT's community services) **should be reported via the Trust's Incident Reporting System (HIRS).**

Investigations (as per NICE CG134)(10)

- **Adults and young people aged 16 years or older:**
After a suspected anaphylactic reaction, take *timed* blood samples for **mast cell tryptase** testing as follows (clotted sample tube - same as used for U&Es):
 - a) a sample as soon as possible after emergency treatment has started (do not delay treatment)
 - b) a second sample ideally within 1–2 hours (but no later than 4 hours) from the onset of symptoms.
- **Children younger than 16 years:**
After a suspected anaphylactic reaction, consider taking *timed* blood samples for **mast cell tryptase** testing as follows, if the cause is thought to be venom-related, drug-related or idiopathic (clotted sample tube - same as used for U&Es):
 - a) a sample as soon as possible after emergency treatment has started (do not delay treatment)
 - b) a second sample ideally within 1–2 hours (but no later than 4 hours) from the onset of symptoms.
- Inform the person (or, as appropriate, their parent and/or carer) that a blood sample may be required at follow-up with the specialist allergy service to measure baseline mast cell tryptase (to be done no less than 24h post-reaction).

8. OBSERVATION, DISCHARGE AND FOLLOW UP (as per NICE CG134)

Notes

- **For Wythenshawe Hospital only:** Use the appropriate '[Anaphylaxis and Allergic Reactions Integrated Care Pathway \(ICP\)](#)'- adults (similar ICP for children under development).
- **For Royal Manchester Children's Hospital:** use the '[Pink](#)' developed specifically for Anaphylaxis in ED, available on MFT's intranet.

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See the Intranet for the latest version.	Version Number: 1.0 (Apr 2022)	

Period of observation following emergency treatment (as per NICE CG134)(10)

- **Adults and young people aged 16 years or older** who have had emergency treatment for suspected anaphylaxis should be observed for 6–12 hours from the onset of symptoms, depending on their response to emergency treatment.

Note: 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 or close to discharge; this is to be decided after senior review.*

- **Children younger than 16 years** who have had emergency treatment for suspected anaphylaxis should be admitted to hospital under the care of a paediatric medical team.

Referral to Allergy Services (as per NICE CG134)(10)

- After emergency treatment for suspected anaphylaxis, all patients should be referred to an Allergy Service in order to accurately investigate, diagnose, monitor and provide ongoing management of, and patient education about, suspected anaphylaxis.
- **Adults and young people aged 16 years or older** should be referred to either:
 - The **Allergy Centre at Wythenshawe Hospital** – by emailing the completed ‘Anaphylaxis & Allergic Reactions Integrated Care Pathway’ (ICP) to the Allergy Centre and copy of paramedic sheet (if arrived by 999) to AllergyCentre@mft.nhs.uk (telephone is 0161 291 4055); or post to the Allergy Centre at Wythenshawe Hospital.
 - The **Immunology and Allergy Service at Manchester Royal Infirmary** – by emailing clinical.immunology@mft.nhs.uk. For queries call 0161 276 6686.
- **Children younger than 16 years** should be referred to either:
 - The **Paediatric Allergy Service at Wythenshawe Hospital** by posting/faxing the completed ‘Paediatric ED admission documentation to Dr Naveen Rao’s secretary (fax 0161 291 5307).
 - The **Paediatric Allergy Service at The Royal Manchester Children’s Hospital** – by completing the Paediatric Anaphylaxis and Allergy pathway, and the Paediatric Allergy referral form
 - The **Paediatric Allergy Service at North Manchester General Hospital** – via post and telephone (switch 0161 764 6081)
- **For perioperative anaphylaxis or following any interventional procedure**, please refer patients to either:
 - The **Allergy Centre at Wythenshawe Hospital** – by emailing or posting the completed appropriate proforma ‘Investigation of anaphylaxis during general anaesthesia’/ ‘Investigation of anaphylaxis during interventional procedures’ (on the [Allergy Service, Wythenshawe Hospital intranet page](#)) to the Allergy secretaries (AllergyCentre@mft.nhs.uk ; telephone 0161 291 4055).
 - The **Anaesthetic Reaction Clinic at Manchester Royal Infirmary** – by emailing a referral form (available on intranet or from <http://bit.ly/ARCref>) with a copy of anaesthetic charts and relevant notes to anaesthetic.reaction@mft.nhs.uk. For urgent advice please contact Dr Andrew Parkes, Consultant Anaesthetist.

