First version: Maya Ballantine, Pamela Bowman, Jonna Männistö, Jacob Roberts, Sarah Dearman, Indi Banerjee, Sarah Flanagan 25/03/2026. Updated: 30-06-2026

Inheritance of Focal Congenital Hyperinsulinism

This information sheet summarises what we know about **inheritance** of **focal congenital hyperinsulinism** (shortened to HI). This sheet is intended for information only and should not replace personalised advice or genetic counselling for you or your family. For information on other forms of inheritance, check out our other information sheets here.

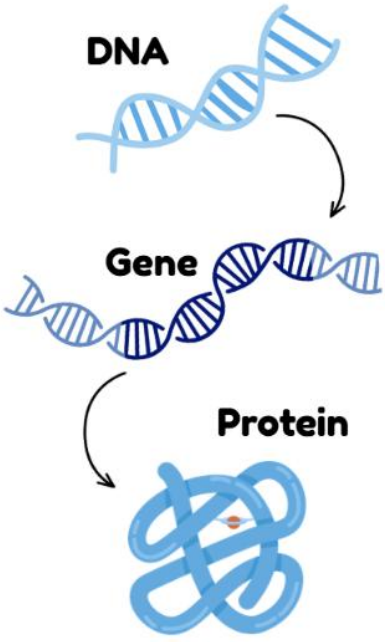
All terms highlighted in **blue** can be found in our glossary, linked here.

Key Points

- **Congenital HI** is often **caused by genetic variants** that have been passed down from parents
- Focal congenital HI happens when **2 separate genetic events** come together: **Dad passes a recessive variant in *ABCC8* or *KCNJ11*** to their child, and when the baby is developing in the womb **Mum's copy of the gene is lost** and **Dad's gene is duplicated**
- The cells in the pancreas then start to **multiply** and make **a focal lesion** and because each **cell has two copies of Dad's gene**, they start to **produce too much insulin**, causing HI
- The chance of a **Dad with a recessive *ABCC8* or *KCNJ11*** variant having a **child with focal HI** is about **1 in 540 (less than 1%).**

What are Genes and Genetic Variation?

We are all **made up of trillions of cells**, and in each cell, there is a very important molecule called **DNA**. DNA is the body's **instruction manual** that tells the cell what it needs to do to function properly. These instructions are contained in **small sections of DNA** called **genes**.



Each person will have **two copies of a gene**, one **inherited** from their **mother**, and one inherited from their **father**. These genes each provide a **unique code** that makes **different proteins**, and these proteins **help the body grow, function and stay healthy**.

It is **normal to have some variation** in this **genetic** code between individuals because that is what makes us all different and unique. Sometimes though a **change (or variant) in a gene** can cause a **protein to not function properly**, leading to **health problems**. These are often called **genetic**, **congenital**, or **inherited conditions**.

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What is Inheritance?

Inheritance is how an individual's **characteristics** **are passed from parents to their children** through variants in their genes.

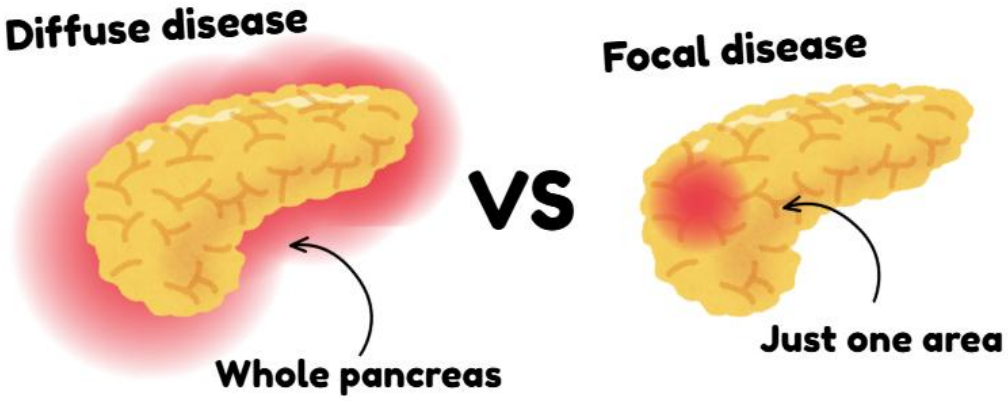
Some variants cause disease when they are in **one copy of a gene inherited from one parent**, these are called **dominant variants**.

