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HEREDITARY ANGIOEDEMA IN FEMALES

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Introduction

Hereditary angioedema (HAE) is a rare genetic condition that causes periodic episodes of severe swelling. It may affect one or more parts of the body, including the skin, gastrointestinal tract, mouth, and throat. Potential symptoms include swelling, pain, bloating, nausea, and vomiting. It may also cause difficulty breathing, which in rare cases can be fatal. HAE attacks often develop spontaneously, but certain triggers may bring on an attack. These include emotional stress, injury, infection, medical or dental procedures, as well as changes in certain hormone levels. Doctors diagnose the condition based on symptoms and bloodwork. Sometimes genetic testing is also used to diagnose HAE.

Women with HAE report more frequent attacks of symptoms than men, which may reflect the effects of female sex hormones. In particular, increased levels of estrogen appear to increase HAE symptoms. Estrogen levels are higher during certain periods of the female lifecycle—including puberty, ovulation, and pregnancy. Estrogen levels also increase when people take medications that contain estrogen, such as combination oral contraceptives or estrogen replacement therapy.

Understanding how hormone levels affect HAE may help people manage potential triggers and symptoms. Doctors may recommend changes to a person's HAE treatment plan, fertility treatments, contraceptives, or other medications to help reduce symptoms.

Puberty

Most people with HAE first develop symptoms during childhood or adolescence. In females, attacks tend to become more frequent following puberty, when estrogen levels increase. In a 2008 survey of 150 women with HAE, 62% said the condition worsened at puberty. Some identified ovulation (14%) or menstruation (35%) as a symptom trigger.

If someone with HAE develops severe abdominal pain while menstruating, it may be difficult to tell whether the cause is HAE or another condition—such as endometriosis. Their doctor may order tests such as an ultrasound to determine the cause.

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Fertility and family planning

HAE does not appear to affect fertility. However, certain fertility treatments may increase the risk of HAE attacks. This may include injections of fertility drugs known as gonadotropins, which may increase estrogen production.

Certain types of birth control may also affect symptoms of HAE. Many women use hormonal contraceptives to prevent pregnancy. Examples include oral contraceptives (birth control pills), skin patches, vaginal rings, implants, and hormone-containing intrauterine devices (IUD). Some hormonal contraceptives include the hormone progestin alone, while others contain a combination of progestin and estrogen. Using contraceptives that contain estrogen may trigger first-time symptoms of HAE or cause more frequent attacks in people who have HAE. Using progestin-based or hormone-free alternatives may help limit symptoms.

In the 2008 survey above, 80% said the condition got worse when they took oral contraceptives with estrogen, while 64% said it improved when they took progestin-based oral contraceptives without estrogen. Another study of 55 women with HAE found that using progestin-based oral contraceptives without estrogen reduced the frequency of HAE attacks in more than 80% of participants.

When discussing fertility treatments or contraceptives with healthcare providers, people with HAE should let them know about their condition. Their healthcare provider can help them learn more about the potential benefits and risks of different fertility treatments and birth control methods. As part of the family planning process, their provider may also recommend genetic testing. A genetic counselor can help people understand the genetic mutations that cause HAE and the risk of passing those mutations on to their children.

To find a Genetics Clinic near you, click here.

Pregnancy and childbirth

Pregnancy may also change the frequency of HAE attacks. In the 2008 survey above, 38% reported more frequent attacks during pregnancy, 30% reported fewer attacks, and 32% reported no change. The frequency of attacks may vary from one pregnancy to another, even in the same person.

More research is needed to learn whether HAE affects pregnancy outcomes. Some studies have found higher rates of premature labour, miscarriage, and stillbirth among those with HAE. Other studies have found similar rates among women with and without HAE.

According to international HAE Guidelines published in 2019, people with HAE should be closely monitored during pregnancy by an HAE expert. This specialist can help them learn if their current treatment plan is safe for pregnant people. In some cases, they may ask the person to stop taking certain treatments while pregnant or breastfeeding. For example, attenuated androgens are not suitable for pregnant or breastfeeding people.

People who become pregnant should also let their obstetrician and gynecologist know if they have a personal or family history of HAE. In some cases, it may be hard to tell the difference between abdominal symptoms of an HAE attack and other pregnancy-related complications. If someone with a history of HAE develops abdominal symptoms, their doctor may order an ultrasound exam or other tests to diagnose the cause.

Optimal management of patients with HAE during pregnancy and delivery requires coordinated effort of the patient and appropriate healthcare providers. Given the potential risk of an angioedema attack and associated complications, it is recommended that patients with HAE deliver in a hospital setting and closely followed up for at least 72 hours after delivery.

The healthcare team should be consulted about short-term, long-term, and/or on-demand treatment options to manage HAE attacks during pregnancy and delivery.

Children of parents with HAE should be tested for the condition, but doctors usually wait until an infant is at least one year old before conducting the test. In some cases, a doctor may recommend testing at a younger age.

Menopause

More research is needed to study how menopause itself affects symptoms of HAE. Although some women with HAE have reported worse symptoms following the onset of menopause, others have reported improvements or no change.

Some women use hormone replacement therapy (HRT) to manage the symptoms of menopause. Depending on the specific type of HRT, a person may receive estrogen replacement, progesterone or progestin replacement, or a combination of both. Estrogen replacement may trigger more frequent attacks of HAE. As a result, people with HAE should generally avoid this treatment. Their doctor may recommend nonhormonal treatments or progesterone- or progestin-only treatments to manage symptoms of menopause.

Conclusion

People with HAE may experience more frequent attacks of symptoms during certain times of life or following certain triggers. Managing HAE may be particularly challenging for many women, due to estrogen-related changes across the female lifecycle. Females may have more frequent symptoms when their estrogen levels increase. This may affect how they manage healthcare decisions related to puberty, family planning, pregnancy, childbirth, and menopause.

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