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Updated: 19-09-2026

Understanding *De Novo* Variants

This information sheet explains what ***de novo* variants** are and what they mean for a family. This resource is intended for information only and should not replace personalised advice or genetic counselling for you or your family.

For more information on congenital hyperinsulinism (shortened to HI), see our other information sheets here.

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

Key Points

- A ***de novo* variant** is a **new genetic change** identified in a person. It is not detected in the samples tested from their biological parents.
- *De novo* variants can happen in **genes related to HI**.
- A *de novo* variant can happen when an **egg or sperm is being formed**, or early in a baby's **development in the womb**.
- Sometimes, a genetic change may be in **some of the parent's egg or sperm cells**, even though it is **not found in their blood** sample. This is called **germline (or gonadal) mosaicism**. This means there may be a small chance of the same genetic change happening in another child.
- For most parents who have one child with HI because of a *de novo* variant, the chance that any of their future children will have HI **is usually very low**. The exact chance can **depend on the genetic change** and the **individual family**.
- A person who has HI because of a *de novo* variant **may be able to pass the genetic change on to their own children**. A child who inherits the genetic change may also develop HI. The chance of this happening **depends on the specific genetic change**.
- Your **genetics team** can explain what your family's results mean for **future pregnancies.**

What Is a *De Novo* Variant?

De novo is a Latin term meaning "**new**." In genetics, it describes a **genetic change** (also called a **genetic variant**) that is **found in a person** but is **not found in** the samples tested from **their biological parents**. These samples are usually blood or saliva.

De novo variants **happen by chance**, usually as a **random** event.

When do *De Novo* Variants happen?

A de novo variant can happen when an **egg or sperm cell is being formed** in a parent, or during the **development of the baby in the womb**.

Sometimes, a parent may have the genetic change in **some of their egg or sperm cells**, even though it is **not found in their blood or saliva sample**. This is called **germline (or gonadal) mosaicism**. To find out more about this, have a look at our information sheet on **mosaic variants** linked here.

It is often not possible to tell exactly whether a *de novo* variant arose in an egg or sperm cell or during the baby's early development in the womb. This is not usually investigated as part of routine genetic testing.

How Common are *De Novo* Variants?

Everyone is born with new genetic changes (*de novo* variants) that are not found in their parents. Most of these changes do not affect a person's health. Changes and differences in our **DNA** are a normal part of **genetic variation,** and this is what makes us all **unique and different**.

Occasionally, a *de novo* variant affects a **gene** **that is important for making sure the body works properly**. Some of these changes can **cause health conditions,** including some forms of **hyperinsulinism (HI)**.

De novo variants that cause HI have been reported in several genes, including ***ABCC8, GCK, GLUD1, HNF4A, HNF1A, HK1, KCNJ11, KDM6A, KMT2D and SLC16A1*** as well as **large deletions on chromosome 9** and **chromosome 20.**

What Does This Mean for Siblings?

For most families, the chance of having another child with the same *de novo* variant is **very low, but it is not zero**.

One reason for this is **germline (gonadal) mosaicism** which is explained above. When a parent has the genetic change in **some of their egg or sperm cells** there is a chance that another child could **inherit** the same genetic change and develop HI.

The chance of this happening **varies between families and depends on the specific genetic change** involved. Your genetics team can discuss what this may mean for future pregnancies.

To find out more about mosaicism, see our information sheet on **mosaic variants** here.

Could Someone with a *De Novo* Variant Pass the Genetic Change to Their Children?

Yes. A person with a *de novo* variant may be able to **pass the genetic change on to their children**.

There are **two things to consider**: the **chance of passing the genetic change** on to a child, and whether a **child who inherits the genetic change will develop HI**. These are not always the same.

For example, for some genetic changes, such as those in the ***GLUD1* or *GCK* genes**, the chance of **passing the genetic change** on to future children may range from **0% to 50%** (1 in 2) in each pregnancy.

Whether a child who inherits the genetic change develops HI can **depend on several factors**. These include the **gene involved**, the **specific genetic change** and **how the genetic change affects the gene**.

Your **genetics team** can explain what **your genetic result** may mean for future children. They can discuss the chance of passing the genetic change on to your children and what it could mean for a child who inherits it.

Getting Individualised Information and Accessing Genetic Counselling Services

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

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

- **More on *de novo* variants:** https://www.genomicseducation.hee.nhs.uk/genotes/wp-content/uploads/2026/03/VCA_DNV_v1.2.pdf
- **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