

Following up patients after treatment for anaphylaxis

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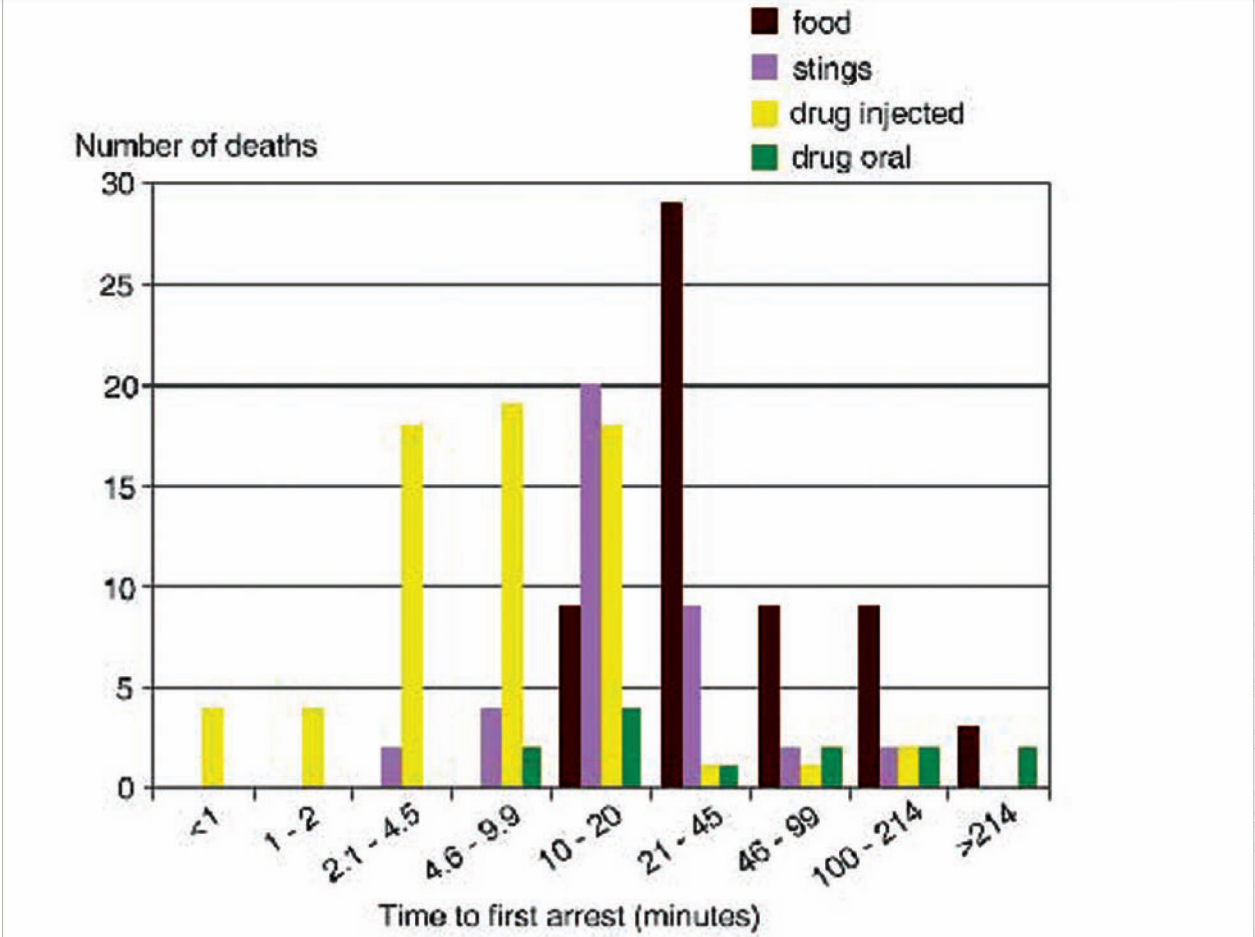


FIGURE 1
Time interval from exposure to trigger to first arrest⁵

Why is specialist referral important?

How should diagnosis be confirmed?

What is the role of primary care?



