

## Angioedema

**Angioedema is a condition in which small blood vessels leak fluid into the tissues, causing swelling. There is no known cure, but it may be possible to prevent the swelling with medications or occasionally diet. Allergy is a very rare cause of angioedema.**

### How common is angioedema?

Angioedema is not rare. Around 1 in 10 people will develop urticaria (hives) at some time in their life and around 1 in 3 of these will have angioedema as well. Having angioedema on its own (without urticaria) is much less common.

Angioedema eventually disappears in most people. It may reappear following infection, when under stress or for no particular reason that can be identified. Occasionally it is a recurrent problem that reappears throughout life.

### Where does angioedema occur?

The most common areas of the body involved are the face, lips, tongue, throat and genital areas, but anywhere in the body can swell. Swelling in one area usually lasts between 1 and 3 days. Occasionally, swelling of internal organs like the oesophagus or stomach can trigger chest or stomach pains as well.

Angioedema may be itchy, tingling, or burning but often there are no symptoms other than the discomfort of the swelling. Sometimes the swelling can be painful, particularly when it occurs over joints. These swellings can be very big and may last for days.

### How is angioedema different to urticaria (hives)?

Weal like swellings on the surface of the skin are called urticaria (hives). Angioedema involves deeper swellings, affecting even the dermis in the skin. Unlike urticaria, angioedema usually requires urgent medical treatment.

### Angioedema can occur alone, or with urticaria (hives)

There are 3 major patterns of angioedema:

- Angioedema plus urticaria: the hives itch, and the angioedema is itchy or hot or painful.
- Angioedema alone: itchy/hot/red swellings, often very big and uncomfortable.
- Angioedema alone: skin-coloured swellings, not itchy or burning, often unresponsive to antihistamines.

### Is angioedema dangerous?

Angioedema does not damage internal organs like kidneys, liver or lungs. The only danger is if the throat or the tongue swell severely. Since this can cause difficulty breathing, it is a symptom that needs to be taken seriously. Severe throat swelling requires early use of medication and transfer to hospital or your doctor.

Swelling that interferes with breathing is uncommon even in those with recurrent angioedema. Swelling on the outside of the neck is uncomfortable but does not affect breathing.

### Should I see a specialist?

All people with recurrent angioedema should be referred by their doctor to a medical specialist (Allergist / Clinical Immunologist) to look for an underlying cause and optimise treatment. Although angioedema is seldom caused by a serious underlying disease, nor does it make you sick or cause damage to organs such as kidneys, liver or lungs, further investigation will normally be required.

### When to suspect an allergic cause

Allergic causes for isolated angioedema are rare but should be suspected with short-lived episodes of swelling that occur under similar circumstances, such as after taking certain foods or medicines. Allergy to foods or drugs usually causes urticaria (hives) or itching as well as angioedema at the same time.

