

### What is VLCAD deficiency?

VLCAD deficiency is an inherited metabolic disease characterized by lethargy, weakness, and low blood sugar. Individuals with VLCAD deficiency have deficiencies of the very long-chain acyl-CoA dehydrogenase enzyme, which helps to break down very long-chain fatty acids (a type of fat) that are used for energy in cells.<sup>1</sup> Symptoms associated with VLCAD deficiency are due to low levels of energy and the toxic build-up of fatty acids in cells, especially in the heart, liver, and muscles.<sup>2</sup>

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

Symptoms of VLCAD deficiency are variable in severity and age at onset, but are typically seen in infancy or early childhood.<sup>1</sup> Children with the most severe, early-onset form of VLCAD deficiency are at risk for serious complications such as liver problems and life-threatening heart problems.<sup>2</sup> Children or adults with a later-onset form may have intermittent muscle-related or no symptoms.<sup>3</sup> Signs and symptoms are often triggered by fasting, illness, or exercise and may include:<sup>2,3</sup>

- Episodic hypoglycemia (low blood sugar)
- Irritability
- Lethargy (lack of energy)
- Muscle weakness
- Cardiomyopathy (abnormal heart muscle)
- Abnormal heart rhythms
- Hepatomegaly (enlarged liver)
- Intermittant rhabdomyolysis (breakdown of muscle tissue)

Treatment focuses on prevention of complications and management of symptoms through dietary modifications and avoidance of dehydration and fasting. Acute episodes may be treated with intravenous glucose.<sup>2,3</sup>

VLCAD deficiency is included in all state newborn screening profiles in the United States.<sup>4</sup>

### How is VLCAD deficiency inherited?

VLCAD deficiency is an autosomal recessive disease caused by mutations in the *ACADVL* gene.<sup>1</sup> An individual who inherits one copy of an *ACADVL* gene mutation is a carrier and is not expected to have related health problems. An individual who inherits two *ACADVL* mutations, one from each parent, is expected to be affected with VLCAD 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 VLCAD deficiency?

VLCAD deficiency is a rare condition that can occur in individuals of all races and ethnicities. The incidence of VLCAD deficiency is approximately 1 in 200,000 and the carrier frequency is 1 in 222.<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/very-long-chain-acyl-coa-dehydrogenase-deficiency>

National Organization for Rare Disorders (NORD): <http://rarediseases.org/rare-diseases/very-long-chain-acyl-coa-dehydrogenase-deficiency-lcad/>

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

### References

1. Very long-chain acyl-CoA dehydrogenase deficiency. *Genetics Home Reference*. Available at <http://ghr.nlm.nih.gov/condition/very-long-chain-acyl-coa-dehydrogenase-deficiency>. Accessed February 8, 2016.
2. Leslie ND, et al. Very Long-Chain Acyl-Coenzyme A Dehydrogenase Deficiency. *GeneReviews*. Available at: <http://www.ncbi.nlm.nih.gov/books/NBK6816/>. Accessed on February 8, 2016
3. Very Long Chain Acyl CoA Dehydrogenase Deficiency (LCAD). *National Organization for Rare Disorders*. Available at <http://rarediseases.org/rare-diseases/very-long-chain-acyl-coa-dehydrogenase-deficiency-lcad/>. Accessed February 8, 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. Naylor EW, et al. Automated tandem mass spectrometry for mass newborn screening for disorders in fatty acid, organic acid, and amino acid metabolism. *Journal of Child Neurology*. 1999;14:S4-S8