Post-reaction care prior to discharge (as per NICE CG134)

- After emergency treatment for suspected anaphylaxis, offer people (or, as appropriate, their parent and/or carer) an appropriate **adrenaline auto-injector (AAI)** as an interim measure *before* the specialist allergy service appointment. Below are the currently available AAIs in the UK at the time of updating this guideline (which may change – please ensure you are aware of the AAIs available):
 - In **adults** (weighing more than 50 kg), the available adrenaline auto-injectors are Jext® 300 microgram, Epipen® 300 microgram, Emerade 300 microgram and Emerade 500 microgram.
 - In **children**, the weight-appropriate adrenaline auto-injector should be selected from the options available: Jext® 300 microgram / 150 microgram, or Epipen® 300 microgram / 150 microgram. Please follow the advice on the Paediatrics Allergy ‘Pink’ document for the RMCH site.
 - Note that in cases of *anaphylaxis confirmed due to drug allergy/hypersensitivity*, prescription of an adrenaline auto-injector is *not required*; instead, patients should receive advice on strict avoidance of the culprit drug (further information and advice to be given by the specialist once patient is reviewed following referral, including registration with MedicAlert or similar, provision of a ‘Drug Allergy Card’ and details marked in notes - Red Alert Card and patient electronic records).
 - Before discharge a healthcare professional with the appropriate skills and competencies should offer people (or, as appropriate, their parent and/or carer) the following:
 - **information about anaphylaxis**, including the signs and symptoms of an anaphylactic reaction*
 - information about the risk of a **biphasic reaction***
 - information on what to do if an anaphylactic reaction occurs (use the adrenaline injector and call emergency services)*
 - a 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 (Anaphylaxis Campaign)*
- * **For adults** - This information is available in a **Patient Information leaflet (PIL)** on ‘Anaphylaxis and use of adrenaline auto-injectors’ and an ‘**Anaphylaxis Action Plan**’ (Appendices 5 and 6)
- * **For children**- action plans, parent information leaflets and training videos on correct use of all AAIs can be accessed at www.allergynorthwest.nhs.uk
- * **Patients with disabilities (learning, hearing, or sensory impairments)**- should be provided with accessible information. If required, reasonable adjustments should be made for these patients.

In those *exceptional* cases when patients are not required to be admitted – adults only, please refer them to either of the below services; an adrenaline auto-injector will be prescribed (if required), and post-reaction care given within 7 days of presentation:

- The **Allergy Centre at Wythenshawe Hospital** – by emailing the completed ‘Anaphylaxis & Allergic Reactions Integrated Care Pathway’ (ICP) to the Allergy Centre and copy of paramedic sheet (if arrived by 999) to AllergyCentre@mft.nhs.uk (tel 0161 291 4055); or post.
- The **Immunology and Allergy Service at Manchester Royal Infirmary** – by either completing the Rapid Access Anaphylaxis referral form on ICE or emailing clinical.immunology@mft.nhs.uk. For queries call 0161 276 6686.

Specific guidance for patients presenting with anaphylaxis at MFT's community services

All patients should be assessed/diagnosed and managed as per guidance in corresponding sections, above.

As per above guidance, most adult patients may require to be transported to one of MFT's Emergency Departments for further assessment/observation and treatment, as appropriate; all children should be admitted to hospital under the care of a paediatric medical team.