### Causes of angioedema

- **ACE (angiotensin converting enzyme)inhibitor medicines** In around 1/200 people who take these heart and blood pressure tablets, swellings will start to appear within the first few months of treatment, but sometimes the onset can be delayed for months to years. Sometimes angioedema only appears when the dose is increased. Why some people seem to get swellings and others don't is not totally clear, but simply switching to another brand or type of ACE inhibitor doesn't seem to help. The swellings from these medicines are not itchy or painful, usually occur around the face, tongue and throat and are not accompanied by urticaria (hives). Strictly speaking, these are not allergic reactions and can't be proven by any skin or blood allergy test. In patients with angioedema who take ACE inhibitors, the medicines are usually blamed. If the drugs are stopped, and the symptoms settle, the diagnosis is considered confirmed.
- **Hereditary angioedema (HAE)** This is a rare condition, which occurs in around 1 in 75,000 people. It is characterised by low levels of an enzyme (C 1 esterase inhibitor) that helps keep blood vessels stable and stops leakage of fluid into the tissues. Often the face, tongue and throat are involved, and like those triggered by ACE inhibitors, the swellings are not itchy or painful, and normally skin coloured. Internal swelling is relatively common, resulting in admission to hospital with severe stomach or chest pains without external swelling at the same time. Episodes can be triggered by emotional stress, alcohol, hormonal changes or trauma (such as dental surgery). HAE can be detected on blood testing, and while called "hereditary" due to genetic changes that can be detected, an individual's problem can arise from a genetic change in them that was not present in their parents. That is, they can be the first of their generation to have the condition. This condition usually presents quite young in life (adolescence rather than in infancy), but presentation can also be delayed. It is important to note that HAE is not associated with urticaria (hives), but sometimes a red circular rash can occur.
- **Acquired C 1 esterase inhibitor deficiency** The same enzyme can sometimes be very low in people with some types of cancer called lymphoma, and in some types of autoimmune disease such as Systemic Lupus Erythematosus (SLE). The swellings are much the same as that described above.
- **Infection** is one of the most common causes of urticaria (hives) and angioedema, particularly in young infants.
- **Food or drug allergy** is usually severe, dramatic and resolves within 24 hours, although exceptions occur.
- **Other causes** Thyroid gland disease and some types of inflammatory arthritis are more common in people with urticaria (hives) and angioedema. In some people whose swellings persist for years without an obvious cause, an autoimmune process may be responsible. This means that part of the body's immune system may be attacking the skin. Unfortunately, in the vast majority of cases, a cause is rarely found. Angioedema can be associated with nasty symptoms, but *rarely* with nasty underlying disease.

Generally, when someone has recurrent swellings for days or weeks at a time, the cause is almost never allergic.

### What makes angioedema worse?

Common aggravating factors include heat, hormonal changes of the menstrual cycle, emotional stress, medications (such as aspirin) or occasionally dietary factors such as alcohol, spicy food, food additives/colours and some naturally occurring substances within food. Stress is an aggravating factor rather than cause in most cases.

### Swellings that can look like angioedema

- **Contact allergy** (such as from animals or plants) is usually localised to the site of direct contact and is often itchy, short-lived, does not cause internal swelling and causes blistering rashes that weep and peel after a few days.
- **Animal allergy** can cause itchy urticaria (hives) and angioedema, but is almost always accompanied by severe allergic rhinitis (hay fever) and/or asthma.
- **Insect stings** from bees, wasps and some ants can cause severe local reactions, but these are usually transient and obvious.
- **Palindromic rheumatoid arthritis.** This can cause transient swellings lasting a few days at a time, usually over joints and mainly affecting the limbs. Swellings are usually painful and hot rather than itchy. Some of those affected will eventually go on to develop rheumatoid arthritis.

### Aspirin, painkillers and angioedema

If you are allergic to aspirin or similar painkillers, then taking a tablet may trigger swelling. Even if you are not allergic to aspirin or similar painkillers, around 1 in 3 people who already have angioedema, will quickly have their swellings made much worse if they take aspirin. It is therefore better to take paracetamol instead for pain. If you are already on aspirin regularly and without symptoms then there is no need to stop taking it.

### Why do tests?

The main reason is to exclude underlying diseases, which may appear as angioedema *first* and other conditions *later*. These conditions might need separate treatment or investigation. That is why a physical examination is also carried out in patients who have angioedema as well as blood tests, to exclude rare conditions as a cause. In most cases, test results are normal.

### How long does angioedema last?

This depends on the cause. If a treatable cause is found or if the cause is an ACE-inhibitor which is stopped, then the episodes of swelling should cease. If no cause is found, the swellings may stop after a few weeks or months or may continue for years, and it is not possible to predict when it will go away.

### Management of angioedema

1. **Do tests to confirm or exclude an underlying cause.** This is important but in most cases test results are normal.
2. **Time may be the healer.** Some people only have a single episode whereas others suffer from recurrent bouts which eventually stop for no apparent reason.
3. **Avoid aggravating factors.** Non-specific measures such as avoiding excessive heat, spicy foods or alcohol are often useful. Since Aspirin can make swellings worse, it should be avoided.

