First version: Maya Ballantine, Pamela Bowman, Indi Banerjee, Sarah Dearman, Sarah Flanagan
Updated: 09-07-2026

When Genetic Testing Does Not Find a Cause for Congenital HI

This information sheet is for individuals and their families who have **had genetic testing for congenital hyperinsulinism** (shortened to HI) **but no genetic cause has been found**.

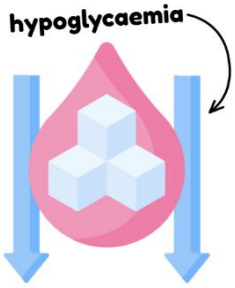
This sheet is intended for information only and should not replace personalised advice or genetic counselling for you or your family. For more information on congenital HI, check out our other information sheets here.

All terms highlighted in **blue** can be found in our glossary, linked here.

Key Points

- **Congenital HI** can be **caused by genetic changes** that affect **genes** involved in **controlling the release of insulin**
- Genetic testing can **help identify whether a genetic change is causing HI**
- For many families, genetic testing **does not find the cause of the HI**, this can happen for **lots of different reasons**
- Not finding a genetic cause **does not always mean the HI is not genetic**, it means that a cause has not yet been identified
- It is **important to keep talking to your doctor** about your genetic results

What Are the Genetics of Congenital HI?



In **congenital HI,** the **pancreas releases too much insulin,** causing **low blood sugar** (called **hypoglycaemia**).

HI that continues **beyond the first few weeks of life** can be caused **by a genetic change (or a variant) in a person's DNA**. These genetic changes **affect genes that make proteins that are important for controlling the release of insulin**.

Genetic changes in more than 30 different genes are currently known to cause congenital HI. How these genetic changes are **inherited is different for each gene and between individuals**. These genetic changes can be found by doing a **genetic test** using **a blood sample** (or rarely from **a sample of the pancreas** after an operation).

As congenital HI can be caused by genetic changes in so many different genes, genetic testing is an important way to **help doctors better understand the condition in each individual.**

First version: Maya Ballantine, Pamela Bowman, Indi Banerjee, Sarah Dearman, Sarah Flanagan
Updated: 09-07-2026

Why Would a Genetic Test Not Tell Me the Cause of My HI?

Up to **50% of people** with congenital HI **do not receive a genetic diagnosis** after genetic testing. This does **not necessarily mean there is no genetic cause**, it often means that current testing has not identified the cause. For some families, living without a genetic diagnosis **can be unsettling** and **leave important questions unanswered**.

There are **many reasons** why you might not have a genetic diagnosis, like:

- Testing may have found **a genetic change,** but laboratory scientists are **unsure if it is the cause of the HI**. These genetic changes are called **variants of uncertain significance (**or **VUS),** which means that there is not currently enough evidence to know whether the genetic change **causes HI or not**. You can find out more about VUS in our information sheet linked here.
- The genetic test **may not have included all the genes or genetic changes** known to cause congenital HI. Or the genetic cause of HI **may not have been discovered yet**.
- In some people the cause of HI **may not be genetic at all**.

What Happens Next?

Not having a genetic diagnosis **will not affect access to appropriate monitoring and treatment for HI.** Doctors will recommend the most appropriate care **based on the symptoms and individual needs** of the person.

It is **still important to keep talking to your doctor** about your genetic testing results for a few reasons:

- **Further genetic testing** may be possible. **New genetic causes of congenital HI are being discovered** all the time, and advances in testing may find a cause that could not be found when your original test was done.
- **Your results may need to be reviewed over time.** A genetic change that was previously a VUS may be **reclassified in the future** as we learn more about it.
- If your child is seen by **different specialists or at different hospitals**, it is helpful to make sure your doctors are **aware of any new findings** or changes to your child's care. This includes if you have had other types of genetic testing done through different genetic testing programmes and the results of these tests.
- It is helpful to **share as much information as possible** about your **child's health and your family history** with your doctor. This includes any **history of HI**, **unusual forms of diabetes**, or other **health conditions** in your wider family. **Even information that may not seem relevant to HI can sometimes provide useful clues.**

First version: Maya Ballantine, Pamela Bowman, Indi Banerjee, Sarah Dearman, Sarah Flanagan
Updated: 09-07-2026

You may be able to take part in research. Research studies may offer **more detailed genetic testing,** helping scientists to discover new genetic causes of congenital HI. Although doing this **may not give you an immediate diagnosis**, it could **benefit** your family in **the future** and **improve understanding of HI** for others. Any results from these studies would be fed back to your doctor who can talk through the findings with you.

Getting Individualised Information and Accessing Genetic Counselling Services

Meeting with a **genetic counsellor** or **clinical geneticist** can be helpful, particularly if you have a family history of HI. They can help you **understand what your results mean**, discuss what they may mean **for your family**, and **answer questions about future pregnancies or testing options**. The guidance you receive will be **personalised to you**.

This support can help you make **informed decisions** and **plan for the future**. To book any appointment you will usually need a **referral from your family doctor** (GP in the UK) or a **specialist doctor**.

Where Can I Find More Support?

Not having an explanation for why HI has happened **can be difficult for some families**. If you would like more information or support, you can also **contact HI patient advocacy organisations**, such as the **Children's Hyperinsulinism Charity**. These organisations can **connect you with other families** affected by congenital HI, including families who are living without a genetic diagnosis.

Useful Resources

- **VUS explained:** https://www.genomicseducation.hee.nhs.uk/genotes/knowledge-hub/variant-of-uncertain-significance-vus/
- **The role of the Genetic Counsellor:** https://www.genomicseducation.hee.nhs.uk/genotes/knowledge-hub/roles-in-clinical-genetics/#genetic-counsellors
- **The Children's Hyperinsulinism Charity:** https://hyperinsulinism.co.uk/

This leaflet was developed by the Exeter Hyperinsulinism Genes team (www.hyperinsulinismgenes.org) in collaboration with The Children's Hyperinsulinism Charity UK (https://hyperinsulinism.co.uk/). Registered Charity: 1165562, Company Number: CE005407