Anaphylaxis (pronounced ana-fill-ax-is) is a severe and potentially life-threatening allergic reaction. The common causes of anaphylaxis include food, insect stings, latex and medicines, but sometimes there may be no obvious trigger for the reaction.

If after medical testing and investigation the cause of the reaction is not found, the reaction is then labelled as ‘idiopathic anaphylaxis’ (which means ‘cause unknown’). This does not necessarily mean the reaction took place without something triggering it; it simply means that no trigger can be identified.

Sometimes it could mean there is an unusual external trigger, such as a rare food allergen for which there is no skin or blood test, or which tests fail to pick up. Sometimes it means there is no external trigger; instead, the cause is a temporary increase in the reactivity of the immune system. This increased reactivity usually clears up within a few weeks or months, although in some cases the condition may take a year or two to settle. A key message in all cases is to visit your GP and ask for a referral to an allergy clinic.

This Factsheet aims to answer some of the questions that you and your family might have if you are diagnosed with idiopathic anaphylaxis. Our aim is to provide information that will help you understand your allergy and minimise risks.

**Symptoms of anaphylaxis**

Mild symptoms may include nettle rash (also known as hives or urticaria) anywhere on the body, or a tingling or itchy feeling in the mouth. There may be lip or face swelling, which is not serious in itself unless any of the more severe symptoms listed below are also present.

More severe symptoms may include:

- Swelling of the throat, tongue or mouth
- Difficulty breathing
- Severe wheezing
- Severe abdominal pain, nausea and vomiting
- Feeling faint, dizzy or sleepy

In extreme cases there could be a dramatic fall in blood pressure (anaphylactic shock). The person may become weak and floppy and may have a sense of impending doom. This may lead to collapse and unconsciousness.
The speed at which life-threatening symptoms occur varies from person to person. Symptoms may begin suddenly and progress quickly.

In general, the first episode of idiopathic anaphylaxis tends to be the most frightening because the person affected has no understanding of what is happening or what to do about it. After that, they may recognise the initial symptoms and act quickly.

**Getting a diagnosis**

It is important to see your GP as soon as possible if you suffer any symptoms that you think may be caused by an allergy. Even mild cases need to be medically assessed because the next reaction, in some cases but not all, could be more severe.

Some GPs have a clear understanding of allergies and similar conditions, but it's more likely your doctor will need to refer you to an allergy clinic. Guidance issued by the National Institute of Health and Care Excellence (NICE) recommends that following emergency treatment for suspected anaphylaxis, people should be offered referral to a specialist allergy service (NICE clinical guideline 134, 2011). Your GP can locate an allergy clinic in your area by visiting the website of the British Society for Allergy and Clinical Immunology (www.bsaci.org).

Once you get a referral, the consultant will discuss your symptoms with you in detail as well as your medical history. The results of skin prick tests and blood tests may help the specialist identify the cause of the problem. If no cause can be found, then the term idiopathic anaphylaxis is used. Sometimes the cause of the first attack may not be obvious but the trigger can become clearer if you experience further attacks.

Food should be considered as a prime suspect. Foods eaten a few minutes before the start of an attack are the most likely culprits. While it is less likely when food was eaten more than an hour before the start of an attack, there are some rare causes where there is a longer delay such as with red-meat allergy (see below; Delayed allergy to red meat).

The most common food triggers are shellfish, fish, peanuts, tree nuts (such as cashews, walnuts or Brazils), milk, eggs and wheat, although many other foods have been known to trigger anaphylaxis. If a particular food is suspected, but skin or blood tests are unexpectedly negative, the consultant may suggest an oral food challenge test to remove this food from the investigation. This is where you eat a very small amount of the suspect food while under medical observation, gradually building up the amount eaten until symptoms occur or it is shown that the food is not the cause of the reaction. This should never be performed at home. There are also situations where a food allergy only causes a reaction if followed by intense exercising (see below; Food plus exercise).
Prescribed drugs, insect stings and latex may also be considered as the cause of the reaction. Any medication taken for years may suddenly cause anaphylaxis. If skin tests are not available for a suspected medication, you may be required to stop taking it for a short time and then take a test dose. This must be done under supervision in hospital.

