

Anaphylaxis: assessment to confirm an anaphylactic episode and the decision to refer after emergency treatment for a suspected anaphylactic episode

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Introduction

Anaphylaxis is a severe, life-threatening, generalised or systemic hypersensitivity reaction. It is characterised by rapidly developing, life-threatening problems involving: the airway (pharyngeal or laryngeal oedema) and/or breathing (bronchospasm with tachypnoea) and/or circulation (hypotension and/or tachycardia). In most cases, there are associated skin and mucosal changes^[1].

In emergency departments a person who presents with the signs and symptoms listed above may be classified as having a 'severe allergic' reaction 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'.

People who have had a mild or moderate allergic reaction are at risk of, and may subsequently present with, suspected anaphylaxis. Certain groups may be at higher risk, either because of an existing comorbidity (for example asthma) or because they are more likely to be exposed to the same allergen again (for example people with venom allergies or reactions to specific food triggers). These groups were not included within the scope of this guideline, which is specific to those who have received emergency treatment for suspected anaphylaxis.

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 nonallergic 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, nonallergic or idiopathic varies considerably with age.

Food is a particularly common trigger in children, while medicinal products are much more common triggers in older people. In the UK it is estimated that 500,000 people have had a venom-induced anaphylactic reaction and 220,000 people up to the age of 44 have had a nut-induced anaphylactic reaction^[2].

There is no overall figure for the frequency of anaphylaxis from all causes in the UK. Because anaphylaxis presents mainly in accident and emergency departments and outpatient settings,

few estimates of prevalence are available from NHS sources. Anaphylaxis may not be recorded, or may be misdiagnosed as something else, for example, asthma. It may also be recorded by cause, such as food allergy, rather than as an anaphylactic reaction.

Available UK estimates suggest that approximately 1 in 1333 of the population of England has experienced anaphylaxis at some point in their lives^[3]. There are approximately 20 deaths from anaphylaxis reported each year in the UK, with around half the deaths being iatrogenic^[4], although this may be an underestimate.

After an acute anaphylactic reaction, it is believed that many people do not receive optimal management of their condition. One reason for this is healthcare professionals' lack of understanding when making a diagnosis, for example failing to differentiate anaphylaxis from less severe histamine-releasing reactions or from other conditions that mimic some or all of its clinical features. Another reason is a lack of understanding of when or where to refer patients. This can affect the likelihood of the person receiving a definitive diagnosis, which can lead to anxiety, inappropriate management and recurrent reactions. It can also lead to avoidable costs for the NHS and increase the need for acute care.

Drug recommendations

The guideline does not make recommendations on drug dosage; prescribers should refer to the [British national formulary](#) for this information. The guideline also assumes that prescribers will use a drug's summary of product characteristics to inform decisions made with individual patients.

Who this guideline is for

This document is for staff in primary, secondary and tertiary settings who care for people with suspected anaphylaxis.

^[3] Resuscitation Council (UK) 2008. Emergency treatment of anaphylactic reactions. Guidelines for healthcare providers.

^[2] Ewan PW for the British Society for Allergy and Clinical Immunology (2006) The nature and extent of allergy in the United Kingdom. A report to the Department of Health Review of Allergy Services.

^[3] Stewart AG, Ewan PW (1996) The incidence, aetiology and management of anaphylaxis presenting to an accident and emergency department. *Quarterly Journal of Medicine* 89 (11): 859–64

^[4] Pumphrey RS (2000) Lessons for management of anaphylaxis from a study of fatal reactions. *Clinical and Experimental Allergy* 30(8): 1144–50

Patient-centred care

This guideline offers best practice advice on the care of adults, young people and children following emergency treatment for suspected anaphylaxis. For the purpose of this guideline all patients under 16 are classed as children. Those aged 16 and 17 are classed as young people and those aged 18 and over as adults.

Treatment and care should take into account patients' needs and preferences. People with suspected anaphylaxis should have the opportunity to make informed decisions about their care and treatment, in partnership with their healthcare professionals. If patients do not have the capacity to make decisions, healthcare professionals should follow the [Department of Health's advice on consent](#) and the [code of practice that accompanies the Mental Capacity Act](#). In Wales, healthcare professionals should follow [advice on consent from the Welsh Government](#).

If the patient is under 16, healthcare professionals should follow the guidelines in [Seeking consent: working with children](#).

Good communication between healthcare professionals and patients is essential. It should be supported by evidence-based written information tailored to the patient's needs. Treatment and care, and the information patients are given about it, should be culturally appropriate. It should also be accessible to people with additional needs such as physical, sensory or learning disabilities, and to people who do not speak or read English.

Families and carers should be given the information and support they need.

Care of young people in transition between paediatric and adult services should be planned and managed according to the best practice guidance described in [Transition: getting it right for young people](#).

Adult and paediatric healthcare teams should work jointly to provide assessment and services to young people with suspected anaphylaxis. Diagnosis and management should be reviewed throughout the transition process, and there should be clarity about who is the lead clinician to ensure continuity of care.

