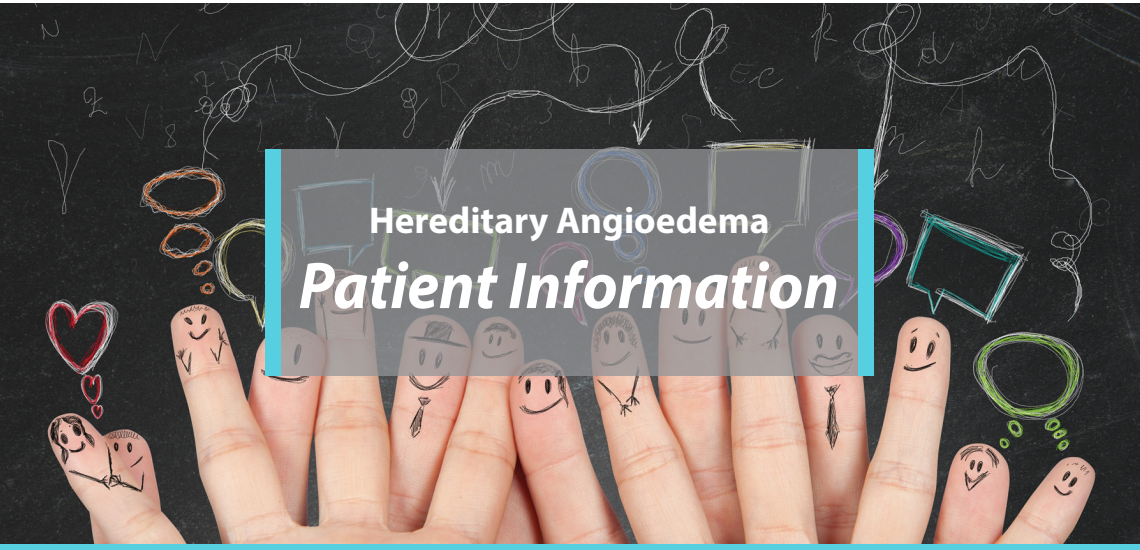
HAEUK
Living for today....
Planning for tomorrow.



Hereditary Angioedema
Patient Information

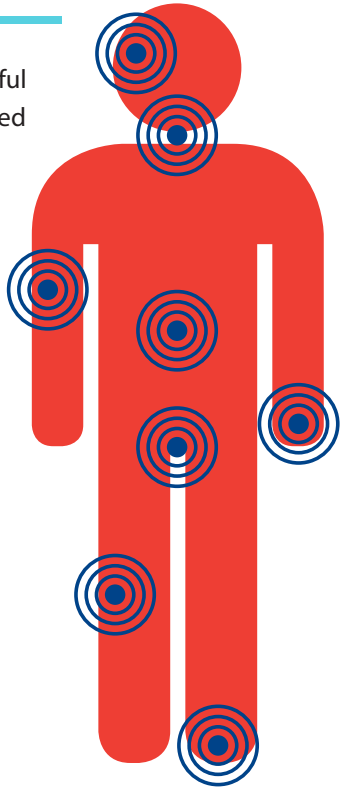
Hereditary Angioedema (HAE) is a very rare genetic (inherited) condition. It affects between 1:20,000 and 1:50,000 people. There is a 50% chance of an affected parent passing the gene onto their children, but it cannot 'skip' a generation. HAE affects both men and women.

The gene affected controls production of a blood plasma protein called C1 Esterase Inhibitor, or C1-INH for short. C1-INH in turn controls **Bradykinin** which causes fluid from capillary vessels to flood into subcutaneous (below the skin) cells. If there is a fault in the production of C1-INH this swelling goes uncontrolled and can reach enormous size in a short time. Any area of the body can be affected, but most common are hands, feet, limbs, genitals, face, tongue and throat. Abdominal swellings also occur frequently and are very painful, causing nausea and vomiting and often leading to mistaken diagnosis such as appendicitis or irritable bowel syndrome. **Swellings in the mouth, tongue and throat are particularly dangerous as they can obstruct the airways, sadly sometimes fatally**.

Most people with HAE will know of a family history of unexplained swellings even if not a firm diagnosis. However it is possible for the gene to mutate spontaneously, and this can occur in up to 15% of cases.