In those *exceptional* cases when patients are not required to be admitted – adults only and are deemed suitable for discharge from a community service, please refer them to either of the below services; an adrenaline auto-injector will be prescribed (if required), and post-reaction care given within 7 days of presentation:

- The **Allergy Centre at Wythenshawe Hospital** – by emailing the completed 'Anaphylaxis & Allergic Reactions Integrated Care Pathway' (ICP) to the Allergy Centre and copy of paramedic sheet (if available) to AllergyCentre@mft.nhs.uk (tel 0161 291 4055); or post.
- The **Immunology and Allergy Service at Manchester Royal Infirmary** – by either completing the Rapid Access Anaphylaxis referral form on ICE or emailing clinical.immunology@mft.nhs.uk. For queries call 0161 276 6686.

9. SPECIFIC GUIDANCE FOR PERIOPERATIVE ANAPHYLAXIS AND ANAPHYLAXIS DURING INTERVENTIONAL PROCEDURES

Patients presenting with perioperative anaphylaxis should be managed as per this guideline and guidance by the Association of Anaesthetists of Great Britain and Ireland (AAGBI), available at <https://anaesthetists.org/Home/Resources-publications/Safety-alerts/Anaesthesia-emergencies/Anaphylaxis-and-allergies>

and their Quick Reference Handbook (QRH) – Anaphylaxis, available at:

<https://anaesthetists.org/Home/Resources-publications/Safety-alerts/Anaesthesia-emergencies/Quick-Reference-Handbook/PDF-version>

All patients presenting with **perioperative anaphylaxis or suspected anaphylaxis** should be referred to either:

- The **Allergy Centre at Wythenshawe Hospital**
 - via a specific referral proforma (adapted from the AAGBI), available on the [Allergy Service intranet page](#) – ‘Referral form (GA) - investigation of reactions during General Anaesthesia’. Referring anaesthetists should enclose copies of all relevant documentation: a) photocopy of the anaesthetic record and any other previous anaesthetic records; b) photocopy of the prescription record; c) photocopy of the recovery room documentation; d) photocopy of any relevant ward documentation.
- The **Anaesthetic Reaction Clinic at Manchester Royal Infirmary**
 - by emailing a referral form (available on intranet or from <http://bit.ly/ARCref>) with a copy of anaesthetic charts and relevant notes to anaesthetic.reaction@mft.nhs.uk
 - For urgent advice please contact Dr Andrew Parkes, Consultant Anaesthetist
- The **Peri-anaesthetic Allergy Clinic at RMCH – Paediatric perioperative anaphylaxis**
 - Referring anaesthetists should complete the referral form on <http://bit.ly/ARCref>, enclose copies of all relevant documentation: a) photocopy of the anaesthetic record and any other previous anaesthetic records; b) photocopy of the prescription record; c) photocopy of the recovery room documentation; d) photocopy of any relevant ward documentation and email to vibha.sharma@mft.nhs.uk or andrew.parkes@mft.nhs.uk

Patients presenting with **anaphylaxis or suspected anaphylaxis during other interventional procedures** should be referred to either:

- The **Allergy Centre at Wythenshawe Hospital**
 - via a specific referral proforma, available on the [Allergy Service intranet page](#) – ‘Referral form (Interv procedures) - investigation of reactions during interv proc’, along with any other relevant documentation.
- The **Anaesthetic Reaction Clinic at Manchester Royal Infirmary**
 - by emailing a referral form (available on intranet or from <http://bit.ly/ARCref>) with a copy of anaesthetic charts and relevant notes to anaesthetic.reaction@mft.nhs.uk
 - For urgent advice please contact Dr Andrew Parkes, Consultant Anaesthetist