A diagnosis of idiopathic anaphylaxis should only be made after an extensive medical investigation. This should include a review of all hospitalisation and A&E records.

**Treating symptoms of anaphylaxis**

So that you can treat severe symptoms yourself, your doctor is likely to prescribe injectable adrenaline (also called epinephrine).

The adrenaline auto-injectors prescribed in the UK are EpiPen®, Jext® and Emerade®, which are designed for self-administration. You should be prescribed and carry two adrenaline auto-injectors at all times.

After adrenaline is administered, someone must always dial 999 in case the symptoms return. Guidelines state that you should lie flat with your legs raised (Resuscitation Council UK, 2008 and BSACI 2017), although this is not recommended if there is breathing difficulty, when sitting with arms anchored makes it easier. If you feel as though you may be sick, your head should be turned to one side. If you feel weak or faint, you must lie-down preferably with legs angled above the head.

You will need to know how and when to use your adrenaline injector, so training should be given by a medical professional such as your doctor, local practice nurse or pharmacist. You can also find help on the website relevant to the injector you carry.

- EpiPen®: [www.epipen.co.uk](http://www.epipen.co.uk)
- Jext®: [www.jext.co.uk](http://www.jext.co.uk)
- Emerade®: [www.emerade-bausch.co.uk](http://www.emerade-bausch.co.uk)

Anaphylaxis can progress rapidly and without early warning signs. Watch out for any combination of the following signs and then act fast:

- **Airway**: choking, can’t breathe, tongue or throat swelling, can’t speak clearly
- **Breathing**: unusually wheezy, noisy breathing, shortness of breath
- **Circulation**: pale or clammy skin, weak or rapid pulse, faintness, passing out

Use your adrenaline injector, even if unsure. Adrenaline is very safe for everyone but those with underlying heart disease. Even with underlying heart disease, if there are Airway, Breathing or Circulation symptoms, the risk from untreated anaphylaxis is likely
to be higher than the risk from adrenaline. Some drugs (such as beta-blockers) can interfere with the action of adrenaline, and these drugs are often avoided in patients who carry adrenaline auto-injectors.

If you carry antihistamines for any reason (for example, to treat hay-fever or hives) bear in mind that these cannot be relied upon in cases of anaphylaxis, even if the symptoms are in their early stages and apparently mild. Oral antihistamine treatment delivers no measurable activity within 30 minutes of the dose, and peak activity is not reached for about three hours. Adrenaline injected into the thigh muscle is the first line of defence in the treatment of anaphylaxis.

If you suffer from asthma – especially if it is poorly-controlled – it is likely to increase the severity of an allergic reaction. If you have asthma, go to your GP and request a review of your asthma to ensure that you are using the most effective treatment.

Some cases of idiopathic anaphylaxis have an internal cause – a temporary increase in the reactivity of the immune system. Cases in which attacks are occurring frequently may require a few weeks or months of regular treatment such as a daily oral antihistamine or steroid to prevent further attacks and help the condition to settle down. Anaphylaxis may occur for up to two years before finally burning itself out.

We advise people who have experienced anaphylaxis – whether the cause is known or not – to wear a medical identification bracelet or talisman.

Finally, we believe it is important to let your family, friends or work colleagues know where you keep your adrenaline injector and what needs to happen in an emergency. In the case of children, the school will need a written care plan and staff must be trained in the use of the injector.

A few possible causes

When someone suffers a suspected allergic reaction, they may be tempted to consider one of the common food allergens as the culprit, such as peanut or shellfish. Indeed, this may prove to be the case, either because the allergen was present in the food eaten or because of cross-contamination somewhere in the food production process. However, the cause of the problem may be less obvious. A few possibilities are presented here.