- 4. Antihistamines are the mainstays of treatment.** The release of histamine within the skin seems to be the trigger for swelling in most people. Antihistamines block this effect. Since they take 1-2 hours to help, it is often better to take them preventatively rather than as needed. The aim is to stop the episodes of swelling, or to make them less frequent or less severe. In people with severe angioedema, it is often better to take them every day, stopping every month or two to see if they are needed and restarting them if they are. *Different* people respond best to different antihistamines, and therefore you will be the one to decide which drug works best for you. Non-drowsy antihistamines are available over the counter without prescription. Unfortunately, these are less effective for angioedema than for urticaria (hives), and are often totally ineffective for the non-itchy angioedema, in which histamine appears to play no significant role.
- 5. Other medications.** Because the likelihood of side effects is greater, other drugs are usually reserved for when antihistamines fail to prevent angioedema, and are generally given under specialist supervision. Examples include corticosteroid tablets (e.g prednisolone or prednisone), but there are many others such as danazol or tranexamic acid. These types of medicines are more likely to be needed in people with frequent non-itchy swellings and in those with the C1 inhibitor deficiency (whether inherited or acquired). Pure C1 inhibitor enzyme concentrate has also recently become available and is used to manage those with this enzyme deficiency. Finally, adrenaline by injection (EpiPen or Anapen adrenaline autoinjectors) may be needed to treat severe episodes of tongue and throat swelling. They are not currently subsidised on the PBS for this condition.
- 6. Elimination diets.** If angioedema episodes have been continuing for more than a few months and are reasonably frequent, for example several per month, you may be advised by your doctor to try an elimination diet under the supervision of a dietitian, to remove some artificial chemicals, preservatives as well as some natural substances (eg. salicylates) from your diet. In some patients, this may reduce or eliminate the episodes of angioedema. This is based on the principle that food intolerance may be triggering or worsening the angioedema. There is no test for food intolerance that can predict whether the diet is likely to work.

### Diet, food allergy and food intolerance in people with angioedema

Food allergy reactions are usually severe, dramatic and often associated with symptoms like trouble breathing, a drop in blood pressure, stomach upset and itchy urticaria (hives) as well as angioedema. Symptoms usually occur within 1 or 2 hours of eating the offending food and disappear within 12 to 24 hours. Allergy tests can be useful for this type of reaction, but it is important to note that food allergy is a very rare cause for isolated angioedema. Food intolerance (not the same as food allergy) can be an underlying factor in some people with recurrent angioedema (see "elimination diet" section above).

### Drugs during Pregnancy and Breast feeding

#### Pregnancy

Treatment of angioedema, like other allergic conditions, is complicated in pregnancy and medical advice should always be sought. Antihistamines thought to be safe generally cause sedation. Other medicines are usually avoided where possible.

#### Breastfeeding

There are few studies examining the use of medicines for treating angioedema and their effect on breastfed infants, particularly with the newer medications. Some antihistamines may cause short term irritability or sedation in breastfed infants, in the same way that they can in adults. Periacin and Polaramine have been used for many years without reports of ill effect. There is no evidence that taking antihistamines will diminish milk supply. Medical advice should always be sought.

## Heart tablets and Urticaria/Angioedema

ACE (angiotensin converting enzyme) inhibitors and Beta-blockers are used to treat high blood pressure and heart failure. They may need to be avoided in patients with recurrent and severe throat or tongue swelling, even if they are not considered to be the cause. Current opinion is that using these medicines may make severity a lot worse.

### © ASCIA 2015

The Australasian Society of Clinical Immunology and Allergy (ASCIA) is the peak professional body of clinical immunology and allergy specialists in Australia and New Zealand.

Website: [www.allergy.org.au](http://www.allergy.org.au)

Email: [projects@allergy.org.au](mailto:projects@allergy.org.au)

Postal address: PO Box 450 Balgowlah, NSW Australia 2093

### Disclaimer

This document has been developed and peer reviewed by ASCIA members and is based on expert opinion and the available published literature at the time of review. Information contained in this document is not intended to replace medical advice and any questions regarding a medical diagnosis or treatment should be directed to a medical practitioner. The development of this document is not funded by any commercial sources and is not influenced by commercial organisations.

**Content last updated January 2010**