10. REFERENCES

1. Guidance: Anaphylaxis | Resuscitation Council UK [Internet]. 2021 [cited 2021 Jul 13]. Available from: <https://www.resus.org.uk/library/additional-guidance/guidance-anaphylaxis>
2. Jose R, Clesham GJ. Survey of the use of epinephrine (adrenaline) for anaphylaxis by junior hospital doctors. *Postgrad Med J* [Internet]. 2007 Sep [cited 2021 Jul 13];83(983):610–1. Available from: <https://pubmed.ncbi.nlm.nih.gov/17823230/>
3. Lindor RA, McMahon EM, Wood JP, Sadosty AT, Boie ET, Campbell RL. Anaphylaxis-related malpractice lawsuits. *West J Emerg Med* [Internet]. 2018 Jul 1 [cited 2021 Jul 13];19(4):693–700. Available from: <https://pubmed.ncbi.nlm.nih.gov/30013706/>
4. Patel N, Chong KW, Yip AYG, Ierodiakonou D, Bartra J, Boyle RJ, et al. Use of multiple epinephrine doses in anaphylaxis: A systematic review and meta-analysis. *J Allergy Clin Immunol* [Internet]. 2021 [cited 2021 Jul 13]; Available from: <https://pubmed.ncbi.nlm.nih.gov/33862009/>
5. Muraro A, Worm M, Alviani C, Cardona V, DunnGalvin A, Garvey LH, et al. EAACI guidelines: Anaphylaxis (2021 update). *Allergy* [Internet]. 2022 Feb;77(2):357–77. Available from: <https://onlinelibrary.wiley.com/doi/10.1111/all.15032>
6. Cardona V, Ansotegui IJ, Ebisawa M, El-Gamal Y, Fernandez Rivas M, Fineman S, et al. World allergy organization anaphylaxis guidance 2020. *World Allergy Organ J* [Internet]. 2020 Oct 1 [cited 2021 Jul 13];13(10). Available from: <https://pubmed.ncbi.nlm.nih.gov/33204386/>
7. Sampson HA, Muñoz-Furlong A, Campbell RL, Adkinson NF, Bock SA, Branum A, 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* [Internet]. 2006 Feb;117(2):391–7. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0091674905027235>
8. Erlewyn-Lajeunesse M, Dymond S, Slade I, Mansfield HL, Fish R, Jones O, et al. Diagnostic Utility of Two Case Definitions for Anaphylaxis. *Drug Saf* [Internet]. 2010 Jan;33(1):57–64. Available from: <http://link.springer.com/10.2165/11318970-000000000-00000>
9. Loprinzi Brauer CE, Motosue MS, Li JT, Hagan JB, Bellolio MF, Lee S, et al. Prospective Validation of the NIAID/FAAN Criteria for Emergency Department Diagnosis of Anaphylaxis. *J Allergy Clin Immunol Pract* [Internet]. 2016 Nov;4(6):1220–6. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S2213219816301829>
10. NICE. Surveillance report – Anaphylaxis: assessment and referral after emergency treatment (2011). *Clin Guidel* [Internet]. 2016 [cited 2021 Jul 13];CG134 www.nice.org.uk. Available from: <https://www.nice.org.uk/guidance/cg134>
11. Simons FE, Arduoso LR, Bilo MB, El Gamal YM, Ledford DK, Ring J, et al. World Allergy Organization anaphylaxis guidelines: summary. *J Allergy Clin Immunol*. 2011;127(3):587–93.
12. Turner PJ, Gowland MH, Sharma V, Ierodiakonou D, Harper N, Garcez T, 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* [Internet]. 2015 Apr 1 [cited 2021 Jul 13];135(4):956-963.e1. Available from: <https://pubmed.ncbi.nlm.nih.gov/25468198/>
13. Baseggio Conrado A, Ierodiakonou D, Gowland MH, Boyle RJ, Turner PJ. Food anaphylaxis in the United Kingdom: Analysis of national data, 1998-2018. *BMJ*. 2021 Feb 17;372.
14. Panesar SS, Javad S, De Silva D, Nwaru BI, Hickstein L, Muraro A, et al. The epidemiology of anaphylaxis in Europe: A systematic review [Internet]. Vol. 68, *Allergy: European Journal of Allergy and Clinical Immunology*. Allergy; 2013 [cited 2021 Jul 13]. p. 1353–61. Available from: <https://pubmed.ncbi.nlm.nih.gov/24117770/>
15. Harper NJN, Cook TM, Garcez T, Farmer L, Floss K, Marinho S, et al. Anaesthesia, surgery, and life-threatening allergic reactions: epidemiology and clinical features of perioperative anaphylaxis in the 6th National Audit Project (NAP6). *Br J Anaesth* [Internet]. 2018 Jul;121(1):159–71. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/29935567>