- Lupin: The seeds from some varieties of lupin are milled to make flour, which is used in baked goods such as pastries, pies, pancakes and in pasta. Allergy to lupin has been recognised for some time in mainland Europe, where lupin flour is used fairly commonly in food products. In the UK, cases of lupin allergy are less common because lupin is rarely used in foods. If you suffer an allergic reaction and discover
that lupin was present in a food you have eaten, you might consider this as the possible trigger. By law, lupin must be declared in the ingredients list when present in pre-packed food.

- **Buckwheat:** Buckwheat use is relatively uncommon in the UK and as a result allergy to buckwheat is rare, but can be missed. Buckwheat does not have to be highlighted as an allergen in ingredient lists by UK law. Despite its name, buckwheat is unrelated to wheat. Buckwheat is sometimes used in gluten free foods, some savoury pancakes/crepes and Japanese noodles.

- **Natural Rubber Latex (NRL):** This is found in thousands of everyday products. Reports of allergy to Natural Rubber Latex have become increasingly common over the past 25 years and severe reactions occur quite frequently. Many people associate allergy primarily with food – but latex should be considered as a possible cause if a reaction occurs during an operation, during a medical or dental procedure, or just after handling an item made of soft rubber. Some adhesives used in food packaging contain latex (often known as cold-seal, for example in wrappers around chocolate bars), which may cause confusion in identifying the cause.

- **Flour contaminated by mites:** In 2009 the World Allergy Organisation (WAO) published information on allergy to wheat flour contaminated with mites. The condition is known colloquially as Pancake Syndrome; the medical term is Oral Mite Anaphylaxis. According to the WAO paper, Oral Mite Anaphylaxis occurs shortly after the intake of foods made with mite-contaminated wheat flour. The condition is seen most frequently in tropical or subtropical environments, but cases are occasionally seen in the UK. Reactions have been reported when cereals have been stored for extended periods at home and the sufferer may mistakenly believe the cause was wheat allergy.

- **The oleosins in sesame:** A research team reported that proteins called oleosins, which are major allergens of sesame seeds, accounted for about a third of all cases of sesame allergy among the people they studied. However, because oleosins do not dissolve in water, they cannot be identified by allergy skin or blood tests. Therefore, an allergy could mistakenly be classed as idiopathic when the true cause is sesame seeds. To address this problem, an oral food challenge test may be used for cases where sesame allergy is suspected but cannot be proved.

- **Exercise induced anaphylaxis (EIA):** This is an uncommon condition in which anaphylaxis occurs after physical activity. It is potentially serious for people affected and requires expert diagnosis. If you think you suffer from EIA, the best course of action is to ask your GP to refer you to an NHS allergy clinic. EIA can also
occur in combination with other factors such as a food (see below; More than one trigger?).

- **Cold induced urticaria/anaphylaxis:** In rare cases, anaphylaxis can be caused by cold. For example, a nine-year-old girl suffered urticaria (hives all over her body) and lost consciousness while swimming in cold water. She was immediately removed from the water and regained consciousness. In the previous two years she had experienced urticaria many times while swimming in unheated water. People who suffer from cold urticaria will develop hives when their skin is chilled by cold rain, cold water or cold weather. If you think you suffer from cold urticaria, you may be at risk of cold anaphylaxis and the best course of action is to ask your GP to refer you to an NHS allergy clinic.

- **Delayed allergy to red meat:** A surprising and unexpected cause of anaphylaxis was discovered in the USA. An allergen in red meat can lead to anaphylaxis several hours after being eaten if the affected person has been previously sensitised (sensitisation is the process in which someone becomes allergic to something in the first place). The condition was first identified in certain areas of the USA, although cases are now being identified in other countries including the UK, Europe and South Africa. The allergen is called alpha-gal (galactose-α-1,3-galactose), which is a sugar molecule found in most mammals. Sensitisation occurs when someone is bitten by a certain variety of tick (hence the reason why the condition is concentrated in certain geographical areas). It has been proposed that it arises if the tick has recently feasted on the alpha-gal-containing blood of a farm animal, however, this may not be the case as alpha-gal is present in laboratory bred ticks.