NICE HAS RECENTLY PUBLISHED GUIDELINES ON THE CARE AND FOLLOW-UP OF PATIENTS

who have received emergency treatment for anaphylaxis.¹ The definition of anaphylaxis used by the guidelines as a severe, life-threatening, generalised or systemic hypersensitivity reaction is widely accepted.² Diagnosis is based on the presenting symptoms and clinical signs which classically develop rapidly, typically evolving over minutes but in some cases hours. Various

combinations of airway and/or breathing and/or circulatory problems are possible as illustrated in case 1, p22 (severe bronchospasm, urticaria, and hypotension i.e. anaphylactic shock). Skin and/or mucosal changes (typically urticaria and/or angioedema) are seen in around 75% of cases, but importantly, these features alone are insufficient for a diagnosis of anaphylaxis. This point was illustrated by the case history in a previous article in this journal.³

Full details of how to resuscitate a

patient presenting acutely as a medical emergency with anaphylaxis have been covered previously.^{3,4}

KEY RECOMMENDATIONS

NICE recommends that as soon as possible after successful emergency treatment, timed (labelled) blood samples should be taken for the mast cell tryptase (MCT) test.⁵

MCT is normally stored in mast cells but is released in large amounts in anaphylaxis. Because MCT has a very short half life, diagnostic serum



Case 1

Typical (uniphasic) immediate IgE-mediated anaphylaxis

A 25-year-old man, with known peanut allergy, felt extremely ill within five minutes of eating a curry in a city restaurant. He had eaten in the same restaurant before without any problems. His mouth and throat were immediately itchy, and he felt increasingly nauseous.

On this occasion he had forgotten to bring both his salbutamol inhaler and his adrenaline autoinjector device. He felt faint and was advised to lie down. Paramedics arrived 10 minutes later, by that time a global urticarial rash had developed, and the patient complained that his breathing was increasingly 'tight'.

Anaphylaxis, most likely due to accidental exposure to nuts, was diagnosed. An adult dose of adrenaline was administered intramuscularly midquadriceps (0.5 ml of 1/1,000 dilution), and nebulised salbutamol was given. Almost immediately the patient felt much better. He was now able to talk normally, and his peak expiratory flow (which had been immeasurable) was improving. Blood pressure readings before and after adrenaline were 60/0 mmHg and 90/60 mmHg respectively.

Although keen to go home, the patient was detained overnight for observation. He continued to improve and by two hours after the first symptoms seemed to have fully recovered. A new adrenaline autoinjector device was prescribed because of worries that the home device was out of date. Blood samples were taken for mast cell tryptase (MCT) testing at 2 hours, 4 hours, and immediately before discharge at 12 hours.

The patient was reminded of the importance of attending his booked appointment in the specialist allergy clinic within the next few weeks. MCT levels at 2 and 4 hours were markedly elevated supporting anaphylaxis. MCT had returned to normal in the 12-hour sample. Skin prick testing in a clinic setting confirmed sensitivity to almond and hazelnut in addition to peanut. The patient had not realised that he was allergic to several tree nuts in addition to peanut. He was now advised to avoid all nuts lifelong.

He was provided with a MedicAlert bracelet. The need for caution when eating out (especially after alcohol) was emphasised. Asthma review and follow-up in the asthma clinic was arranged. Daily inhaled steroid and improved inhaler technique led to improved peak expiratory flow rates. A written management plan was provided.

samples need to be taken within 1–2 hours but no later than 4 hours from the onset of symptoms. If possible a second paired and timed sample within the same time frame is useful. Routine clotted blood bottles are required, and blood samples are stable overnight at room temperature.

MCT test results may strongly support anaphylaxis, but normal test results do not confidently exclude the diagnosis.

It is important to document the acute clinical features (record blood pressure, respiratory rate etc) and in particular, the time course of the onset of symptoms/signs and their resolution.

The circumstances immediately before the onset of symptoms should also be recorded to try to identify possible triggers. A study of fatal anaphylaxis⁵ showed that the majority of triggers provoke symptoms within

one hour of exposure (see figure 1, p21). Injected agents including medical drugs or bee/wasp venom act most rapidly, with some reactions following foods and oral medicines producing delayed reactions after a couple of hours. Food typically triggers symptoms within a few minutes, and is more likely in a child whereas new onset food allergy is far less likely in adults.

Because of the risk of relapse i.e. biphasic reactions, see case 2, opposite, the guidelines recommend that patients should be observed for 6–12 hours after the onset of symptoms especially for under 16 year olds. Possible confusion will be avoided if monitoring is advised for all cases who have been resuscitated following life-threatening anaphylaxis. Children younger than 16 years should be admitted and supervised by a hospital paediatrician.