Other variants only cause disease when present **in both copies of a gene, one inherited from each parent.** These are called **recessive variants**.

This **inheritance pattern** depends on the **type of variant and the gene** it is in.

How Does This Relate to Congenital HI?

In congenital **hyperinsulinism** the **pancreas** **releases too much** **insulin** causing **low blood sugar** (called **hypoglycaemia**). Some people have **diffuse** disease, where the **whole pancreas** releases too much insulin. Others have **focal** disease, where too much insulin is released from a **smaller area of the pancreas**.



In some, but not all people, **congenital HI is caused by genetic variants**. These variants **affect genes that make proteins that are important for controlling insulin secretion**.

Variants in over 30 different genes can cause congenital HI. How these variants are inherited **differs by gene and between individuals**. These variants can be identified by performing a **genetic test** using **a blood sample** (or rarely from **the pancreatic sample** after an operation).

This information sheet is about **focal congenital HI which is caused by recessive variants.**

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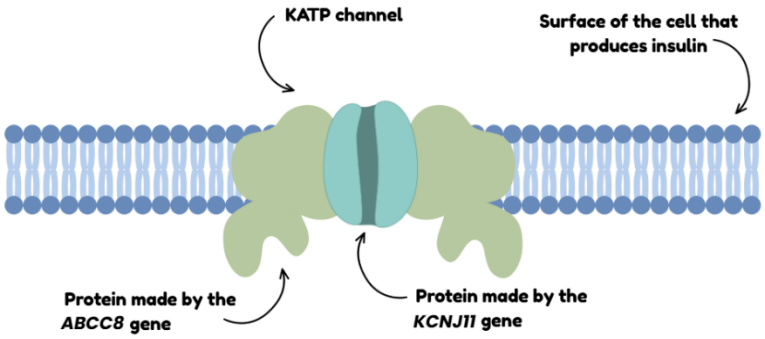
Changes in the *ABCC8* and *KCNJ11* Genes Cause Focal Disease

Focal congenital HI involves changes in one of two genes: ***ABCC8*** and ***KCNJ11***.

These genes code for proteins that make **the potassium channel**, also called the **KATP channel**. The KATP channel sits at the surface of **cells in the pancreas** and **controls when insulin** is **released** into the blood.



In congenital HI, changes in these genes can cause the **channel to stop working properly**. Because of this, cells in the pancreas **release insulin** even when **blood sugar (glucose) levels are low**, leading to **repeated episodes of hypoglycaemia**.

How Does a Focal Lesion Develop?

Focal disease happens when **2 separate genetic events** come together:

Genetic event 1: First, a child inherits a single **recessive variant** in one copy of the ***ABCC8*** or ***KCNJ11*** gene from their **unaffected Dad**. This variant on its own does not cause congenital HI, which is why the Dad does not have the condition.

Genetic event 2: The second event happens as **the baby is growing in the womb**. A cell in the pancreas **loses Mum's copy of the same gene** and **Dad's copy of the gene is duplicated**. The cell then has 2 identical copies of Dad's gene, both of which have the variant. This is a **random event** that happens **by chance** within a cell **in the pancreas.**

This situation **has 2 consequences** within the pancreas:

- The cell starts to **multiply more than normal**, producing lots of cells to **form a focal lesion**
- All these cells within the lesion have **2 copies of the variant** causing them **to release too much insulin**

