

### What is ornithine transcarbamylase deficiency?

Ornithine transcarbamylase deficiency is an inherited disease with variable severity and age at onset.<sup>1</sup> Individuals with ornithine transcarbamylase deficiency have a defect in the ornithine transcarbamylase enzyme. This enzyme is a component of the urea cycle, which helps the body eliminate nitrogen in the form of urea.<sup>2</sup> When the urea cycle is disrupted, nitrogen is converted to ammonia.<sup>2</sup> Signs and symptoms of ornithine transcarbamylase deficiency are due to the toxic buildup of ammonia in the blood,<sup>2</sup> which can be life-threatening.<sup>1</sup> Neuropsychological complications are due to the sensitivity of the nervous system to ammonia.<sup>1,3</sup> Ornithine transcarbamylase deficiency belongs to a group of diseases called urea cycle disorders.<sup>3</sup>

### What are the symptoms of ornithine transcarbamylase deficiency and what treatment is available?

The severity and age at onset for symptoms can be variable, with the most severely affected individuals showing signs within a few days of birth.<sup>3</sup> Symptoms may include:<sup>1,3</sup>

- Progressive lethargy (lack of energy)
- Vomiting
- Poorly-controlled breathing rate and body temperature
- Seizures
- Hypotonia (poor muscle tone)
- Coma
- Developmental delay
- Intellectual disability
- Hepatomegaly (enlarged liver) and progressive liver damage
- Skin lesions and brittle hair
- Cerebral palsy
- Ataxia (loss of muscle coordination)

There is no cure for ornithine transcarbamylase deficiency. Treatment is supportive and may include dietary restrictions, oral nitrogen-scavenging drugs, and vitamin supplementation.<sup>1</sup>

### How is ornithine transcarbamylase deficiency inherited?

Ornithine transcarbamylase deficiency is an X-linked recessive disease caused by mutations in the *OTC* gene.<sup>3</sup> A male who inherits one copy of an *OTC* gene mutation is affected with ornithine transcarbamylase deficiency. A female who inherits one copy of an *OTC* gene mutation is a carrier and is not expected to have related health problems, but in some cases may have symptoms.<sup>3</sup> A female who inherits two *OTC* mutations, one from each parent, is affected with ornithine transcarbamylase deficiency, although this is an uncommon occurrence.

If a female is a carrier, the risk for each son to be affected is 50% and the risk for each daughter to be a carrier is 50%. If a male is affected, each son is unaffected and each daughter is an obligate carrier.

### Who is at risk for ornithine transcarbamylase deficiency?

Ornithine transcarbamylase deficiency is a rare condition that can occur in individuals of all races and ethnicities. The incidence is estimated to be 1 in 56,500 in the general population.<sup>4</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/ornithine-transcarbamylase-deficiency>

National Organization for Rare Disorders (NORD): <http://rarediseases.org/rare-diseases/ornithine-transcarbamylase-deficiency/>

New England Consortium of Metabolic Programs: <http://newenglandconsortium.org/for-professionals/acute-illness-protocols/urea-cycle-disorders/ornithine-transcarbamylase-deficiency-otc/>

### References

1. Ornithine Transcarbamylase Deficiency. *National Organization for Rare Disorders*. Available at: <http://rarediseases.org/rare-diseases/ornithine-transcarbamylase-deficiency/>. Accessed March 25, 2016.
2. OTC. *Genetics Home Reference*. Available at: <https://ghr.nlm.nih.gov/gene/OTC>. Accessed March 25, 2016.
3. Ornithine transcarbamylase deficiency. *Genetics Home Reference*. Available at: <https://ghr.nlm.nih.gov/condition/ornithine-transcarbamylase-deficiency>. Accessed March 25, 2016.
4. Summar ML, *et al*. The incidence of urea cycle disorders. *Mol Genet & Metab*. 2013;110:179-180.