Inheritest®
CARRIER SCREEN

Systemic primary carnitine deficiency

What is systemic primary carnitine deficiency?

Systemic primary carnitine deficiency is an inherited metabolic disease with variable severity and age at onset. Individuals with systemic primary carnitine deficiency have absent or defective organic cation transporter proteins, which causes a shortage of carnitine in the cells of the body.[1,2] Carnitine is used to process fats and produce energy.[1] Signs and symptoms of systemic primary carnitine deficiency are due to the buildup of fatty acids in cells, which can damage the liver, heart, and muscles, along with reduced energy production in cells, which can lead to muscle weakness and hypoglycemia.[1] Systemic primary carnitine deficiency is also known as carnitine transporter deficiency and carnitine uptake defect.[1,3]

What are the symptoms of systemic primary carnitine deficiency and what treatment is available?

Typically, signs and symptoms of systemic primary carnitine deficiency are seen during infancy or early childhood.[1] Some individuals with systemic primary carnitine deficiency may appear to have no symptoms.[1] All individuals with systemic primary carnitine deficiency are at risk for coma, liver problems, heart failure, and sudden death.[1] Signs and symptoms may include:[3]

- Metabolic episodes triggered by fasting or common illness
- Vomiting
- Irritability
- Lethargy (lack of energy)
- Hypoglycemia (low blood sugar)
- Coma
- Encephalopathy (brain dysfunction)
- Hepatomegaly (enlarged liver)
- Cardiomyopathy (enlarged and weakened heart)
- Skeletal muscle weakness
- Hypotonia (poor muscle tone)

There is no cure for systemic primary carnitine deficiency. Treatment is supportive and may include avoidance of fasting and dietary supplementation.[3] Infantile and childhood forms of the disease can lead to death if not treated; however, the long-term prognosis can be favorable with dietary supplementation.[3]

Systemic primary carnitine deficiency is included in newborn screening in most states in the United States.[4]

How is systemic primary carnitine deficiency inherited?

Systemic primary carnitine deficiency is an autosomal recessive disease caused by mutations in the *SLC22A5* gene.[1] An individual who inherits one copy of a *SLC22A5* gene mutation is a carrier and is not expected to have related health problems. An individual who inherits two *SLC22A5* mutations, one from each parent, is expected to be affected with systemic primary carnitine 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 systemic primary carnitine deficiency?

Systemic primary carnitine deficiency can occur in individuals of all races and ethnicities and has a worldwide carrier frequency of 1 in 130.[5] It has been found to occur more frequently in Japan and the Faroe Islands.[3]

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/primary-carnitine-deficiency

Screening, Technology And Research in Genetics (STAR-G): http://www.newbornscreening.info/Parents/fattyaciddisorders/Carnitine.html

National Organization for Rare Disorders (NORD): http://rarediseases.org/rare-diseases/systemic-primary-carnitine-deficiency/

References

1. Primary Carnitine Deficiency. *Genetics Home Reference.* Available at: http://ghr.nlm.nih.gov/condition/primary-carnitine-deficiency. Accessed on February 17, 2016.
2. SLC22A5. *Genetics Home Reference.* Available at: http://ghr.nlm.nih.gov/gene/SLC22A5. Accessed on February 17, 2016.
3. El-Hattab AW. Systemic Primary Carnitine Deficiency. 2012 Mar 15 [Updated 2014 Jun 26]. In: Pagon RA, Adam MP, Ardinger HH, et al., editors. GeneReviews®. Seattle (WA): University of Washington, Seattle; 1993-2016. Available at: http://www.ncbi.nlm.nih.gov/books/NBK84551/. Accessed on February 17, 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. Feuchtbaum L, *et al*. Birth prevalence of disorders detectable through newborn screening by race/ethnicity. *Genetics in Medicine*. 2012;14(11):937-945.