16. Turner PJ, Jerschow E, Umasunthar T, Lin R, Campbell DE, Boyle RJ. Fatal Anaphylaxis: Mortality Rate and Risk Factors. *J Allergy Clin Immunol Pract* [Internet]. 2017 Sep 1 [cited 2021 Jul 13];5(5):1169–78. Available from: <https://pubmed.ncbi.nlm.nih.gov/28888247/>
17. Kraft M, Scherer Hofmeier K, Ruëff F, Pföhler C, Renaudin JM, Bilò MB, et al. Risk Factors and Characteristics of Biphasic Anaphylaxis. *J Allergy Clin Immunol Pract* [Internet]. 2020 Nov 1 [cited 2021 Jul 13];8(10):3388-3395.e6. Available from: <https://pubmed.ncbi.nlm.nih.gov/32763470/>
18. 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* [Internet]. 2015 [cited 2021 Jul 13];3(3):408-416.e2. Available from: <https://pubmed.ncbi.nlm.nih.gov/25680923/>
19. Kim TH, Yoon SH, Hong H, Kang HR, Cho SH, Lee SY. Duration of Observation for Detecting a Biphasic Reaction in Anaphylaxis: A Meta-Analysis. *Int Arch Allergy Immunol* [Internet]. 2019 May 1 [cited 2021 Jul 13];179(1):31–6. Available from: <https://pubmed.ncbi.nlm.nih.gov/30763927/>
20. 2021 Resuscitation Guidelines | Resuscitation Council UK [Internet]. 2021 [cited 2021 Jul 13]. Available from: <https://www.resus.org.uk/library/2021-resuscitation-guidelines>

