IONIS

HEREDITARY ANGIOEDEMA (HAE)

What is HAE?

HAE is a **rare and potentially life-threatening genetic condition that involves recurrent attacks of severe swelling** (angioedema) in various parts of the body, including the hands, feet, genitals, stomach, face and/or throat.[1–6]

Types of HAE

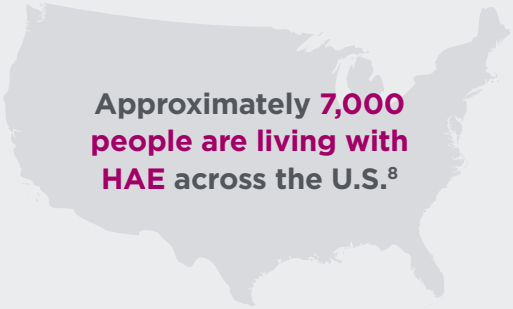
Type I
The most common form, representing 80 to 85% of HAE cases. People with HAE Type I have levels of the C1-inhibitor protein that are considerably below normal.[6]

Type II
Makes up approximately 15 to 20% of HAE cases. People with HAE Type II have adequate or even elevated levels of C1-inhibitor protein, however, it does not function properly.[6]

HAE with Normal C1-inhibitor
A rare form in those living with HAE. People with HAE and normal C1-inhibitor levels can experience swelling attacks similar to HAE Types I and II.[6]

HAE can impact multiple family members, and because the disease is hereditary, **children have a 50% chance of inheriting HAE** if one of their parents has the condition.[7]

However, as many as **25% of HAE cases** result from a **spontaneous genetic mutation,** or change, without a family history of HAE.[7]



Approximately 7,000 people are living with HAE across the U.S.[8]

Approximately **50% of people** living with HAE will experience **at least one laryngeal attack** in their lifetime, which means they experience swelling of the throat and/or tongue, and as a result can experience loss of consciousness or death.[7]

Even if not life-threatening, attacks can cause **severe pain and significantly disrupt daily life.** Abdominal attacks, for example, occur in up to 90% of people with HAE, and can lead to severe abdominal pain as well as vomiting and diarrhea.[7]

What is the disease burden?

People living with HAE still experience significant symptom burden day to day and may continue to experience attacks, despite preventative treatment.[7,9]

HAE can make it difficult to carry out daily tasks, go to work or school, leave the house, walk or travel.[7] This can negatively impact mental and emotional health, as well as the ability to maintain a job and relationships with friends, family and romantic partners.[7,9]

Because attacks are unpredictable, **simple activities are significantly more challenging,** and people living with HAE may experience anxiety daily as they feel they need to always be prepared for the possibility of an attack.[9] Many avoid activities all together that may trigger an attack.[7,9]

According to an Ionis-sponsored Harris Poll*

72% **of patients surveyed** reported they make **tradeoffs in their daily lives** due to unpredictability of attacks.

The vast majority,

89% have **missed or avoided events** due to their HAE in the past 12 months, including:

- 53% **days of work**
- 46% **social events like cookouts, concerts or dates**
- 35% **personal travel and/or vacation plans**

**This research was sponsored by Ionis Pharmaceuticals and conducted online in the U.S. by The Harris Poll among 150 U.S. adults aged 18 and older who have been diagnosed with HAE by a HCP. The patient survey was conducted from November 13–December 5, 2024, using a 70-question questionnaire consisting primarily of closed-ended pick-list and scale questions. Full research methodology is available upon request.*

What causes HAE?

HAE is caused by a genetic change that results in either reduced levels or poor functioning of a protein in the blood called C1-inhibitor.[8-11]

When the body doesn't have enough C1-inhibitor, or if the C1-inhibitor does not function correctly, it can lead to overactivity of prekallikrein (PKK).[8-11] PKK is a key factor in an inflammatory pathway that results in an excess of a protein called bradykinin, which ultimately leads to HAE attacks.[8-11]

What triggers an attack?

Every experience is different, and **some attacks appear to be spontaneous or unrelated to any specific cause.[7]**

While there are no consistent triggers for HAE attacks, common examples include:[1,6,12]

- **Anxiety**
- **Stress**
- **Common illnesses**, such as colds/flu/other viral infections
- **Minor trauma**, such as a fall
- **Surgery** or **dental procedures**
- Change in **temperature**

How is HAE diagnosed?

Symptoms of HAE usually appear early in life, most often by puberty, and may increase in severity with age.[7,8,13]

A diagnosis is typically confirmed through a blood test.[7,8,13]

Because HAE is so rare, in some cases **it can take up to a decade to obtain an accurate diagnosis** after symptoms are first experienced. On average, it takes five years to diagnosis.[9]

How can people manage their HAE?

Clinical guidelines recommend two categories of treatment:

Prophylactic Therapies

To help prevent and reduce the frequency and severity of attacks when taken regularly.[14]

Administration for prophylactic therapies can be as frequent as daily, or up to once every eight weeks.[14,15]

Acute Therapies

Used on-demand as an HAE attack is occurring to reduce swelling and minimize the impact of an attack.[5]

For more information on HAE, visit the following resources:

People living with HAE:

HAEVN™

HAEVNhub.com

or

haea.org

U.S. Hereditary Angioedema Association (HAEA)

Healthcare providers:

HAE UNCOVERED

HAEuncovered.com

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