Written by: Jacob Roberts, Maya Ballantine, Lara Gulec, Sarah Dearman, Pam Bowman, Sarah Flanagan. First version: 01/07/2026

How a Deletion on Chromosome 20 Can Cause Congenital Hyperinsulinism

This information sheet summarises what we currently know about **congenital hyperinsulinism** (shortened to HI) **caused by a deletion on chromosome 20**. Our understanding of how this deletion results in HI is still growing, which means some of the information we provide here is still very new and will be updated as we discover more.

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

Key Points

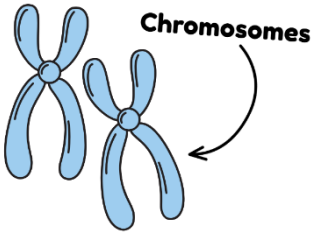
- A **deletion of a section of chromosome 20** has been linked to **HI** in 5 children
- Specifically, the deletion of the ***FOXA2* gene** is believed to be the cause
- This form of HI is considered **rare**, but may be **underdiagnosed** as it is not routinely tested for
- The standard treatment is **diazoxide**, which resolved or managed the symptoms in four of the five children
- Because this form of HI has **only recently been discovered**, researchers are now **working to understand more** about the condition and the **long-term treatment** options

What are Genes, Chromosomes, 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 **instructional 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**.

Within each cell, the **DNA forms structures** called **chromosomes**. A person has **46 chromosomes** in each cell; 23 of them inherited from their mother, and 23 of them inherited from their father. These chromosomes are **numbered 1 to 22** not including the sex chromosomes. For the sex chromosomes, a male will usually have an X and Y chromosome, and a female will usually have two X chromosomes.



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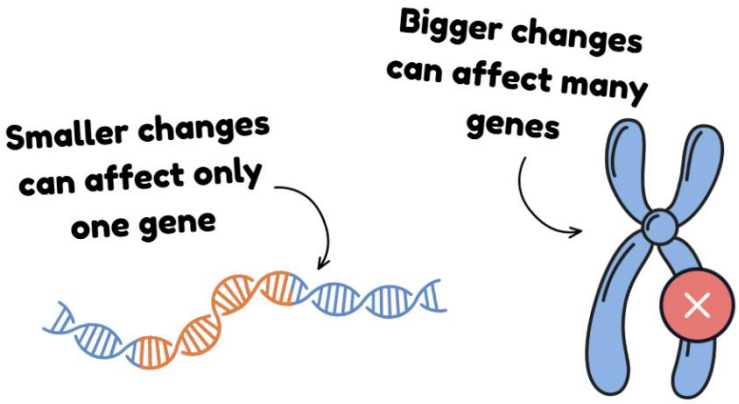
It is **normal to have some** variation in your genetic code because that is what makes us all different and unique. Sometimes though, a **change** (or a variant) **in our DNA** can make a **protein stop working properly**, leading to **health problems**. These changes can be small variants **that affect a single gene** or can be larger variants that **affect multiple genes**.



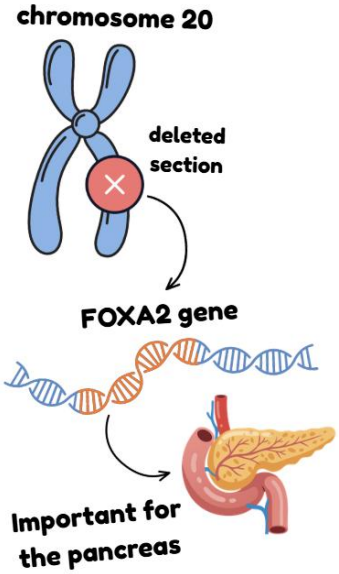
An example of a larger variant can involve a **deletion of multiple genes**, where whole **sections of DNA can be lost**. This is the case with the deletion on chromosome 20.

How Can a Deletion on Chromosome 20 Cause HI?

We have recently discovered that **deletions of a section of DNA on chromosome 20 are a cause of HI**. Within this deletion, there are many genes missing, including all or parts of a gene called ***FOXA2***.

