

HCU DISEASE CHECKLIST

Homocystinuria: A treatable disorder

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The Homocystinurias are a group of inherited metabolic disorders leading to accumulation of homocysteine and its metabolites in the blood and urine. The most common of these disorders is known as classical homocystinuria (HCU) and is caused by a deficiency in the enzyme known as cystathionine beta-synthase or CBS. There are other very rare metabolic causes of homocystinuria that are quite different from HCU. The other forms of homocystinuria are not discussed in this checklist.

The international reported birth incidence of classical homocystinuria varies between 1 in 50,000 and 1 in 200,000^[1]. In Australia it is about 1 in 100,000. The true prevalence, especially of milder cases, is unknown.

In Australia homocystinuria is included in the disorders screened at birth by newborn screening. Screening does not detect all cases of homocystinuria. If not diagnosed by newborn screen, delays are on average 4.5 years from disease onset to accurate diagnosis^[2].

Could it be classical homocystinuria?

Whilst the disorder is present at birth, the symptoms and signs may develop in infancy, childhood or even in adulthood^[3]. The symptoms associated with classical homocystinuria are highly variable with some affected individuals only having mild signs of the disorder; others may have many different symptoms including some potentially life-threatening complications^[4].

The most commonly affected areas are: the brain; the eyes; the skeleton; and the vascular system. Due to the symptoms and signs being non-specific this often leads to misdiagnosis and late diagnosis^[3,5].

Key warning signs and symptoms include:

The eyes:

- severe and progressive near sightedness (myopia) at a young age
- lens dislocation

The brain:

- developmental delays
- intellectual deficit
- seizures
- clumsiness
- psychiatric disorders: anxiety, depression, obsessive-compulsive disorder
- behavioural problems

The skeleton:

- marfanoid features
- restricted joint mobility in the hands
- excessive growth and thinning or lengthening of the long bone
- abnormally protruding or sunken chest
- highly arched foot
- knock knees
- premature osteoporosis
- scoliosis

The vascular system:

- blood clots especially DVTs
- strokes (especially sagittal sinus thrombosis)
- pulmonary embolism
- mildly affected individuals may present as adults with blood clots as only problem

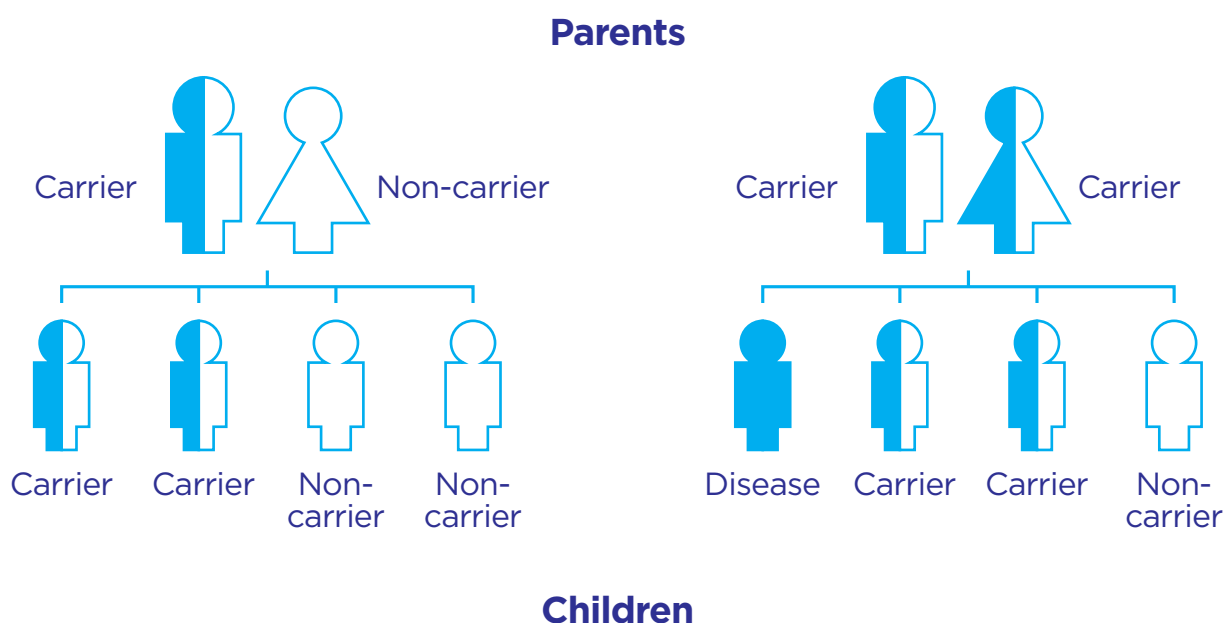
It is important to note that early treatment can prevent the development of symptoms listed above or prevent further complications and worsening of symptoms which are already present^[3].

