

What is familial hyperinsulinism?

Familial hyperinsulinism is an inherited disease characterized by hypoglycemia due to unregulated release of insulin from cells in the pancreas.¹ Symptoms are the result of increased levels of insulin in the blood, which causes decreased blood sugar levels (or hypoglycemia). Familial hyperinsulinism is also known as congenital hyperinsulinism.

What are the symptoms of familial hyperinsulinism and what treatment is available?

Familial hyperinsulinism is a disease that varies in severity and age at presentation, even within families. The disease can involve the entire pancreas (diffuse form) or can be limited to confined areas of the pancreas (focal form); however, the symptoms are similar.^{1,2}

Symptoms of severe familial hyperinsulinism diagnosed soon after birth may include:¹

- Increased birth weight
- Very low blood sugar (hypoglycemia) that may be difficult to manage
- Seizures
- Poor feeding
- Low muscle tone (hypotonia)
- Difficulty breathing (apnea)

If untreated, symptoms may lead to irreversible brain damage and can be fatal.²

Individuals who are diagnosed in childhood or early adulthood usually have a milder form of the disease with varying degrees of low blood sugar.

Treatments include medications and dietary control to help normalize blood sugar and prevent brain damage. For individuals with the focal form of familial hyperinsulinism, partial removal of the pancreas may be curative, whereas a near total removal of the pancreas may improve symptoms for individuals with the diffuse form of familial hyperinsulinism.¹

How is familial hyperinsulinism, *ABCC8*-related, inherited?

Familial hyperinsulinism is a disease that is caused by mutations in one of at least five known genes, the most common of which is the *ABCC8* gene (previously known as *SUR*).¹

Most often, *ABCC8*-related familial hyperinsulinism is inherited in an autosomal recessive pattern.¹ With autosomal recessive inheritance, an individual who inherits one copy of an *ABCC8* gene mutation is a carrier and is not expected to have related health problems.³ An individual who inherits two *ABCC8* mutations, one from each parent, is expected to be affected with the diffuse form of familial hyperinsulinism. If both members of a couple are carriers, the risk for an affected child is 25% in each pregnancy; therefore, it is especially important that the reproductive partner of a carrier be offered testing.

In rare cases, individuals who inherit one copy of an *ABCC8* mutation from their father, but not from their mother, can be affected with focal familial hyperinsulinism.¹ Symptoms are usually relatively mild and may not appear until early adulthood. If only the male in a couple is a carrier, there appears to be a less than 1% chance for an affected child in each pregnancy.¹

Who is at risk for familial hyperinsulinism, *ABCC8*-related?

Familial hyperinsulinism can occur in individuals of virtually all races and ethnicities. In the Ashkenazi Jewish population, the incidence of *ABCC8*-related familial hyperinsulinism is approximately 1 in 10,800 (for diffuse familial hyperinsulinism), and the carrier frequency is 1 in 52.² The calculated carrier frequency in the Finnish population is approximately 1 in 101.³

Having a relative who is a carrier or is affected can increase an individual's risk of being a carrier. Consultation with a genetics professional may be helpful in determining carrier risk and appropriate testing.

What does a positive test result mean?

If a gene mutation is identified, an individual should speak to a physician or genetics health professional about the implications of the result and appropriate testing for the reproductive partner and at-risk family members.

What does a negative test result mean?

A negative result reduces, but does not eliminate, the possibility that an individual carries a gene mutation. The likelihood of being a carrier is also influenced by family history, medical symptoms, and other relevant test results.

Where can I get more information?

National Center for Advancing Translational Sciences (NCATS) – Genetic and Rare Diseases (GARD) Information Center: http://www.rarediseases.info.nih.gov/GARD/Condition/3947/Familial_hyperinsulinism.aspx

References

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3. Otonkoski T *et al.* A point mutation inactivating the sulfonylurea receptor causes the severe form of persistent hyperinsulinemic hypoglycemia of infancy in Finland. *Diabetes* 1999; 48: 408-415