

### What is cobalamin C disease?

Cobalamin C disease, also known as methylmalonic aciduria with homocystinuria, is an inherited disease characterized by hypotonia, lethargy, mental retardation, seizures, vision problems, and blood-related problems. Individuals with cobalamin C disease have defects in a protein used to change vitamin B<sub>12</sub> into a form that the body can use to break down certain amino acids and fats. Symptoms are due to the build-up of these substances and their metabolites in the body's organs and tissues.<sup>1</sup>

### What are the symptoms of cobalamin C disease and what treatment is available?

Cobalamin C disease varies in age of onset and severity. Most individuals show initial symptoms within the first year, often triggered by fasting, illness, infection, or eating large amounts of protein.<sup>1</sup>

Symptoms during infancy may include:<sup>1,2</sup>

- Poor appetite and growth
- Lethargy (lack of energy)
- Hypotonia (low muscle tone)
- Seizures
- Microcephaly (small head size)
- Hydrocephalus ("water on the brain") and other brain abnormalities
- Megaloblastic anemia (red blood cells that are low in number and large in size)
- Developmental delays or intellectual disability
- Vision, heart, and kidney problems
- Skin rashes

A small number of individuals do not develop signs until later in life. Some adults may remain undiagnosed due to atypical or nonspecific symptoms such as behavior problems, tremor, and weakness in the limbs.<sup>1</sup>

There is no cure for cobalamin C disease. Prompt and lifelong treatment with a low protein diet, nutritional supplements, and other medications may lessen the chance of intellectual disability, psychiatric disorders, and serious health problems. If not treated, symptoms can be life-threatening in some cases.<sup>1</sup>

Cobalamin C disease is included in newborn screening profiles in some states.<sup>3</sup>

### How is cobalamin C disease inherited?

Cobalamin C disease is an autosomal recessive disease caused by mutations in the *MMACHC* gene.<sup>2</sup> An individual who inherits one *MMACHC* gene mutation is a carrier and is not expected to have related health problems. An individual who inherits two *MMACHC* gene mutations, one from each parent, is expected to be affected with cobalamin C disease.

If both members of a couple are carriers, the risk for an affected child is 25% in each pregnancy; therefore, it is especially important that the reproductive partner of a carrier be offered testing.

### Who is at risk for Cobalamin C Disease?

Cobalamin C disease can occur in individuals of all races and ethnicities. The exact incidence is not known.

Having a relative who is a carrier or who is affected can increase an individual's risk of being a carrier. Consultation with a genetics health professional may be helpful in determining carrier risk and appropriate testing.

**What does a positive test result mean?**

If a gene mutation is identified, an individual should speak to a physician or genetics health professional about the implications of the result and appropriate testing for the reproductive partner and at-risk family members.

**What does a negative test result mean?**

A negative result reduces, but does not eliminate, the possibility that an individual carries a gene mutation. The likelihood of being a carrier is also influenced by family history, medical symptoms, and other relevant test results.

**Where can I get more information?**

Organic Acidemia Association: <http://www.oaaneews.org/mma.htm>

Screening, Technology and Research in

Genetics: [http://www.newbornscreening.info/Parents/organicaciddisorders/MMA\\_HCU.html](http://www.newbornscreening.info/Parents/organicaciddisorders/MMA_HCU.html)

Children Living with Inherited Metabolic Disorders (CLIMB): <http://www.climb.org.uk/>

**References**

1. Screening, Technology and Research in Genetics. Methylmalonic Acidemia with Homocystinuria. Available at: [http://www.newbornscreening.info/Parents/organicaciddisorders/MMA\\_HCU.html](http://www.newbornscreening.info/Parents/organicaciddisorders/MMA_HCU.html) Accessed on: April 6, 2012.
2. Methylmalonic aciduria and homocystinuria, cb1C type. Available at: <http://omim.org/entry/277400>. Accessed on April, 6, 2012.
3. National Newborn Screening Status Report. November 2, 2014. Available at: <http://genes-r-us.uthscsa.edu/sites/genes-r-us/files/nbsdisorders.pdf> . Accessed January 6, 2016.