There are also cases of **Acquired C1-Inhibitor deficiency or AAE** which result from an underlying condition such as lymphoma or use of ACE inhibitors.

Symptoms of Hereditary Angioedema



- Sudden unexplained swellings, no hives. Can be very painful
- Recurrent, unexplained abdominal pain, often accompanied with swellings elsewhere
- Often more than one 'site' affected
- Symptoms can be mild for a long time, then suddenly a severe one with no warning
- Tend to get worse with puberty, pregnancy, contraceptive pill
- No specific 'triggers' for attacks
- Lack of response to anti-histamines or steroids

Hereditary Angioedema is divided into four categories:

- **Type 1** - Low levels or absence of C1-INH
- **Type II** - C1-INH is present but has very low activity
- **Hereditary angioedema with normal C1-INH** (formally called Type III) - C1-INH is present and active. Possible cause is sudden surges in bradykinin production. Predominantly in women, some cases are associated with a defect in the gene controlling FXII coagulation factor.
- **Acquired C1-Inhibitor Deficiency**

Diagnosis of Hereditary Angioedema – Types I and II

- Family history
- Symptoms
- Testing
- Genetic testing

Testing is usually a simple blood test for C4 levels. This is usually low if C1-INH levels are low. This is then followed by testing of C1-INH levels and activity.

If results show HAE, it is wise for all family members to be tested. Genetic testing is available and becoming more commonly used.

Other forms of Hereditary Angioedema

HAE with normal C1-INH is generally diagnosed by clinical presentation, although now testing for FXII involvement is available. Where there is no positive genetic test and angioedema, it can be difficult to make an accurate diagnosis of the case. You can also can test for kininogenase activity.
Acquired C1-Inhibitor Deficiency is diagnosed from clinical presentation, also testing for C1-INH levels, measurement of C1q and testing for anti C1-INH autoantibodies.

Treatment of Hereditary Angioedema

Once diagnosed, a treatment plan should be agreed with your consultant and care team. Depending on the severity and frequency of your attacks, treatment could be:

- No preventative medication, but a treatment plan in place for possible severe attacks.
- Attenuated androgens (such as Danazol or Oxandrolone) - these are oral tablets taken to prevent attacks, they can work well for many people but some people find unacceptable side effects. You should discuss this with your care team and possibly switch to a lower dose or another type of androgen. There should also be a plan in place for a possible severe attack.
- Tranexamic Acid - This is an oral medication which works well for some people. This type of medication can be used for children.
- Icatibant (Firazyr) - This medication comes in a pre-filled syringe and is injected subcutaneously (under the skin). Icatibant acts to prevent bradykinin production and must be used as soon as an attack is suspected. It also has a short 'half-life' and so a follow up injection may be needed after 6 hours if swelling starts again. Icatibant can also be used for children over the age of two years.
- C1-INH concentrate (Berinert, Cinryze, Ruconest) - The first two are human plasma derived, the third is a human plasma-free therapy. All three are powder which has to be reconstituted in order to be administered as a slow intravenous injection (into the vein). These medications act to replace the missing or non-functioning C1-INH and therefore controls not only the bradykinin production but also controls the entire Hereditary Angioedema cascade. Administration as early as possible in an attack will prevent swellings getting too large.

Remember - Icatibant and C1-INH both act to stop the swelling, but they do not make swellings reduce, this will be done by the body's own circulation. Therefore it is important to **inject sooner rather than later!**

There are NHS guidelines for management of severe attacks of Hereditary Angioedema and also for use of C1-INH prophylaxis. Prophylaxis is the use of treatment to prevent attacks. C1-INH can be used in this way and there is also a new medication called Lanadelumab (Takhzyro).

Lanadelumab is licenced for those over 12 years of age and is a fortnightly subcutaneous injection of a product that works to control kallikrein (a precursor of bradykinin), thereby controlling bradykinin. Clinical trials show it to be effective in reducing the number of attacks and some patients are able to reduce the dose to one syringe per month. It is not a medication for acute attacks and breakthrough attacks must be treated with other products as advised by the Immunologist.

There are new products under development all the time, that will enable people with HAE to have more convenient control of their symptoms and lead even better lives.

A diagnosis of HAE does not mean you cannot lead a good quality of life. Good planning and sensible precautions will enable you to live life to the full.