An adrenaline injector device for intramuscular use only, should be prescribed appropriately for body weight^{3,4} as an interim measure before referral to a specialist allergy clinic. The adrenaline prescription must be accompanied by on-the-spot practical training in when, why, and how to use these devices before discharge.

Information packs should include details on how to recognise and manage future reactions, including the direction to 'use the adrenaline injector and call emergency services'. Interim advice should be given about avoidance of triggers (if known). Contact details for patient support groups should also be provided.

Referral to a specialist allergy service (or specialist paediatric service), is strongly recommended. The BSACI website (www.bsaci.org) lists many suitable clinics with contact details. Diagnosis can be confirmed, and further investigations organised not least with a view to identifying or confirming triggers (though many cases remain idiopathic). Advice on ongoing management, and further patient education can also be provided.

'Because of the risk of relapse i.e. biphasic reactions ... patients should be observed for 6–12 hours after the onset of symptoms'

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

UNIPHASIC AND BIPHASIC REACTIONS

Uniphasic reactions are the norm (see case 1, above) with clinical features (urticaria and/or bronchospasm and/or hypotension etc) peaking at around 30 minutes after the trigger event, and full recovery (either spontaneously or as a result of treatment) within

key points

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Anaphylaxis is defined as a severe, life-threatening, generalised or systemic hypersensitivity reaction. Diagnosis is based on the presenting symptoms and signs which classically develop rapidly, typically evolving over minutes but in some cases hours. Various combinations of airway and/or breathing and/or circulatory problems are possible, as well as urticaria, and hypotension. Skin and/or mucosal changes (typically urticaria and/or angioedema) are seen in around 75% of cases, but importantly these features alone are insufficient for a diagnosis of anaphylaxis.

As soon as possible after successful emergency treatment, timed blood samples should be taken for the mast cell tryptase (MCT) test. Serum samples need to be taken within 1–2 hours but no later than 4 hours from the onset of symptoms. If possible a second paired and timed sample within the same time frame is useful. It is important to document the acute clinical features (record blood pressure, respiratory rate etc) and in particular, the time course of the onset of symptoms/signs and their resolution.

The majority of triggers provoke symptoms within one hour of exposure. Injected agents including medical drugs or bee/wasp venom act most rapidly, with some reactions following foods and oral medicines producing delayed reactions after a couple of hours. Because of the risk of relapse the guidelines recommend that patients should be observed for 6–12 hours after the onset of symptoms. Children younger than 16 years should be admitted and supervised by a hospital paediatrician.

An adrenaline injector device for intramuscular use only, should be prescribed appropriately for body weight as an interim measure before referral to a specialist allergy clinic. Referral to a specialist allergy service (or specialist paediatric service), is strongly recommended. The BSACI website (www.bsaci.org) lists many suitable clinics with contact details. Diagnosis can be confirmed, and further investigations organised not least with a view to identifying or confirming triggers.

Uniphasic reactions are the norm with clinical features peaking at around 30 minutes after the trigger event, and full recovery (either spontaneously or as a result of treatment) within the next 30–60 minutes. Apparently biphasic responses are reported when an apparently fully resolved uniphasic response is followed by relapse without further exposure to the trigger substance.

The only available tests aimed at identifying trigger agents assume an IgE-based mechanism, and therefore are more likely to be helpful when symptom onset is rapid (minutes) rather than delayed (hours). Selection and interpretation of IgE-specific blood testing and/or skin prick testing, is best left to the clinic specialists.

Case 2

Biphasic reaction

A 66-year-old former bee-keeper, with known bee venom hypersensitivity, was stung by a bee on the lower arm. He immediately took two antihistamine tablets and ensured that he had his adrenaline autoinjector to hand. In addition to immediate local swelling and erythema, within 10 minutes the patient noticed his skin and scalp were itchy. He felt weak and faint and needed to lie down.

He decided to use his adrenaline autoinjector and within minutes felt much improved. Nonetheless, he decided to attend hospital (as previously advised) to ensure that nothing else needed to be done. The car journey took approximately 30 minutes.

