Very Long-Chain Acyl-CoA Dehydrogenase (VLCAD) Deficiency
Information for Healthcare Professionals

Very Long-Chain Acyl-CoA Dehydrogenase (VLCAD) deficiency is a rare, but treatable, cause of cardiomyopathy, fatty liver, skeletal myopathy, pericardial effusion, ventricular arrhythmias, and sudden death. Unrecognized, VLCAD deficiency may be rapidly progressive and fatal secondary to its cardiac involvement. It is classified as a fatty acid oxidation disorder.

✓ Clinical Symptoms

There are three forms of VLCAD deficiency: "Early", "Childhood" and "Adult". Initial signs and symptoms of this disorder occur during infancy or childhood and include hypoglycemia, lethargy, fever, vomiting and muscle weakness. People with an early onset of VLCADD are also at risk of serious complications, such as liver abnormalities and life-threatening heart problems. Fatal infantile encephalopathy may be the only indication of the condition. Symptoms that begin in adolescence or adulthood tend to be milder and generally do not involve heart problems. Episodes of VLCADD can be triggered by periods of fasting, illness, and heavy exercise. Periods of hypoglycemia can happen with or without the other symptoms. Hypoglycemia can cause a child to feel dizzy, clammy, weak, and shaky. If not treated, it can lead to coma, and possibly death.

✓ Incidence

VLCAD deficiency is thought to be a rare disorder. VLCADD is estimated to affect greater than 1 in 75,000 newborns.

✓ Genetics of VLCAD Deficiency

Mutations in the ACADVL gene cause VLCAD deficiency. Mutations in the ACADVL gene lead to inadequate levels of very long-chain acyl-coenzyme A dehydrogenase. Without sufficient amounts of this enzyme, very long-chain fatty acids from food and fats stored in the body are metabolized improperly. As a result, these fats are not converted to energy, leading to characteristic signs and symptoms of this disorder, such as lethargy and low blood sugar.

✓ Inheritance Patterns

VLCAD deficiency is inherited in an autosomal recessive pattern. Parents of a child diagnosed with VLCADD are unaffected. These individuals are carriers of the condition and have one normal ACADVL gene and one abnormal ACADVL gene. Each pregnancy between carrier parents has a 25% chance of producing a child affected with VLCADD, a 50% chance of producing an unaffected carrier child, and a 25% chance of producing a child who is unaffected and is not a carrier.

✓ Treatment

Treatment for VLCAD deficiency involves avoiding long periods of fasting and having frequent meals that are high in carbohydrates and low in fat. Infants should have at least one nighttime feeding, or a late-night snack as they get older, to reduce the time they go without eating. Treatment should begin shortly after birth and is life-long. Some dietary supplements may be prescribed. Emergency care must be taken if a person with VLCAD deficiency becomes ill and has difficulty keeping food down. This is usually treated in the hospital. People with VLCAD deficiency require treatment through a specialty clinic with experience in treating this disorder. **Parents should always travel with a letter from the child's physician, including treatment guidelines, for any situation that may necessitate hospital admission during an acute illness.**

✓ Screening Methodology

Newborn screening for VLCADD is performed by tandem mass spectrometry (MS/MS). The primary marker for VLCAD deficiency is tetradecenoylcarnitine (C14:1)**.**

- ✓ **What to do After Receiving Presumptive Positive Very Long-Chain Acyl-CoA Dehydrogenase Deficiency Screening Results:** **MEDICAL EMERGENCY - TAKE THE FOLLOWING IMMEDIATE ACTIONS:**

1) **Consult with pediatric metabolic specialist.**
2) **Evaluate infant for hepatomegaly, cardiac insufficiency; history of sudden unexpected death in a sibling; maternal liver disease during pregnancy, and hypoglycemia. If signs are present or infant is ill, initiate emergency treatment in consultation with metabolic specialist.**
3) **Educate family about signs and symptoms of hypoglycemia and metabolic acidosis. Parents should be warned that if an infant shows warning signs of the disorder, such as lethargy or vomiting, they should immediately seek medical attention.**
4) **Initiate timely confirmatory/diagnostic testing as recommended by specialist.**
5) **Call KS Newborn Screening Program at 785-291-3363 with questions about results.**
6) **Report Clinical Findings to Newborn Screening Program at 785-291-3363.**

- ✓ **Confirmation of Diagnosis**

The diagnosis is confirmed by finding increased long chain fatty acids on blood acylcarnitine analysis and on organic acid analysis in urine. Mutation analysis of the ACADVL gene is also available.

- ✓ **Communication of Results to Parents**

If a baby has a presumptive positive VLCADD newborn screening result, additional testing needs to be performed to confirm a diagnosis. In accordance with Kansas Administrative Regulation 28-4-502, it is the responsibility of the attending physician or other birth attendant to obtain repeat specimens when needed to complete the screening process.

If a baby is diagnosed with VLCAD deficiency, the following points should be conveyed to parents:

- ***Parents should understand that treatment is lifelong and that compliance with diet and avoidance of fasting and prolonged strenuous exercise is critical.***
- ***Although children with VLCADD are usually healthy, any illness (for example, fever, vomiting or injury) where the child is not eating requires prompt notification of the child's physician.***
- ***Parents should be encouraged to keep an individualized written treatment protocol for doctors to utilize in a medical crisis.***
- ***The siblings of a baby with VLCADD have a chance of being affected, even if they haven't had symptoms. Finding out whether other children in the family have VLCADD is important because early treatment may prevent serious health problems.***
- ***People with VLCADD typically receive follow-up care by a team of professionals that is experienced in treating people with metabolic disorders.***
- ***Parents may want to consider a medical emergency bracelet for their child.***

For consultation contact:

Bryce Heese, MD
Biochemical Genetics
Children's Mercy Hospital- Kansas City, MO

Clinic phone: 816-234-3771
Hospital Operator: 816-234-3000
Office Fax: 816-302-9963