1 Recommendations

The following guidance is based on the best available evidence. The [full guideline](#) gives details of the methods and the evidence used to develop the guidance.

1.1 List of all recommendations

- 1.1.1 Document the acute clinical features of the suspected anaphylactic reaction (rapidly developing, life-threatening problems involving the airway [pharyngeal or laryngeal oedema] and/or breathing [bronchospasm with tachypnoea] and/or circulation [hypotension and/or tachycardia] and, in most cases, associated skin and mucosal changes).
- 1.1.2 Record the time of onset of the reaction.
- 1.1.3 Record the circumstances immediately before the onset of symptoms to help to identify the possible trigger.
- 1.1.4 After a suspected anaphylactic reaction in adults or young people aged 16 years or older, take timed blood samples for mast cell tryptase testing as follows:
- a sample as soon as possible after emergency treatment has started
 - a second sample ideally within 1–2 hours (but no later than 4 hours) from the onset of symptoms.
- 1.1.5 After a suspected anaphylactic reaction in children younger than 16 years, consider taking blood samples for mast cell tryptase testing as follows if the cause is thought to be venom-related, drug-related or idiopathic:
- a sample as soon as possible after emergency treatment has started
 - a second sample ideally within 1–2 hours (but no later than 4 hours) from the onset of symptoms.

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- 1.1.6 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.
- 1.1.7 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. In people with reactions that are controlled promptly and easily, a shorter observation period may be considered provided that they receive appropriate postreaction care prior to discharge.
- 1.1.8 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.
- 1.1.9 After emergency treatment for suspected anaphylaxis, offer people a referral to a specialist allergy service (age-appropriate where possible) consisting of healthcare professionals with the skills and competencies necessary to accurately investigate, diagnose, monitor and provide ongoing management of, and patient education about, suspected anaphylaxis.
- 1.1.10 After emergency treatment for suspected anaphylaxis, offer people (or, as appropriate, their parent and/or carer) an appropriate adrenaline injector as an interim measure before the specialist allergy service appointment.
- 1.1.11 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)

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- 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.

1.1.12 Each hospital trust providing emergency treatment for suspected anaphylaxis should have separate referral pathways for suspected anaphylaxis in adults (and young people) and children.

2 Notes on the scope of the guidance

NICE guidelines are developed in accordance with a scope that defines what the guideline will and will not cover. The [scope](#) of this guideline is available.

3 Implementation

NICE has developed [tools](#) to help organisations implement this guidance.

4 Research recommendations

The Guideline Development Group has made the following recommendations for research, based on its review of evidence, to improve NICE guidance and patient care in the future.

4.1 Mediators of anaphylactic reactions

Aside from mast cell tryptase, which other chemical inflammatory mediators offer potential as indicators of anaphylaxis?

Why this is important

Although mast cell tryptase is widely used to support the diagnosis of anaphylaxis, it is not universally suitable. Mast cell tryptase is not always elevated in children, when food is the allergen, or when the main severe feature is respiratory.

It is recommended that a cross-sectional study be carried out into the diagnostic accuracy of other potential chemical inflammatory mediators. The study should be conducted in both adults and children who have had a suspected anaphylactic reaction. The sensitivity and specificity of the proposed mediator should be compared against mast cell tryptase, using clinical assessment in conjunction with immuno-allergic study as the reference standard for both. The diagnostic accuracy of any mediator should be carried out for a range of potential allergens.

4.2 The frequency and effects of biphasic reactions

What are the frequency, timing, severity and predictors of biphasic reactions in people who have received emergency treatment for anaphylaxis?

Why this is important

Limited evidence was found on the frequency, timing severity and predictors of biphasic reactions and the resulting effect of these on morbidity and mortality.

It is recommended that a UK-based prospective cohort study be conducted that follows patients up after emergency treatment for anaphylaxis.

The study should follow people up for 7 days after discharge from the emergency department. The aim is to collect data on the predictors (for example, the person's response to the initial treatment), the time to any reaction, the severity of any biphasic reaction and the effect of the biphasic reaction on morbidity and mortality.

4.3 Length of observation period following emergency treatment for anaphylaxis

For how long should a person who has received emergency treatment for anaphylaxis be observed?

Why this is important

No studies were found that compared different observational periods or the effect of these on relevant patient outcomes.

It is recommended that a cluster randomised controlled trial is conducted for people who have received emergency treatment for anaphylaxis.

The interventions for the trial should be differing time periods of observation, within the secondary care setting, ranging from 1 hour to 24 hours after symptom resolution of the index reaction. Patients should then be followed up for 7 days following the end of the observational period to determine if a biphasic reaction has occurred and the effects of any reaction. The aim is to determine whether differing periods of observation have a detrimental effect on morbidity and mortality and to gather information about resource use.

4.4 Prevalence of anaphylactic reactions and related outcomes

What is the annual incidence of anaphylaxis and its related outcomes within the UK?

Why this is important

Limited evidence exists on the annual incidence of anaphylactic reactions and their associated outcomes within the UK.

It is recommended that a prospective observational study be conducted that records the annual incidence of anaphylactic reactions within the UK.