- **Polyethylene Glycol (PEG) allergy:** PEG, also known as macrogol or E1521, is a commonly used bulking and stabilizing agent. It is used in some medications, household products, cosmetics and processed foods. A recent study showed biphasic reactions can occur with PEG allergy, with the first symptoms occurring shortly after exposure followed by a second reaction several hours later. PEG is found in the Pfizer BioNTech and the Moderna covid-19 vaccines. Chapter 14a of the Green Book states: “The Pfizer BioNTech and Moderna mRNA vaccines contain polyethylene glycol (PEG). PEGs (also known as macrogols) are a group of known allergens commonly found in medicines, many household products and cosmetics. Medicines containing PEG include some tablets, laxatives, depot steroid injections, and some bowel preparations used for colonoscopy.” Individuals with a history of idiopathic anaphylaxis should seek the advice of an allergy specialist before proceeding with vaccination.
More than one trigger?

For a small minority of people, anaphylaxis can occur when a combination of factors is present together. This makes diagnosis difficult and without a thorough investigation the symptoms may be classed as idiopathic. Here we give a few examples taken from medical literature.

- **Food plus exercise:** This is called food-dependent, exercise induced anaphylaxis (FDEIA). The symptoms occur when a food is eaten before exercise. Wheat is often the culprit food, although others including shellfish are sometimes implicated. Looking at the available evidence, we believe that anyone diagnosed with FDEIA should avoid physical activity for 12 hours after eating their trigger food. It would be safer to avoid the food altogether even if it is normally not a problem without exercise. There have also been rare reports of symptoms occurring when the food is eaten immediately after exercise.

- **Food plus exercise and/or aspirin:** A research team examined a patient with a history of FDEIA related to eating wheat before exercise. They found that he also suffered a reaction when aspirin was taken before eating wheat – even without exercising. The combination of aspirin, wheat and exercise triggered symptoms that were even more severe, but wheat alone did not trigger symptoms. The same report describes the case of an 18-year-old man with FDEIA who suffered symptoms with a combination of aspirin, shrimp and exercise. In other cases ibuprofen and other non-steroidal anti-inflammatory drugs (NSAIDs) may act as the responsible co-factor.

- **Exercise and exposure to cold:** Researchers reported on a 16-year-old Japanese boy who had a four-year history of allergic reactions when he exercised in winter. Tests showed it was the combination of cold and strenuous exercise that triggered the symptoms. Food was not thought to be a factor in this case.

- **Cereal mites with exercise:** A 17-year-old boy suffered anaphylaxis while jogging after having eaten a Japanese pancake. The pancake mix, which had been stored for several months after the package had been opened, was examined under a microscope, and live mites were discovered. The researchers concluded that it was a combination of eating the mites and exercise that caused the symptoms. One of our medical advisers tells us he saw the case of a boy who exercised in the snow after eating a breakfast cereal from a packet which had been open for many months. The boy suffered a severe anaphylactic reaction.
• Intolerance to non-steroidal anti-inflammatory drugs (NSAIDS): Painkillers such as aspirin and ibuprofen should also be regarded as a possibility when the cause of an allergic reaction is a mystery.

Diseases that mimic anaphylaxis

• Angioedema: In angioedema, there are recurring episodes of painless swelling that may involve the lips, face (especially around the eyes) tongue, upper airway or anywhere in the body. In many cases no cause for these symptoms can be identified and the attacks stop happening after a few weeks or months. When attacks are persistent, the most common identifiable cause is a side-effect of ACE inhibitors, which are prescribed to treat blood pressure problems. According to research, this treatment sometimes causes angioedema in about 1 person in 300 who takes it. As the attacks may not start for several months or years after the treatment has begun, this possibility may be overlooked.

Note that although angioedema is a condition in its own right, it can also occur during anaphylaxis and with other conditions such as spontaneous urticaria.

