

### **What is Holocarboxylase Synthetase Deficiency?**

Holocarboxylase synthetase (HLCS) deficiency is an inherited disease characterized by vomiting, lethargy, developmental delays, and hypotonia when untreated.<sup>1</sup> It involves abnormalities in the enzyme holocarboxylase synthetase, which uses the vitamin biotin for the normal processing of proteins, fats, and carbohydrates. Symptoms are due to the toxic build-up of these substances in the body. Holocarboxylase synthetase deficiency is also called multiple carboxylase deficiency.<sup>2</sup>

### **What are the symptoms of Holocarboxylase Synthetase Deficiency and what treatment is available?**

Holocarboxylase synthetase deficiency is a disease that varies in severity and age at onset, even within families. Affected individuals typically have onset of symptoms by age two, with the majority showing signs in early infancy. Symptoms are episodic and may include<sup>1</sup>:

- Poor appetite and vomiting
- Lethargy (lack of energy)
- Severe dermatitis (skin rash)
- Hypotonia (low muscle tone)
- Seizures
- Irritability
- Hypoglycemia (low blood sugar)
- Metabolic acidosis (high levels of acidic substances in the blood)

If an episode remains untreated or is nonresponsive to treatment, symptoms may worsen and can include coma or death. Additional long-term symptoms may include<sup>1</sup>:

- Continued skin rashes or infections
- Hair loss
- Learning disabilities or mental retardation
- Developmental delays
- Ataxia (difficulty coordinating movements)
- Spasticity (abnormally tight muscles)
- Hearing and vision loss

There is no cure for HLCS deficiency. Early detection and treatment with biotin supplementation may prevent, manage, and possibly reverse symptoms. With treatment, most affected individuals are expected to have normal growth and development, although some individuals may have life-long learning problems.<sup>1</sup>

Holocarboxylase synthetase deficiency is included on newborn screening panels for most states in the US.<sup>3</sup>

### **How is Holocarboxylase Synthetase Deficiency inherited?**

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

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.



## CARRIER SCREEN

### Who is at risk for Holocarboxylase Synthetase Deficiency?

Holocarboxylase synthetase deficiency can occur in individuals of all races and ethnicities, with an estimated incidence of less than 1 in 100,000 in the United States.<sup>1</sup>

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?

- Screening, Technology and Research in Genetics: Holocarboxylase synthetase deficiency <http://www.newbornscreening.info/Parents/organicaciddisorders/HCSA.html>
- Organic Acidemia Association: <http://www.oaanews.org/mcd.htm>

### References

1. Holocarboxylase synthetase deficiency. *Screening, Technology and Research in Genetics*. Available at: <http://www.newbornscreening.info/Parents/organicaciddisorders/HCSA.html> Accessed March 19, 2012.
2. Holocarboxylase synthetase deficiency. *Genetics Home Reference*. Available at: <http://ghr.nlm.nih.gov/condition/holocarboxylase-synthetase-deficiency>. Accessed March 19, 2012.
3. National Newborn Screening Status Report: Updated 2/15/12. Available at: <http://genes-r-us.uthscsa.edu/nbsdisorders.pdf>.