The overall number of anaphylactic reactions that occur in adults and children should be recorded and these should be classified into those that are first-time reactions, recurrent reactions or biphasic reactions. A clear, pre-defined, definition of what constitutes an anaphylactic reaction should be used, in order to avoid the misclassification of milder reactions. Data should also be collected on any emergency treatment that was delivered (by a clinician, use of an adrenaline injector) and the associated outcomes (morbidity, mortality, adverse events). Data should also be collected on any previous treatment received, such as that from a specialist allergy service or the provision of adrenaline injectors.

4.5 Effect of specialist services on health-related quality of life

For people who have experienced suspected anaphylaxis, what is the effect on health-related quality of life of (a) referral to specialist allergy services and (b) provision of adrenaline injectors, when compared with emergency treatment alone?

Why this is important

The GDG believed that referral to specialist services and/or the provision of adrenaline injectors was likely to provide day-to-day HRQoL benefit for people who have experienced suspected anaphylaxis, as a result of decreased anxiety and ongoing support. However, the health economic model relied on GDG opinion alone to quantify this benefit. Future economic analyses would be greatly improved by a reliable demonstration of this effect and an estimate of its magnitude. It is recommended that data are collected using validated measure(s) of HRQoL, including EQ-5D.

5 Other versions of this guideline

5.1 Full guideline

The full guideline, [Anaphylaxis: assessment to confirm an anaphylactic episode and the decision to refer after emergency treatment for a suspected anaphylactic episode](#) contains details of the methods and evidence used to develop the guideline.

5.2 NICE pathway

The recommendations from this guideline have been incorporated into a [NICE pathway](#).

5.3 Information for the public

NICE has produced [information for the public](#) explaining this guideline.

We encourage NHS and voluntary sector organisations to use text from this information in their own materials about anaphylaxis.

6 Related NICE guidance

Published

- [Food allergy in children and young people](#). NICE clinical guideline 116 (2011).

Under development

NICE is developing the following guidance (details available from www.nice.org.uk):

- Pharmedgen for the treatment of venom allergy. NICE technology appraisal guidance.

7 Updating the guideline

NICE clinical guidelines are updated so that recommendations take into account important new information. New evidence is checked 3 years after publication, and healthcare professionals and patients are asked for their views; we use this information to decide whether all or part of a guideline needs updating. If important new evidence is published at other times, we may decide to do a more rapid update of some recommendations. Please see [our website](#) for information about updating the guideline.

8 Glossary

Anaphylaxis

Anaphylaxis is a severe, life-threatening, generalised or systemic hypersensitivity reaction. It is characterised by rapidly developing, life-threatening problems involving: the airway (pharyngeal or laryngeal oedema) and/or breathing (bronchospasm with tachypnoea) and/or circulation (hypotension and/or tachycardia). In most cases, there are associated skin and mucosal changes^[5].

Biphasic anaphylaxis

After complete recovery of anaphylaxis, a recurrence of symptoms within 72 hours with no further exposure to the allergen. It is managed in the same way as anaphylaxis.

Idiopathic anaphylaxis

Denotes a form of anaphylaxis where no identifiable stimulus 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, for people who present with symptoms of anaphylaxis.

In emergency departments a person who presents with the signs and symptoms of anaphylaxis may be classified as having a 'severe allergic' reaction 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'.

Please see the [NICE glossary](#) for an explanation of terms not described above.

^[5] Resuscitation Council (UK; 2008) Emergency treatment of anaphylactic reactions. Guidelines for healthcare providers.

Appendix A: The Guideline Development Group, National Collaborating Centre and NICE project team

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A Short Clinical Guidelines Technical Team was responsible for this guideline throughout its development. It prepared information for the Guideline Development Group, drafted the guideline and responded to consultation comments.

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Appendix B: The Guideline Review Panel

The Guideline Review Panel is an independent panel that oversees the development of the guideline and takes responsibility for monitoring adherence to NICE guideline development processes. In particular, the panel ensures that stakeholder comments have been adequately considered and responded to. The panel includes members from the following perspectives: primary care, secondary care, lay, public health and industry.

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About this guideline

NICE clinical guidelines are recommendations about the treatment and care of people with specific diseases and conditions in the NHS in England and Wales.

The guideline was developed by the Centre for Clinical Practice at NICE. The Centre worked with a group of healthcare professionals (including consultants, GPs and nurses), patients and carers, and technical staff, who reviewed the evidence and drafted the recommendations. The recommendations were finalised after public consultation.

The methods and processes for developing NICE clinical guidelines are described in [The guidelines manual](#). This guideline was developed using the [short clinical guideline process](#).

The recommendations from this guideline have been incorporated into a [NICE Pathway](#). We have produced [information for the public](#) explaining this guideline. Tools to help you put the guideline into practice and information about the evidence it is based on are also [available](#).

Changes after publication

June 2012: minor maintenance

October 2012: minor maintenance

Your responsibility

This guidance represents the view of NICE, which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer, and informed by the summary of product characteristics of any drugs they are considering.

Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to avoid unlawful discrimination and to have regard to promoting equality of opportunity. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.

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