Prevention of attacks

Some people who have very frequent attacks have various warning signs ('prodromal' symptoms) that can indicate an impending attack. Occasionally this can be a non-itchy 'chicken wire' type rash, a feeling of depression and extreme tiredness, bad temper and a heavy feeling in the limbs.

Whilst HAE does not have regular 'triggers' like an allergy (e.g. peanuts) there are some things that can cause an attack or make an existing attack worse. These can be:

- Stress - including 'happy stress' like parties, events and celebrations
- Minor trauma
- Repetitive actions (for example peeling potatoes or painting)
- Hormonal changes (puberty, contraception, HRT, pregnancy)
- Minor infections (teeth, abscesses etc)
- Surgical and dental interventions (these should be planned for and prophylactic treatment/C1-INH administered before minor surgery, tooth extraction etc)
- Some prescription or over the counter drugs, such as ACE inhibitors or ibuprofen

Children

The gene for HAE is an 'autosomal dominant'. This means that usually most children will have a parent with HAE; they have a 50% chance of inheriting the faulty gene. However, in a few there is no family history; a 'spontaneous mutation'

If there is a family history of HAE and one (or more) parent is affected, it is wise to discuss children as early as possible with your immunologist so that you can be tested and, if needed, have a care plan put in place in case of swellings.

Testing children

In the majority of children blood tests after 3 months of age can accurately confirm or refute if your child has HAE. As children rarely have any swellings in the first years of life and C3, C4 and C1 esterase levels can vary, waiting until at least 1 year old is best.

Cord blood; genetic testing can be carried out; but only if the parent's genetic defect is known.

Symptoms in children

Young children often do not exhibit symptoms but it is important to be alert for signs of an attack as soon as possible. Avoiding triggers can be helpful, but there are some common triggers such as teeth (infected or erupting teeth, dental treatment such as extractions and fillings) minor injuries, childhood illnesses, puberty and stress such as exams, changing school which cannot be avoided and could trigger an attack. Attacks tend to become more frequent with the onset of hormonal changes at puberty especially in girls.

Treatments for children

The only oral treatment for children is tranexamic acid, which can work well for some. Treatment of children will tend to be 'on demand' i.e. when an attack happens. The most likely course is administration of intravenous C1-INH. Icatibant can also be used in children over the age of two.

If the child needs C1-INH, then frequently they will need to be taken to hospital to have an IV line inserted and then administration either by the parent or more likely a nurse or doctor at the hospital. Sometimes a parent is trained to be able to give C1-INH to their child.

A short course (3 days) of the attenuated androgen Danazol is sometimes used in children prior to dental work to increase C1-INH levels. This needs to be discussed with your immunology team. It should not be used in children as a prophylaxis due to the potential effect on puberty.

School and social life

Correctly managed HAE is not a barrier to children enjoying a normal full life. However it is wise to set up a 'care plan', with the treating Immunology centre that provides the local accident and emergency department and the childs school. The care plan* should include as much information as possible about the condition and management; including 'how to manage' and an 'acute attacks' strategy. Individual situations will vary so if there are problems discuss with your immunology team.

* *HAE UK can help with these - contact: support@haeuk.org to discuss what we can offer*

As children grow older their HAE will change and management strategies may change. It is important that your team and you understand this and openly discuss issues with your child. This will improve the quality of life for them and you.

Remember! Children with HAE may not wish to 'broadcast' it to their peers so all plans need to be discussed with them in detail. A 'buddy' system (an older mentor or friend) may help to support them.

Be prepared!

- Set up a treatment plan with your consultant and care team
- Have letters from your consultant detailing your condition and advised treatment that you carry with you at all times
- Make sure you have contact details for your consultant – phone number of clinic
- HAE UK A&E card
- If travelling abroad, get the contact details of the nearest HAE clinic to where you are staying - HAE UK can help with this

Patient support

HAE UK is a dedicated patient support and advocacy association which is affiliated to HAE International.

- A website full of practical information.
- A closed Facebook group which serves our community.
- Dedicated telephone and e-mail support.
- Assistance with school and employment issues.
- Patient Days - annual meetings with presentations from doctors, nurses and other patients
- Social events.
- A specialist HAE medical advisory panel for support.

Contact

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