On arrival at the hospital, he was asked to wait for an available doctor. After a further 30 minutes, he noticed patches of urticaria developing, and his speech was becoming difficult because of marked tongue and throat angioedema. He was rushed into the resuscitation bay where he was given further intramuscular adrenaline, intravenous hydrocortisone, and 100% oxygen by face mask. It was explained that he was having a biphasic reaction and needed to be detained in hospital.

the next 30–60 minutes.

By contrast biphasic responses (see case 2, above) are reported when an apparently fully resolved uniphasic response is followed by relapse without further exposure to the trigger substance. These biphasic reactions are thought to be uncommon but are hard to predict.

Biphasic reactions are managed as for new onset anaphylaxis, often requiring further intramuscular adrenaline injections as appropriate. Biphasic reactions have been documented in children following supervised hospital-based food challenges, and in adults following immunotherapy injections of pollen extract or other allergens.

HOW COMMON IS ANAPHYLAXIS?

Some estimates suggest that as many as 1 in 1,333 of the UK population have experienced anaphylaxis at some point in their lives.⁶ But fatal anaphylaxis in the community setting is, fortunately, extremely rare with only 1 fatal case per 5 million of the UK population per annum.⁷ Note that half of all the fatal cases are related to medicines or other agents within a hospital rather than a community setting.

The question therefore arises, how to reconcile these two numerical estimates. It may be that the former is an overestimate and the latter an underestimate. In part it depends on the definition of anaphylaxis used.

CONFIRMING DIAGNOSIS

Referral to a specialist clinic should take place as soon as possible, ideally within

a few weeks of the acute episode.

Earlier referral (within the first two weeks) may be counterproductive as MCT tests may not have been processed, and though evidence is lacking, there are concerns that IgE-specific blood tests may be less accurate at this time.

‘The diagnosis of anaphylaxis rests largely on presentation with the expected clinical features, rapid onset, and in many, but not all, cases elevated acute MCT levels’

Important background referral details should include details and timings of clinical features (peak expiratory flow, oximetry, blood pressure) both at presentation and after resuscitation. The diagnosis of anaphylaxis rests largely on presentation with the expected clinical features, rapid onset, and in many, but not all, cases elevated »

SPECIAL REPORT

ANAPHYLAXIS FOLLOW-UP

acute MCT levels. Identifying the trigger agent can be difficult.

The only available tests aimed at identifying trigger agents assume an IgE-based mechanism, and therefore are more likely to be helpful when symptom onset is rapid (minutes) rather than delayed (hours). Selection and interpretation of IgE-specific blood testing and/or skin prick testing, is best left to the clinic specialists.

Patients should stop taking antihistamines and/or prednisolone (if possible) several days before clinic attendance to avoid interference with skin prick testing.

ADRENALINE INJECTOR DEVICE TRAINING

It is vital that patients who need to carry an adrenaline injector lifelong, have their training reviewed. Indeed some referred cases may prove not to have had anaphylaxis² and the correct recommendation may be withdrawal of the autoinjector and reassurance. Failure to train patients properly can lead to misuse including unintentional self-injection which is surprisingly common.⁸

At the risk of oversimplification, simple antihistamines, and oral prednisolone tablets should be provided in addition to an adrenaline autoinjector, for mild, moderate, and severe (life-threatening) reactions respectively.

LONG-TERM FOLLOW-UP IN PRIMARY CARE

Once patients have been assessed in a specialist clinic, and provided with a tailored management plan, regular review will be necessary in primary care. Important aspects include ensuring that:

- adrenaline devices are in date
- injection technique refresher sessions are available
- background asthma is well controlled
- any dietary restrictions have not led to an unhealthy diet (e.g. lack of adequate calcium source in patients avoiding dairy products).

CONCLUSION

We know that many anaphylaxis cases are currently not referred to a specialist clinic for review. This specific aspect, and many others, can now be audited against the guidelines. Collection and documentation of presenting features, MCT test results, and clinical outcomes will facilitate research including more accurate data on the frequency of fatal and biphasic reactions.

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Useful information

UK Resuscitation Council
enquiries@resus.org.uk
www.resus.org.uk

Allergy UK
Helpline: 01322 619898
www.allergyuk.org

The Anaphylaxis Campaign
Helpline: 01252 542029
www.anaphylaxis.org.uk

NICE
Copies of the NICE guideline on anaphylaxis (CG134) and the version for patients can be downloaded free from:
www.nice.org.uk

BSACI
Lists specialist allergy services
www.bsaci.org

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