11. APPENDICES

APPENDIX 1

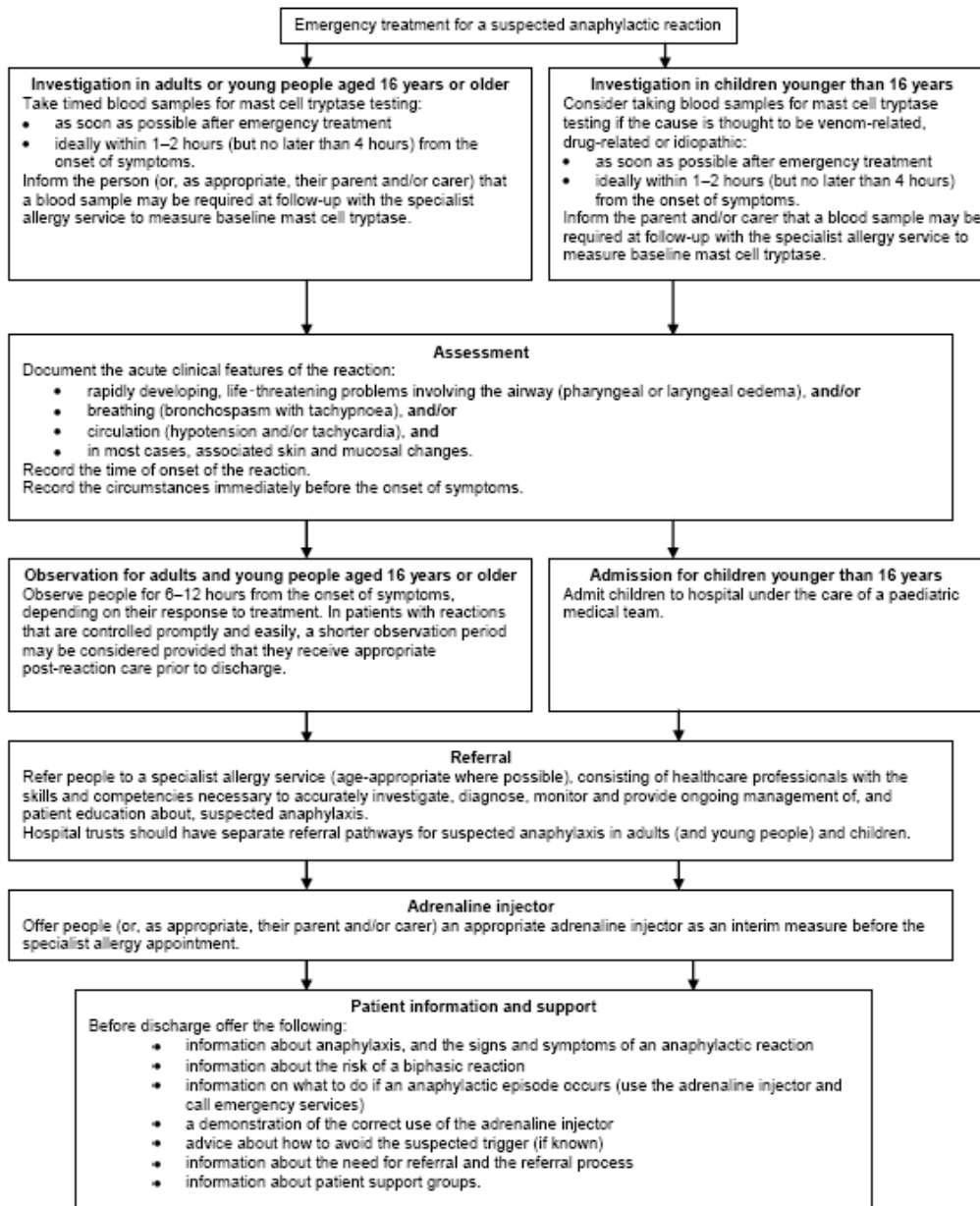
NICE CG 134 Guidance

<https://www.nice.org.uk/guidance/cg134>

APPENDIX 2

NICE CG 134 Care Pathway

2 Care pathway



APPENDIX 3

Anaphylaxis and Allergic Reactions Integrated Care Pathway – Adults Wythenshawe Hospital only

Available on the [Allergy Centre \(Wythenshawe Hospital\) Intranet page](#):

<https://intranet.mft.nhs.uk/content/hospitals-mcs/wtwa/heartlung/respiratory/allergy-1/anaphylaxis>

This document is also available on the ICP page of the Trust’s intranet:

<http://uhsm-intranet/guidelines/IntegratedCarePathways/Pages/IntegratedCarePathways.aspx>

