Very Long-Chain Acyl-Coenzyme A Dehydrogenase (VLCAD) Deficiency

For Healthcare Providers

This is a customized health care provider version of our website. Please visit the main website to find more comprehensive information for families and schools (www.gemssforschools.org).

Fatty Acid Oxidation Disorders Introduction

Note: not all people with VLCAD will have all of these features.

VLCAD is one of several Fatty Acid Oxidation Disorders (FAOD) in which there is an inability to break down fats, caused by an enzyme deficiency. This results in a decreased ability to go for a long time without food or calories (fasting). The fatty acid oxidation (FAO) pathway is a series of four reactions that occur within the mitochondria. The first step involves the four main enzymes known to cause the most common of the FAOD, listed below:

- Short (SCAD that uses C4-C6 fatty acyl-CoAs)
- Medium (MCAD; C6-C10 fatty acyl-CoAs)
- Long (LCAD; C10-C14 fatty acyl-CoAs)
- Very long (VLCAD; C14-C20 fatty acyl-CoAs)

With every pass through this pathway, also known as the fatty acid spiral, the chain length of the fat is shortened by two carbon atoms.

After birth, fat becomes the major energy source, especially for the heart, kidney and skeletal muscle. The liver usually relies directly on absorbed food sources and regulates the short- and medium-term storage of energy. During times of fasting, the liver uses acetyl CoA to generate ketones to be used for energy, particularly by the brain. The brain adapts to fasting by switching to a ketone economy, reducing the need for glucose as the energy source. With exercise, especially prolonged exercise, slow skeletal muscles use longer-chain FAO to generate energy. The enzyme VLCAD is involved in the first step in this transition to alternate food sources. In the absence of VLCAD activity, there is an inability to produce ketones and therefore alternative energy sources.

Physical characteristics and/or symptoms

Note: not all people with VLCAD deficiency will have all of these features.

About one in every 30,000 babies is born with VLCAD deficiency. Newborn screening for VLCAD deficiency is done in all 50 states in the US and in many other countries.

Before VLCAD was included on the newborn screening test, three types of VLCAD were recognized by the severity of the condition:

- A severe early onset form that typically presented in the first months of life and included cardiac disease (cardiomyopathy) and multi-organ failure.
- An early childhood onset form with an enlarged liver that did not include an enlarged heart (cardiomyopathy), and presented with low blood sugar (hypoglycemia).
    - Weak, shaky, dizzy with clammy cold skin
    - If not treated it can result in coma and possible death.
- A milder, later childhood or adult onset form that affects muscles. It presents with intermittent breakdown of muscle tissue (rhabdomyolysis), muscle cramps and/or pain, and/or exercise intolerance. Depending upon the length of time newborn screening has been done for VLCAD in your area, older teenagers may still present with this form and is still a recognized cause of myoglobinuria.

Now that VLCAD can be detected through newborn screening, the determination of the type of VLCAD is determined through genetic and biochemical testing. With treatment from infancy, children with all types of VLCAD are expected to live a full life. However, they are still at risk for complications in times of illness, stress, and prolonged or extreme physical activity.

Children with VLCAD do not have any distinct physical features, but can have symptoms during times of fasting, illness, stress, or prolonged physical activity. These includes

- Recurrent episodes of hypoglycemia, which can lead to multiple emergency room visits or hospitalizations, particularly within the first years of life
- Lack of energy (lethargy)
- Muscle weakness
- Liver abnormalities
- Cardiomyopathy

Dietary management is the mainstay of the treatment for VLCAD deficiency

- No prolonged fasting
    - 2-3 hours in newborn infants
    - Increasing to 8-12 hours at night as a toddler

    - Cornstarch at bedtime when longer fasting in more severe forms
- A low fat (<30% of total energy from fat) diet is recommended
    - May mean an almost non-fat diet
    - Supplements of medium-chain triglycerides (MCT) oil and walnut or similar oils in order to get their essential fats without taking in very long chain fats in more severe forms
- Carnitine supplements may benefit some children, although this is still controversial and should not be given unless there is a documented carnitine deficiency.
- Excess food intake is stored in the body as very long chains fats, so controlling the overall calories is also important to avoid obesity.
- During the school day, a student may require low fat/high carbohydrate foods throughout the day.

Be aware, or ask a parent, if the child has a medical alert bracelet.

What you can do

During the school day, a student may require low fat/high carbohydrate foods throughout the day. Parents may leave cereal or other food with the teacher or nurse to use as needed. Multiple snacks during the day may be necessary.

Ensure good hydration and carbohydrate intake during periods of exercise. Low blood sugar (hypoglycemia) must be avoided.

Ensure sick day plans are in place for illness or other times when a child cannot eat.

Notify a parent if you notice changes. Documenting is helpful.

NOTE: A child may appear hydrated and still be heading to a crisis. They still require calories to prevent or help them through the metabolic crisis/stress.

