

### What is carbamoyl phosphate synthetase I deficiency?

Carbamoyl phosphate synthetase I deficiency is a rare inherited disease with variable severity and age at onset.<sup>1</sup> Individuals with carbamoyl phosphate synthetase I deficiency have a deficiency of the enzyme carbamoyl phosphate synthetase I, which helps the body break down excess nitrogen so that it can be excreted. If excess nitrogen is not excreted, the body stores the nitrogen in the form of ammonia, leading to excess ammonia accumulation in the blood (hyperammonemia).<sup>2</sup> Individuals with severe carbamoyl phosphate synthetase I deficiency rapidly develop hyperammonemia in the newborn period and, after the initial crisis, are chronically at risk for repeated bouts of hyperammonemia. Hyperammonemia can cause developmental delays, intellectual disability, failure to thrive, and hypotonia.<sup>3</sup> Carbamoyl phosphate synthetase I deficiency belongs to a group of diseases called urea cycle disorders.<sup>1</sup>

### What are the symptoms of carbamoyl phosphate synthetase I deficiency and what treatment is available?

Symptoms of carbamoyl phosphate synthetase I deficiency often occur in the first few days of life. In less severe cases, symptoms may not occur until later in life.<sup>1</sup> Symptoms may include<sup>1,3</sup>:

- Vomiting
- Refusal to eat
- Lethargy (lack of energy)
- Irritability
- Respiratory distress
- Poorly-regulated body temperature
- Seizures
- Abnormal movements
- Coma
- Intellectual disability
- Developmental delays
- Failure to thrive
- Hypotonia (poor muscle tone)

Treatment is primarily dietary. In severe cases, even with treatment high ammonia levels and associated complications may still occur.<sup>3</sup>

Carbamoyl phosphate synthetase I deficiency is included in newborn screening panels in some states in the United States.<sup>4</sup>

### How is carbamoyl phosphate synthetase I deficiency inherited?

Carbamoyl phosphate synthetase I deficiency is an autosomal recessive disease caused by mutations in the *CPS1* gene.<sup>1</sup> An individual who inherits one copy of a *CPS1* gene mutation is a carrier. Carriers are not affected with carbamoyl phosphate synthetase I deficiency. An individual who inherits two *CPS1* mutations, one from each parent, is expected to be affected with carbamoyl phosphate synthetase I deficiency.

If both members of a couple are carriers of mutations in the same gene, 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 carbamoyl phosphate synthetase I deficiency?

Carbamoyl phosphate synthetase I deficiency is rare, but can occur in individuals of all races and ethnicities. The worldwide incidence is estimated to be 1 in 1,300,000 with a carrier frequency of 1 in 570.<sup>5</sup>

Having a relative who is a carrier or who is affected can increase an individual's risk to be 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?

Genetics Home Reference: <http://ghr.nlm.nih.gov/condition/carbamoyl-phosphate-synthetase-i-deficiency>

National Organization for Rare Disorders (NORD): <http://rarediseases.org/rare-diseases/carbamoyl-phosphate-synthetase-i-deficiency/>

New England Consortium of Metabolic Programs: <http://newenglandconsortium.org/for-professionals/acute-illness-protocols/urea-cycle-disorders/carbamyl-phosphate-synthetase-deficiency-cps/>

### References

1. Carbamoyl phosphate synthetase I deficiency. *Genetics Home Reference*. Available at <http://ghr.nlm.nih.gov/condition/carbamoyl-phosphate-synthetase-i-deficiency>. Accessed February 5, 2016.
2. CPS1. *Genetics Home Reference*. Available at: <http://ghr.nlm.nih.gov/gene/CPS1>. Accessed February 5, 2016.
3. Carbamoyl Phosphate Synthetase I Deficiency. *National Organization for Rare Disorders*. Available at <http://rarediseases.org/rare-diseases/carbamoyl-phosphate-synthetase-i-deficiency/>. Accessed February 5, 2016.
4. 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.
5. Summar ML, et al. The incidence of urea cycle disorders. *Mol Genet & Metabolism*. 2013;110:179-180