The *FOXA2* gene provides the instructions to make a protein. That protein has many functions but one of them is to **help with the development and function of the** pancreas.

This is important because the pancreas is the organ which **secretes** insulin, and our research suggests that it is the **loss of this *FOXA2* gene** that is **causing this form of HI**.



How Common Is This Form of HI?

This form of HI is considered **rare**. Currently, we know **5 individuals** with this type of deletion that have been diagnosed with congenital HI. However, this genetic form of HI is **not routinely tested for**, so we believe it may be **underdiagnosed**. Because of this, we are **actively raising awareness** of this condition worldwide.

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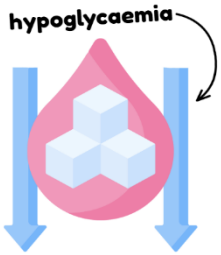
How Is This Deletion Inherited?

This chromosome 20 deletion is a **dominant variant**, and further information on what this means can be found on **our information sheet on dominant inheritance** linked here.

In 4 of the 5 children, this deletion **occurred for the first time in the child**, meaning the parents did not have this deletion in their own genes. This is called a ***de novo* variant**. In the fifth child, this deletion **was inherited from their Mum**, whose blood sugar levels had not been investigated previously.

What Are the Features of HI Caused by a Chromosome 20 Deletion?



All 5 of the children with this form of HI have **low blood sugar levels** (known as **hypoglycaemia**) that was **diagnosed before they were 1 year old**. 3 of the children were diagnosed within the first week of their life, one child was diagnosed at 3 months old, and the final child was diagnosed at the age of 1 year.

There were a range of other clinical features that were seen in all 5 of these children, but it is important to note that **these features vary between individuals** and likely reflect the **differences in the size of the deletion** that they have. For example, some children may have more genes missing because of this deletion than others, which can cause different features to develop.

We also know that the ***FOXA2* gene** has an important role in other organs in the body, like the **brain** and the **liver**. This could explain why some children **developed other conditions**.

The other features that have been reported in the 5 children include:

- Distinctive **facial features**
- **Learning difficulties**, including slower than expected development of movement skills (e.g. sitting, walking, and coordination)
- Difficulties with **feeding** and/or **slower growth**
- Changes in the level of **hormones** from the **pituitary gland** in the brain
- Some issues with the **heart, kidneys, and genitals (in males)** which could be treated and managed. In some children, these features **got better with time**.

NOTE: Not every person will develop these features and **how severe** these features are can be **very different between individuals**.

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How Do You Treat and Manage This Form of HI?

Four of the five children with this chromosome 20 deletion were given the drug **diazoxide**. This is the **standard treatment** for congenital HI.

For one of these children, the **HI resolved when they were 6 months old** and they no longer needed treatment. The other 3 children are **continuing to take diazoxide** to manage their ongoing hypoglycaemia. Currently, the average age of these children is 4 years old, with the youngest being 3 and the oldest being 12. In the fifth child, the **diazoxide treatment did not properly control their blood glucose levels**, so they underwent **surgery** that removed **some of their pancreas** to help manage their HI.

Because this form of congenital HI has **only recently been discovered**, researchers are working hard to understand which **treatments** will work best in the **long term**.

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 each family's genetics are unique, the guidance you receive will be **personalised to your situation**.

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

This medical paper describes the discovery of the chromosome 20 deletion in HI:

Laver, T.W., Wakeling, M.N., Caswell, R.C., Bunce, B., Yau, D., Männistö, J.M.E., Houghton, J.A.L., Hopkins, J.J., Weedon, M.N., Saraff, V., Kershaw, M., Honey, E.M., Murphy, N., Giri, D., Nath, S., Tangari Saredo, A., Banerjee, I., Hussain, K., Owens, N.D.L. and Flanagan, S.E. (2024). Chromosome 20p11.2 deletions cause congenital hyperinsulinism via the loss of FOXA2 or its regulatory elements. *European journal of human genetics: EJHG*. doi:https://doi.org/10.1038/s41431-024-01593-z. PMID: 38605124

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