**Angio-oedema**

Episodes of angio-oedema cause swelling of deeper skin tissues, most commonly around the eyes and mouth. Sometimes the tongue and throat are affected which may affect breathing. Other parts of the body such as hands, feet and genital areas may be affected less commonly. There are various causes. Some people have recurring episodes. Each episode usually clears within a few days. Antihistamines and steroid tablets ease symptoms in many cases. If your breathing is affected then go straight to your local accident and emergency department or call for an ambulance urgently.

**What is angio-oedema?**

Angio-oedema is a condition that can cause swelling of:

- The deeper layers of the skin - these are called the dermis and subcutaneous tissues.
- The tissues just under the lining of the airways, mouth and gut - these are called the submucosal tissues.

The swelling of angio-oedema occurs when certain chemicals are released in the body which cause the tiny blood vessels in the affected tissues to become leaky. The chemicals usually involved are called histamine and bradykinin. These chemicals affect the cells lining the small blood vessels. Fluid then leaks out of these small blood vessels into the surrounding areas, which makes them swell. The swelling can occur under any part of the skin or submucosal tissues. However, it commonly affects the eyelids, lips, genitals, hands and feet.

Sometimes the tongue, throat and airway are affected and become swollen. The swelling sometimes becomes bad enough to cause difficulty with breathing. Occasionally the tissues lining parts of the gut are affected. This causes swelling of the lining of the gut which gives you tummy pains and cramps.

**What causes angio-oedema?**

There are a number of different possible causes of angio-oedema. The cause will affect the symptoms and the treatment.

**Idiopathic angio-oedema**

In many cases there is no known cause and it is not clear why it occurs. This is called idiopathic angio-oedema. In up to half of cases there is a link to an autoimmune disorder. Autoimmune disorders are conditions where your body's own immune system over-reacts and causes damage. Examples of conditions which may be linked to idiopathic angio-oedema include:

- Chronic hives (urticaria). About half of people who have chronic urticaria also have regular episodes of angio-oedema.
- Systemic lupus erythematosus (SLE).
- Thyroiditis (hypo thyroidism).
Allergic reactions
Some people develop angio-oedema as part of an allergic reaction. Something triggers the immune system, which triggers mast cells in the skin to release histamine. For example:

- Allergy to foods - for example, nuts, shellfish, milk, eggs.
- Allergy to medicines - for example, penicillin, aspirin.
- Allergy to latex
- Allergy to insect bites or stings.

The symptoms that may develop with an allergic reaction can vary. For example:

- Some people develop weals (hives) - an urticarial rash.
- Some people develop angio-oedema.
- Some people develop an urticarial rash and angio-oedema.
- Some people develop a very severe reaction called anaphylaxis. This usually includes an urticarial rash, angio-oedema, and other symptoms. Other symptoms may be dangerous, such as low blood pressure, severe breathing problems, and collapse. Anaphylaxis is rare but is the most serious type of allergic reaction and can be fatal unless promptly treated.
- Various other symptoms can develop to localised allergies. For example, nasal symptoms if you have hay fever (are allergic to pollen), etc.

Non-allergic reaction to a medicine
Some medicines can cause angio-oedema as a side-effect. Medicines for high blood pressure or heart problems, particularly angiotensin-converting enzyme (ACE) inhibitors, are known to do this. This is caused by the release of the chemical bradykinin rather than histamine.

Hereditary angio-oedema
Some people inherit a tendency to develop episodes of angio-oedema. This is due to a lack of a blood protein called C1 esterase inhibitor. The lack of this protein results in too much bradykinin, which in turn can cause angio-oedema when triggered. This condition is called hereditary C1 esterase deficiency. There are three different types of hereditary angio-oedema.

About 1 person in 50,000 inherits the gene for C1 esterase deficiency. Half the children born to people with this condition will inherit the condition. Although it is hereditary and most cases first develop in childhood, in some cases the angio-oedema first develops in early adulthood.

Acquired C1 esterase inhibitor deficiency
People with angio-oedema due to acquired C1 esterase inhibitor deficiency have similar symptoms to those with the hereditary condition. Symptoms are due to excess bradykinin, but they develop the condition rather than inheriting it. In some cases this is due to a type of cancer called a lymphoma. In others it is due to a different condition called systemic lupus erythematosus (SLE).

How common is angio-oedema?
The number of people affected by angio-oedema is not known. However, it is thought that fewer than 1 in 10 people have some episode in their lifetime. Women are affected more often than men. It can occur at any age. However, it most commonly affects people aged 40-60 years (apart from hereditary angio-oedema, which often develops in children). Hereditary angio-oedema is rare (around 1 in 50,000 people as described above.)
What are the symptoms of angio-oedema?

Symptoms of each episode develop quickly, over minutes or hours.

A typical episode is as follows:

- Areas of the skin become more and more swollen. Most commonly this affects the eyelids, lips, genitalia, hands and feet.
- The surface of the skin may appear normal - it is the tissues just beneath the skin that swell.
- The swellings are often more painful than itchy.
- An itchy urticarial rash often develops at the same time on various parts of the body. See separate leaflets called Acute Urticaria and Chronic Urticaria for more details.
- The swelling takes up to 72 hours to ease and to go.

