

# CLASSICAL HOMOCYSTINURIA (HCU)

## What are **homocystinurias**?



**Classical homocystinuria, HCU for short**, is a rare metabolic disorder that **prevents the normal breakdown of protein**. Babies with HCU inherit **two faulty copies of the affected gene**, one from each parent. With HCU, an enzyme called **cystathionine beta-synthase is deficient or missing**, leading to **problems breaking down the amino acid methionine**. This causes methionine and a substance called **homocysteine to build up in the body** and blood.<sup>1</sup>

**Genetic mutations in different genes cause most types of HCU**. Two of the most common mutations are **G307S for B6 non-responders** and **I278T for the B6 responders**. Elevation of homocysteine, however, may be observed in non-genetic conditions such as deficiency of vitamin B12.<sup>2</sup>

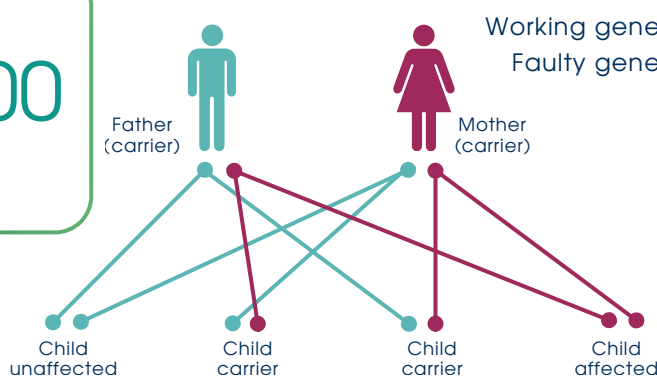
The **most common type** of **homocystinuria** affects

# 1 : 200,000 to 335,000

people worldwide.<sup>2</sup>

### **Cystathionine beta-synthase (CBS) deficiency:**

The **most common type** and is known as **classical homocystinuria**. This occurs when the **CBS gene produces little to no CBS enzyme** or when it **produces CBS enzyme that doesn't work properly**. The CBS enzyme requires **vitamin B6** to function.

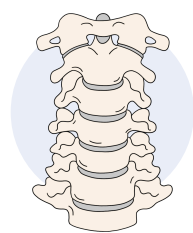


When both parents are carriers, in each pregnancy the risk to the baby is:

- **25% chance (1 in 4) of HCU**
- **50% chance (1 in 2) for the baby to be a carrier of HCU**
- **25% chance (1 in 4) for the baby to have two working genes and neither have HCU or be a carrier**

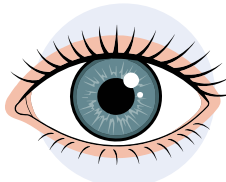
## Signs and symptoms

The main signs and symptoms of homocystinuria usually develop **during childhood**, but some people don't develop any symptoms **until into adulthood**.



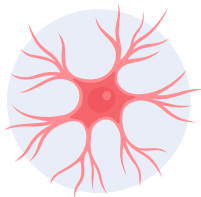
### **Bones**

**Excessive growth, knock knees, sunken or protruding chest, curvature of the spine and long limbs**, fingers and toes, and sometimes **scoliosis** and **osteoporosis**.



### **Eyes**

**Dislocation of the lenses** of the eyes and **severe short-sightedness**.



### **Brain**

**Developmental delays, seizures, learning problems.**



### **Vascular system**

Increased **risk of blood clots**, which **can lead to strokes** or **pulmonary embolisms**.<sup>2</sup>

## Diagnosis



HCU is currently included on the newborn screening test (NBS) in **most areas**. However, the testing threshold (methionine level) **varies from region to region**. The NBS screening test measures the amount of some amino acids in the blood. **A high level of the amino acids methionine and total homocysteine** suggests a baby **may have HCU**. However, It's important to remember that newborn **screening tests aren't always accurate**, and some people aren't diagnosed until after symptoms appear.

If a person is recognised as having symptoms of HCU, their healthcare provider should order **a homocysteine test (tHcy)**. A genetic test is needed to confirm an HCU diagnosis. In approximately 10-15% of individuals, treatment with high-dose vitamin B6 alone is sufficient to lower their homocysteine to safer levels. These individuals are called B6-responsive. However, studies from around the world show that nearly half of individuals with the B6 non-responsive form of HCU struggle to achieve levels of homocysteine deemed safe.

## Treatment

In some babies, homocysteine levels in the blood can be reduced by administering vitamin B6 (also known as pyridoxine), however, not all are responsive to this treatment.<sup>1</sup> If this is unsuccessful, a strict low-protein diet is prescribed, from birth or immediately on diagnosis. This includes a special formula and adapted diet which restricts protein intake and requires strict adherence for optimum outcomes.<sup>3</sup> Patients with HCU need regular blood tests to monitor levels of homocysteine in their blood to guide treatment plans.<sup>3</sup>

## Support

For more information about HCU and more support:

### **HCU Network Australia:**

Visit [hcunetworkaustralia.org.au](http://hcunetworkaustralia.org.au)

### **HCU Network America:**

Visit [hcunetworkamerica.org](http://hcunetworkamerica.org)

### **Metabolic Support:**

Visit [metabolicsupport.org](http://metabolicsupport.org)

### References

1. [gov.uk/government/publications/hcu-suspected-description-in-brief/homocystinuria-hcu-detailed-information](http://gov.uk/government/publications/hcu-suspected-description-in-brief/homocystinuria-hcu-detailed-information)
2. [my.clevelandclinic.org/health/diseases/25160-homocystinuria](http://my.clevelandclinic.org/health/diseases/25160-homocystinuria)
3. [galenmedicalnutrition.com/metabolics/homocystinuria-hcu/](http://galenmedicalnutrition.com/metabolics/homocystinuria-hcu/)