Speak with your doctor about your child's symptoms and take this HCU Disease Checklist along to your appointment.

Genetic Inheritance

It is suggested that relatives of a family member recently diagnosed with homocystinuria should be tested^[5].

Homocystinuria is an autosomal recessively inherited disorder. This means that an individual inherits the same defective copy of the CBS gene from each parent. The risk is the same for males and females.



What to do if there is a suspicion of HCU?

If an individual is showing any of the signs above then classical homocystinuria should be considered as a potential diagnosis. It is important to measure the plasma total homocysteine level and if high (above $50 \mu\text{M}$) and homocystinuria is suspected refer patient to a metabolic center for further investigation and early treatment where appropriate^[1].

The metabolic clinics available in Australia are:

NEW SOUTH WALES

Children's Metabolic Clinic

The Children's Hospital, Westmead
Hawkesbury Rd & Hainsworth St,
Westmead, NSW 2145
ph. (02) 9845 2525

Sydney Children's Hospital

High St,
Randwick, NSW 2031
(02) 9382 1111

Adult Metabolic Clinic

Westmead Hospital
Cnr Darcy Rd & Bridge St,
Westmead, NSW 2145
ph. (02) 98459 780

VICTORIA

Children's Metabolic Clinic

Royal Children's Hospital
50 Flemington Road,
Parkville VIC 3052
ph. (03) 9345 6180

Adult Metabolic Clinic

Royal Melbourne Hospital
300 Grattan St,
Parkville VIC 3050
ph. (03) 9342 7074

SOUTH AUSTRALIA

Children's Metabolic Clinic

Women's and Children's Hospital
72 King William Rd,
North Adelaide, SA 5006
ph. (08) 8161 7295

Adult Metabolic Clinic

Royal Adelaide Hospital
North Terrace,
Adelaide, SA 5000
ph. (08) 8222 5174

WESTERN AUSTRALIA

Children's Metabolic Clinic

Princess Margaret Hospital
Roberts Rd,
Subiaco, WA 6008
ph. (08) 9340 8222

Adult Metabolic Clinic

Royal Perth Hospital
197 Wellington St,
Perth, WA 6000
ph. (08) 9224 3511

QUEENSLAND

Children's and Adult Metabolic Clinic

Lady Cilento Children's Hospital
501 Stanley Street,
South Brisbane, QLD 4101
ph. (07) 3068 1111

Classical homocystinuria is a treatable disease and early diagnosis and treatment can prevent the development or progression of the complications associated with the disease. If untreated, classical homocystinuria is a serious and potentially fatal disease. Timely diagnosis and treatment of classical homocystinuria is important in preventing or reducing the symptoms associated with the disorder^[1]. Early diagnosis and treatment can make a real difference to patient outcomes^[6].

HCU Network Australia

For more information about classical homocystinuria or patient support please visit www.hcunetworkaustralia.org.au.

HCU Network Australia is a Health Promotion Charity established in 2014, with the vision “to be a driving force in the journey to a cure, improving quality of life along the way”. Our aim is to achieve meaningful progress and best health outcomes for the HCU community.

If you would like to contact HCU Network Australia, please send us an email at info@hcunetworkaustralia.org.au.

References:

- [1]Medscape. <http://emedicine.medscape.com/article/1952251-overview>.
- [2]HCU Network Australia, unpublished data.
- [3]García-Jiménez MC, Baldellou A, García-Silva MT, Dalmau-Serra J, Garcia-Cazorla A, Gomez-Lopez L, Pedron Giner C, Alonso Luengo O, Pena Quintana L, Luz Couce M, Martinez-Pardo M, Lambruschini N (2012), Epidemiological study of the metabolic diseases with homocystinuria in Spain. *Anales de Pediatría*, 76, 133-139
- [4]Morris, A.A.M., Kožich, V., Santra, S (2016), Guidelines for the diagnosis and management of cystathionine beta-synthase deficiency, *J Inherit Metab Dis*, 40, 49-74
- [5]Refsum H, Smith AD, Ueland PM, Nexø E, Clarke R, McPartin J, Johnston C, Engbaek F, Scheede J, McPartin C, Scott JM (2004), Facts and recommendations about total homocysteine determinations: an expert opinion, *Clinical Chemistry*, 50, 3-32
- [6]Schiff M, Blom HJ (2012), Treatment of inherited homocystinurias. *Neuropediatrics* 43, 295-304