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Dominant Inheritance of Congenital Hyperinsulinism

This information sheet summarises what we know about **dominant inheritance** of **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.

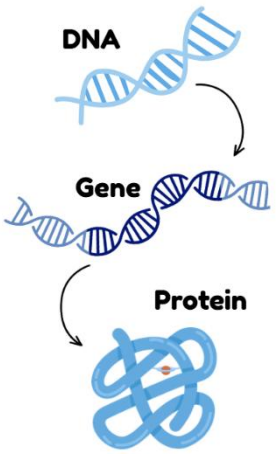
All terms highlighted in **blue** can be found in our glossary, linked here.

Key Points

- **Inheritance** is how **characteristics are passed from a parent to their child**
- **Congenital HI** is often **caused by genetic changes** that have been passed down from parents
- A **dominant variant** means that only **one genetic change on one copy of a gene** is needed to cause disease
- If someone has dominant congenital HI, each of their **children has a 1 in 2 (50%) chance of inheriting the genetic change and developing congenital HI**
- Dominant variants cause **diffuse pancreatic disease** where the **whole pancreas releases too much insulin**

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 genetic changes in their genes.

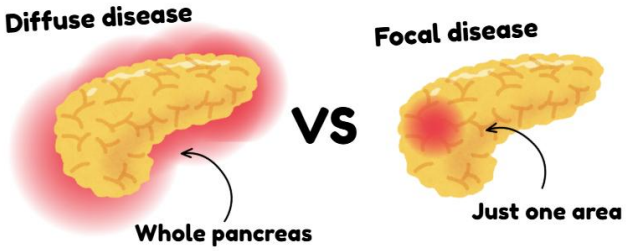
Some genetic changes cause disease when they are in **one copy of a gene inherited from one parent**, these are called **dominant variants**.

Other genetic changes 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 genetic change and the gene** it is in.

How Does This Relate to Congenital HI?

In congenital HI 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 changes**. These genetic changes **affect genes that make proteins that are important for controlling insulin secretion**.

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

This information sheet is about **dominant inheritance.**

Dominant Variants

To be affected with a **dominant condition**, only **one genetic change on one copy of the gene** is needed. Dominant conditions can be **passed down through generations of a family** or **appear for the first time** in an individual (a ***de novo* variant**). These ***de novo* variants** can happen in a **parent's egg or sperm cell** or when the baby is growing in the **womb**.

If someone has dominant congenital HI, **each of their children has a 1 in 2 (50%) chance of inheriting the genetic change and developing congenital HI**. Likewise, each child has a **1 in 2 (50%) chance of not inheriting the genetic change** and **being unaffected**.

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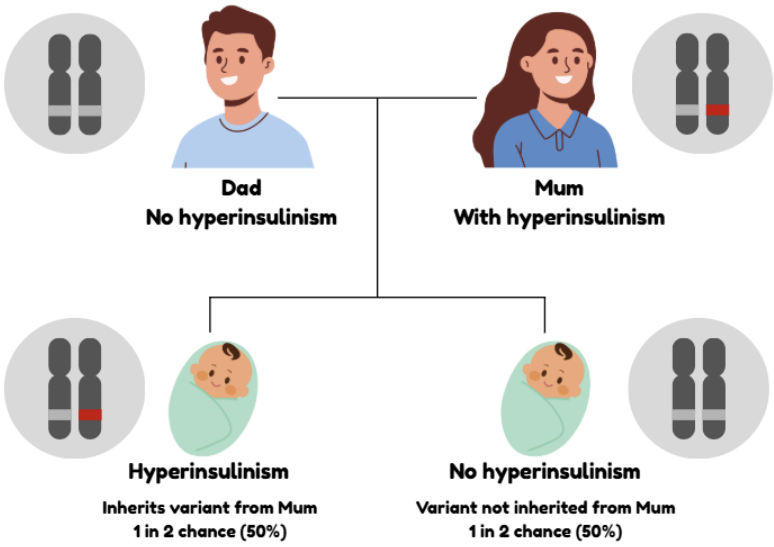
For parents of children with a *de novo* variant, there is a small **chance that they could have another child with HI**. This can happen if the **genetic change is present** in one of the **parent's egg or sperm cells**.

Changes in genes, such as ***ABCC8***, ***GCK***, ***GLUD1***, ***HK1***, ***SLC16A1, KMT2D, CACNA1D*** or ***HNF4A*** can cause dominantly inherited congenital HI.



Dominant variants cause **diffuse pancreatic disease**, which is where the **whole pancreas releases too much insulin**.

Dominant variants can also show **variable penetrance.** This means that **not everyone with the genetic change will develop congenital HI**. Variable penetrance is explained more in our information sheet linked here.

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

- **Dominant inheritance explained:** https://www.genomicseducation.hee.nhs.uk/genotes/knowledge-hub/autosomal-dominant-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