• Hereditary angioedema: is a rare, inherited, non-allergic form of angioedema. In addition to external swelling, there may also be stomach cramps, abdominal pain, nausea and diarrhoea. The episodes may follow localised injury such as dental work. The angioedema (swelling) tends to be painful and slow in onset. This disorder can be differentiated from non-inherited angioedema and anaphylaxis by blood test findings and the lack of other symptoms of anaphylaxis. There are very specific and effective treatments for this condition and therefore accurate diagnosis is vital.

• Spontaneous urticaria: Urticaria (commonly called hives) can occur as part of an allergic reaction, but can also occur when there is no allergy present. Non-allergic urticaria is called spontaneous urticaria and affects 10-20% of people at some point in their lives, and if it persists for more than 6 weeks is known as chronic spontaneous urticaria. Up to 50% of people with spontaneous urticaria, will also have angioedema (swellings) with an attack. However, airway, breathing, circulatory and abdominal symptoms are not features of spontaneous urticaria.

• Histamine poisoning: Histamine can sometimes be present in spoiled fish (especially tuna and mackerel) and can cause similar symptoms to allergy called scombroid poisoning. Unlike an allergy, this usually affects everyone who has eaten the offending food, although some people might be more susceptible than others.
Mastocytosis: This is a rare condition caused by too many ‘mast cells’ gathering in the tissues of the body. These are the cells that release histamine and other chemicals involved in allergic reactions, causing symptoms such as a skin rash, itchy skin and anaphylaxis. The condition is diagnosed by a special blood test, and it is standard medical practice to offer this blood test to any patient who is suffering from unexplained anaphylaxis.

Tips and advice

If you suffer allergy-like symptoms but the cause is a mystery, keep a detailed account of your experience. Important points to note down are:

- Where you were at the time of the reaction
- The time of day
- What you had eaten or drunk within the hours leading up to the reaction
- Whether you had taken a painkiller or other medication within a few hours before the reaction
- Whether you were taking a medication known to be associated with allergic reactions
- Your general state of health
- Whether you were particularly hot, cold or stressed
- Whether you had been exercising at the time of the reactions or just before

All these details might help to build a picture of the problem and possibly identify a common thread.

Some other things to consider

- Do you suspect that a food is responsible? If so, try to get a detailed list of the ingredients of any foods, sweets or snacks eaten within the hour before the reactions.
- If a takeaway or restaurant meal is suspected, it will help your doctor find a cause for the reaction if you obtain a full list of the ingredients.
- Have you considered latex as a possible trigger? Itchy or swollen lips after attempting to blow-up a balloon is a common sign.
- Have you considered a medication as a possible trigger?

Feedback

Please help us to improve our information resources by sending us your feedback at: -

https://www.anaphylaxis.org.uk/information-resources-feedback/
Sources

All the information we produce is evidence-based or follows expert opinion and is checked by our clinical and research reviewers. If you wish to know the sources we used in producing any of our information products, please contact info@anaphylaxis.org.uk and we will gladly supply details.

Reviewers

The content of this Factsheet has been Peer Reviewed by Prof John Warner, Emeritus Professor of Paediatrics National Heart and Lung Institute, Imperial College London; Hon Professor University of Cape Town; and Dr Tariq El-Shanawany, Consultant Clinical Immunologist, University Hospital of Wales.

Disclosures

We are not aware of any conflicts of interest in relation to the review of this Factsheet.

Disclaimer

The information provided in this Factsheet is given in good faith. Every effort has been taken to ensure accuracy. All patients are different, and specific cases need specific advice. There is no substitute for good medical advice provided by a medical professional.

About Anaphylaxis UK

Anaphylaxis UK is the only UK-wide charity solely focused on supporting people at risk of serious, life-threatening allergic reactions. We provide information and support to people living with allergies through our free national helpline and local support groups. We also campaign and fundraise to achieve our ultimate aim, to create a safer environment for all people at risk of serious allergies. Visit our website www.anaphylaxis.org.uk and follow us to keep up-to-date with our latest news. We're on Facebook @anaphylaxixUK, LinkedIn, Instagram @anaphylaxisUK, Twitter @AnaphylaxisUK and YouTube.