In some cases, in addition to the above:

- You may become short of breath, wheezy and have difficulty breathing due to swelling of the lining of throat, main airway, tongue and mouth.
- You may develop tummy (abdominal) pain with being sick (vomiting) or diarrhoea.
- Occasionally, angio-oedema is part of a more severe anaphylactic episode (described above).

Hereditary angio-oedema

- Typically, this causes recurring episodes. In most cases there are one or more episodes per month. These can occur for no apparent reason; however, episodes may be triggered by events such as:
  - Stress.
  - Injury.
  - Infections.
  - Minor operations and dental surgery.
  - Exercise.
  - Periods or pregnancy.

  - Swellings commonly affect the hands or feet and are painless.
  - There are no weals (hives) on the skin (urticaria).
  - There may be involvement of the throat, tongue or airway, with some degree of wheezing or breathing difficulty.
  - Tummy pain is common.
  - Episodes last for 1-4 days.

Do I need any tests?

The diagnosis of angio-oedema is usually apparent when a doctor examines you and no tests are needed. However, tests to determine the cause may well be required. Possible tests include:

- Skin prick tests for allergy.
- Blood tests to exclude other conditions which might be causing the symptoms.
- Blood tests for other autoimmune conditions (for example, tests to check the thyroid gland).
- Blood tests to see if you have a lack of C1 esterase inhibitor.
- Having a sample of skin taken (a biopsy) to send for examination in the laboratory.

What is the treatment for angio-oedema?

Treating each episode

The most important thing is to determine whether an episode of angio-oedema affects breathing, or if it is part of an anaphylactic episode.
If breathing is affected or if you have any symptoms of anaphylaxis:

- You should go straight to your local casualty (accident and emergency department) or call for an ambulance urgently.
- You may be given adrenaline (epinephrine) by injection, a course of antihistamines, and a short course of steroids. These help to prevent symptoms from getting worse, and help to clear the symptoms more quickly than they would do naturally.
- If your angio-oedema is not caused by histamine (for example, if you have hereditary angio-oedema) the above treatments do not work. If this is the case you may be given other treatments such as:
  - Treatment through your veins of the blood protein you are missing (C1 esterase inhibitor such as conestat alfa, Cinryze® or Berinert®).
  - An injection of a medicine which blocks bradykinin, such as icatibant.
- You will be observed until the symptoms subside.
- Help with breathing, and intensive care, may be needed in severe cases.

If breathing is not affected and you feel otherwise OK:

- You may be advised to take a short course of antihistamines and steroid tablets. These help to prevent symptoms from getting worse and help to clear the symptoms more quickly than they would do naturally.
- Most episodes of angio-oedema will clear away within a few days.
- A cool shower or a cold compress on the affected area may ease symptoms.
- If your skin is itchy it is best to try not to scratch, as it may damage the skin. If necessary, rubbing itchy skin with the palms of your hands is better than scratching. Choose clothing that does not irritate the skin. Consider whether any skin creams, soaps, or detergents are making symptoms worse.
- If symptoms get worse and breathing does become affected then go straight to your local casualty (accident and emergency department) or call for an ambulance urgently.

Follow-up and general advice

Most people who have an episode of simple angio-oedema can be safely managed by their GP. More complex cases can be referred to a specialist. This will be an allergy specialist (immunologist) or a skin specialist (dermatologist). This is to confirm the diagnosis and, where possible, to identify a cause. The severity of one episode compared with another is unpredictable. So, if you do have an allergy to something, it is best to be aware of what the allergy is. Those with hereditary angio-oedema will be referred to a specialist centre for that condition as it is so rare.

The specialist will also advise on such things as:

- Whether it is likely to happen again.
- What to do if it does happen again.
- Whether you should carry an injection of adrenaline (epinephrine) with you at all times in case you have a severe episode.
- Avoiding the cause, if you are diagnosed as having an allergy.
- Taking regular tablets such as antihistamines to prevent symptoms.
- Alternative treatments for the types of angio-oedema which do not get better with antihistamines and steroids. This is commonly the case with hereditary, ACE inhibitor and autoimmune angio-oedema. The specialist will be able to prescribe alternative treatments and advise on what to do if minor surgery or a dental operation is needed.

It is advisable to carry a wallet-sized management card that:

- Briefly explains your diagnosis
- Explains the best treatment for your acute attacks
- Provides contact information for the specialist looking after you

What is the outlook (prognosis)?

- For sudden episodes of allergic angio-oedema: In most cases they are not severe or life-threatening and will usually clear in 1-3 days. However, recurrences are common and the severity of each episode can vary. Some episodes are severe and life-threatening, especially if the angio-oedema is part of an anaphylactic episode.
- If your angio-oedema is due to a non-allergic reaction to a medicine, then the episodes of angio-oedema can get more severe if the medicine is not stopped.
- Idiopathic angio-oedema often has a waxing and waning course. The severity of each episode can vary. If you have chronic hives (urticaria) then treatment for this may help to prevent some episodes of angio-oedema.
- Hereditary angio-oedema can vary in severity.

Further reading & references

- BSACI guideline for the management of chronic urticaria and angioedema; British Society for Allergy and Clinical Immunology (Feb 2015)
- Angio-oedema and anaphylaxis; NICE CKS, June 2014 (UK access only)
- Urticaria; NICE CKS, May 2016 (UK access only)

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