Recommended Routine Surveillance

- Routine growth monitoring with particular attention to weight
- Routine monitoring of liver function tests
- Regular assessment of micronutrient needs and essential fatty acids
- Periodic echocardiograms to assess cardiac function in the more severe forms
- Developmental evaluation and therapies as needed

Emergency Protocols

- Individuals should have an emergency letter for health care providers who may not be familiar with VLCAD deficiency. This letter should include recommendations for emergency labs to be drawn with hypoglycemia or lethargy, as well as instructions for IV fluid management
- See the examples listed below in sample forms. Note the emergency protocol should be reviewed by the metabolic specialist following the child.
- The emergency protocol should be in the child's electronic medical record

Specialists Who May Be Involved

Follow up is need on a case-by-case basis. A multidisciplinary team approach to best meet the child's individual needs is recommended. The specialists for VLCAD deficiency may include:

- Geneticist/Genetic Counselor:
  - Diagnosis
  - Coordination of care
  - Genetic risk to the family
  - Clinical trials
- Metabolic Multispecialty Clinic
  - Clinical follow-up as needed with a metabolic specialist
  - Dietician familiar with VLCAD
  - Social Worker
  - Nurse specialist
- Cardiologist
  - Coordination of surveillance and follow-up for cardiomyopathy
- Developmental Pediatrician – if needed
  - Speech therapy
  - Physical therapy
  - Occupational therapy
- Behavioral and psychiatric evaluation
- Nephrologist – if needed
  - To address any renal effects of prolonged or severe rhabdomyolysis

Sample Forms

Samples of emergency protocols/letters:
http://fodsupport.org/pdf/vlcad_protocol.pdf
http://newenglandconsortium.org/protocols/acute_illness/fatty-acid-oxidation-disorders/VLCADD.pdf

Sample paragraph to be used for letters of medical necessity or letter to schools:

My patient _____ has been diagnose with VLCAD deficiency, also known simply as VLCAD. This condition is caused by a lack of an enzyme require to break down fats for energy in times of fasting or stress. In those times, symptoms may include lethargy or just not feeling well. If left untreated, these episodes can lead to life-endangering hypoglycemia and breakdown of muscle mass. Regular treatment involves regular intake of a low-fat diet as well as attention to hydration and extra calories when needed for activities. Because of this, accommodations need to be made for frequent snacks and hydration. He/she must be allowed access to low-fat food and water as well as rest when feeling fatigued.

If an episode occurs, _____'s parents have provided an emergency protocol which must accompany _____ if a hospital or emergency room visit is warranted.

Seven Important Aspects of School Life

"VLCAD at a Glance" will help you talk with parents and schools about:

- Medical / Dietary Needs
- Education Supports
- Behavior & Sensory Supports
- Physical Activity, Trips, Events
- School Absences & Fatigue
- Emergency Planning
- Transitions

Resources

GeneReviews: VLCAD
http://www.ncbi.nlm.nih.gov/books/NBK6816/

New England Consortium of Metabolic Programs
http://newenglandconsortium.org/ and
http://newenglandconsortium.org/protocols/acute_illness/fatty-acid-oxidation-disorders/VLCADD.pdf

Genetics Home Reference
http://ghr.nlm.nih.gov/condition/very-long-chain-acyl-coa-dehydrogenase-deficiency

FOD Family Support Group
https://www.fodsupport.org/medical.htm

MCAD and VLCAD are the most common of the FAOD, but many different disorders are included in this group. Below are links to information on these other FAOD's.

- Medium Chain Acyl-CoA Dehydrogenase (MCAD) Deficiency
http://www.ncbi.nlm.nih.gov/books/NBK1424/

- Long Chain 3-Hydroxyacyl-CoA Dehydrogenase (LCHAD) Deficiency
http://ghr.nlm.nih.gov/condition/long-chain-3-hydroxyacyl-coa-dehydrogenase-deficiency

- Trifunctional Protein (TFP) Deficiency
http://www.newbornscreening.info/Parents/fattyaciddisorders/TFP.html

- Carnitine Transport Defect (Primary Carnitine Deficiency)
http://www.newbornscreening.info/Parents/fattyaciddisorders/Carnitine.html

- Carnitine-Acylcarnitine Translocase Deficiency (Translocase)
http://ghr.nlm.nih.gov/condition/carnitine-acylcarnitine-translocase-deficiency

- Carnitine Palmitoyl Transferase I & II (CPT I & II) Deficiency
http://ghr.nlm.nih.gov/condition/carnitine-palmitoyltransferase-i-deficiency

- 2,4 Dienoyl-CoA Reductase Deficiency
http://www.fodsupport.org/list.htm

- Short Chain Acyl-CoA Dehydrogenase (SCAD) Deficiency
http://ghr.nlm.nih.gov/condition/short-chain-acyl-coa-dehydrogenase-deficiency

- Short Chain L-3-Hydroxyacyl-CoA Dehydrogenase (SCHAD) Deficiency (now called 3-Hydroxy Acyl CoA Dehydrogenase Deficiency (HADH)
http://www.fodsupport.org/list.htm

- Electron Transfer Flavoprotein (ETF) Dehydrogenase Deficiency (GAII & MADD)
http://www.fodsupport.org/list.htm

- 3-Hydroxy-3 Methylglutaryl-CoA Lyase Deficiency (HMG)
http://ghr.nlm.nih.gov/condition/3-hydroxy-3-methylglutaryl-coa-lyase-deficiency