APPENDIX 4

Anaphylaxis - Mechanisms and Triggers

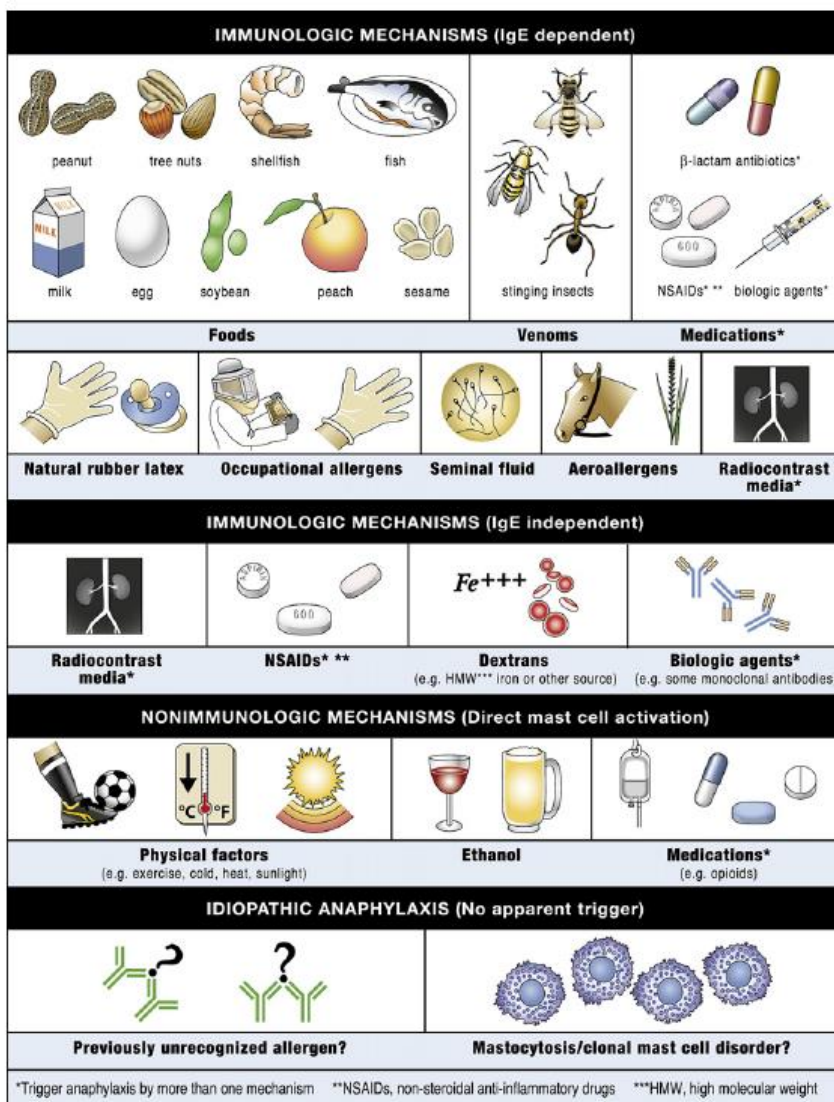


FIG 2. Anaphylaxis mechanisms and triggers. Anaphylaxis typically occurs through an IgE-dependent immunologic mechanism, most commonly triggered by foods, stinging insect venoms, or medications. Medications can also trigger anaphylaxis through an IgE-independent immunologic mechanism and through direct mast cell stimulation. Radiocontrast media can trigger anaphylaxis through both IgE-dependent and IgE-independent mechanisms. In patients with idiopathic anaphylaxis, the possibility of a novel allergen trigger or of underlying mastocytosis or a clonal mast cell disorder should be considered. For

From ref (11) – WAO anaphylaxis guidelines 2011

APPENDIX 5

Patient Information leaflet on Anaphylaxis and the use of Adrenaline Auto-injectors (AAI)

Available on the [Allergy Service \(Wythenshawe Hospital\) Intranet page](#):

<https://intranet.mft.nhs.uk/content/hospitals-mcs/wtwa/heartlung/respiratory/allergy-1>

All information related to Paediatric Allergy is available at www.allergynorthwest.nhs.uk

APPENDIX 6

Anaphylaxis Action Plan

Available on the [Allergy Service \(Wythenshawe Hospital\) Intranet page](#):

<https://intranet.mft.nhs.uk/content/hospitals-mcs/wtwa/heartlung/respiratory/allergy-1>

All information related to Paediatric Allergy is available at www.allergynorthwest.nhs.uk

APPENDIX 7

Additional Patient Information Leaflets on Anaphylaxis

Anaphylaxis Campaign (available on their website):

<http://www.anaphylaxis.org.uk/our-factsheets/>

APPENDIX 8

Plan for Dissemination

This guideline will be available under 'Guidelines' on the Trust intranet. It will also be circulated to the Heads of Nursing and Clinical Directors for dissemination to their divisions.

Training of all clinical staff on recognition and management of anaphylaxis is a mandatory requirement.