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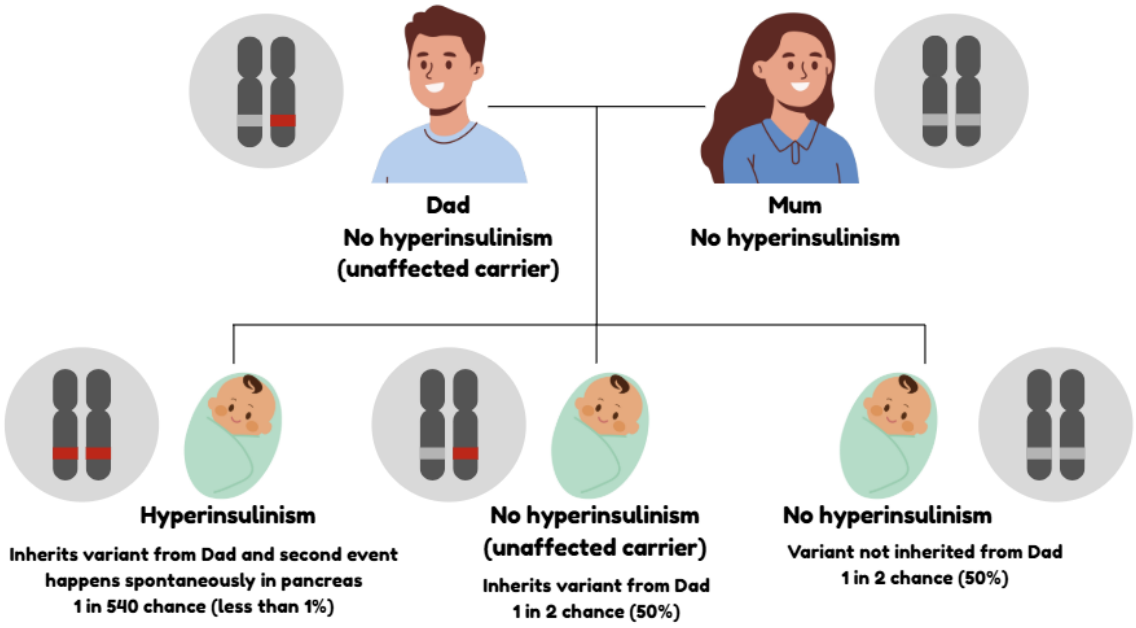
What Are the Chances of Developing Focal HI?

If an **unaffected Dad** carries a recessive variant in one copy of the ***ABCC8* or *KCNJ11* gene**, there is a **50% chance that he will pass it** on to his child (***genetic event 1***). Most children who inherit the variant will be **healthy carriers** and will **not have congenital HI**.

A child develops focal congenital HI only if ***genetic event 2*** also **happens during pregnancy**. This second event is estimated to happen in **about 1 in 270 pregnancies**.

Overall, this means the chance of a Dad with a recessive *ABCC8* or *KCNJ11* variant having a child with focal HI is **about 1 in 540 (less than 1%)**.



What Are the Chances Someone with Focal HI has a Child with HI?

Most children of affected parents will not develop hyperinsulinism.

If the **Dad has focal HI** each child has a **50% (1 in 2) chance** of inheriting the variant and being a **healthy carrier** (***genetic event 1***). For the child to develop focal HI ***genetic event 2* must occur**. The likelihood of this is **1 in 540 (less than 1%).** If the child's **Mum carries a recessive variant** in the same gene there is an **increased chance** of the child having **diffuse congenital HI**.

If the **mother has focal HI** each child has a **50% (1 in 2) chance of inheriting the variant** and being **a healthy carrier**. If the **Dad carries a recessive variant** in the **same gene** there is an **increased chance** of the child having **diffuse congenital HI**.

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The likelihood that a parent with focal hyperinsulinism will have a child with **diffuse HI** is **generally low**. However, the likelihood **increases in 2 specific situations**:

- The partner and the person with focal HI are **related by blood**

OR

- Congenital HI is **particularly common in the population** that the parents are from

Getting Individualised Information and Accessing Genetic Counselling Services

Meeting with a **genetic counsellor** or **clinical geneticist** can be very helpful if you have **a family history of HI**. They can explain how HI might **affect you or your children** and **answer any questions** you have. Because everyone's genetics are unique, the guidance you receive will be **personalised to you**.

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

Additional Resources

- **Recessive inheritance explained:** https://www.genomicseducation.hee.nhs.uk/genotes/knowledge-hub/autosomal-recessive-inheritance/
- **Genes explained:** https://www.genomicseducation.hee.nhs.uk/genotes/knowledge-hub/gene/
- **The role of the Genetic Counsellor:** https://www.genomicseducation.hee.nhs.uk/genotes/knowledge-hub/roles-in-clinical-genetics/#genetic-counsellors

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