VLCAD deficiency

Other Names: Very long-chain acyl-CoA dehydrogenase deficiency; VLCADD

Categories: Congenital and Genetic Diseases (/diseases/diseases-by-category/5); Heart Diseases (/diseases/diseases-by-category/4); Metabolic disorders (/diseases/diseases-by-category/14); See More

Summary

VLCAD deficiency is a condition in which the body is unable to properly breakdown certain fats (called very long-chain fatty acids) into energy, particularly during periods without food (fasting). Signs and symptoms can occur during infancy, childhood or adulthood depending on the form of the condition and may include low blood sugar (hypoglycemia), lack of energy, and muscle weakness. Children affected by the most severe forms of the condition are also at risk of serious complications such as liver abnormalities and life-threatening heart problems. VLCAD deficiency is caused by changes (mutations) in the *ACADVL* (http://ghr.nlm.nih.gov/gene=acadvl) gene and is inherited in an autosomal recessive manner. Treatment is based on the signs and symptoms present in each person.[1][2][3]

Last updated: 6/29/2015

Symptoms

There are three forms of VLCAD deficiency: a severe, early-onset form; a hepatic (liver) or hypoketotic hypoglycemic form; and a later-onset episodic myopathic form.[1]

Signs and symptoms of the severe, early-onset form occur in the first few months of life and include cardiomyopathy (heart disease), pericardial effusion (http://www.mayoclinic.com/health/pericardial-effusion/DS01124/METHOD=print) (fluid around the heart), heart arrhythmias (http://www.nlm.nih.gov/medlineplus/arrhythmia.html) (abnormal heart beat), low muscle tone, enlarged liver, and intermittent hypoglycemia (low blood sugar). The heart problems can be life threatening, but are often improved with early treatment and diet modifications.[1][2]

People affected by the hepatic or hypoketotic hypoglycemic form typically develop symptoms during early childhood. These features may include hypoketotic hypoglycemia and enlarged

liver (without cardiomyopathy). "Hypoketotic" refers to a low level of ketones, which are produced during the breakdown of fats and used for energy. Hypoglycemia refers to low blood sugar. Together, these signs are called "hypoketotic hypoglycemia."[1]

The episodes of hypoglycemia seen in the early-onset form and hepatic/hypoketotic hypoglycemia form can cause a child to feel weak, shaky and/or dizzy with clammy, cold skin. If not treated, it can lead to coma, and possibly death. Periods of hypoglycemia can also occur with other symptoms as part of a metabolic crisis (http://www.newbornscreening.info/GlossaryTerms/metabolicCrisis.html).[4]

Signs and symptoms of the later-onset episodic myopathic form may include intermittent rhabdomyolysis (breakdown of muscle), muscle cramps, muscle pain, and exercise intolerance. It is the most common form of VLCAD deficiency.[1]

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Cause

VLCAD deficiency is caused by changes (mutations) in the *ACADVL* (http://ghr.nlm.nih.gov/gene/ACADVL) gene. This gene encodes an enzyme that is required for the proper break down (metabolism) of a certain group of fats called very long-chain fatty acids. Mutations in the *ACADVL* gene lead to reduced levels of this enzyme which prevents the proper metabolism of these fats. Because very long-chain fatty acids are an important source of energy, particularly for the heart and muscles, this may result in certain symptoms such as lethargy and hypoglycemia. Fats that are not properly broken down can also build-up and damage tissues such as the heart, liver, and muscles, which can cause the other features seen in people with VLCAD deficiency.[3][1][4]

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Inheritance

VLCAD deficiency is inherited in an autosomal recessive manner.[1] This means that to be affected, a person must have a mutation in both copies of the responsible gene in each cell. The parents of an affected person usually each carry one mutated copy of the gene and are referred to as carriers. Carriers typically do not show signs or symptoms of the condition. When two carriers of an autosomal recessive condition have children, each child has a 25% (1 in 4) risk to have the condition, a 50% (1 in 2) risk to be a carrier like each of the parents, and a 25% chance to not have the condition *and* not be a carrier.

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Diagnosis

A diagnosis of VLCAD deficiency may be suspected based on an abnormal newborn screen (http://www.nlm.nih.gov/medlineplus/ency/article/007257.htm) or the presence of

characteristic signs and symptoms (https://rarediseases.info.nih.gov/gard/5508/vlcad-deficiency/resources/9). In both of these cases, additional testing can then be ordered to further investigate the diagnosis. This testing may include specialized tests performed on a sample of blood, urine, skin cells, muscle, and/or liver tissue. Genetic testing for changes (mutations) in the *ACADVL* (http://ghr.nlm.nih.gov/gene/ACADVL) gene can confirm the diagnosis.[1][2]

GeneReview's (http://www.ncbi.nlm.nih.gov/books/NBK6816/#vlcad.Diagnosis) Web site offers more specific information about the diagnosis of VLCAD deficiency. Please click on the link to access this resource.

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Testing Resources

The Genetic Testing Registry (http://www.ncbi.nlm.nih.gov/gtr/conditions/C0342784/) (GTR) provides information about the genetic tests for this condition. The intended audience for the GTR is health care providers and researchers. Patients and consumers with specific questions about a genetic test should contact a health care provider or a genetics professional.

Newborn Screening

An ACTion (ACT) sheet (http://www.acmg.net/StaticContent/ACT/C14.pdf) is available for this condition that describes the short-term actions a health professional should follow when an infant has a positive newborn screening result. ACT sheets were developed by experts in collaboration with the American College of Medical Genetics.

An Algorithm (http://www.acmg.net/StaticContent/ACT/Algorithms/Visio-C14-1_DM.pdf) flowchart is available for this condition for determining the final diagnosis in an infant with a positive newborn screening result. Algorithms are developed by experts in collaboration with the American College of Medical Genetics.

Baby's First Test (http://www.babysfirsttest.org/) is the nation's newborn screening education center for families and providers. This site provides information and resources about screening at the local, state, and national levels and serves as the Clearinghouse for newborn screening information.

National Newborn Screening and Global Resource Center (http://genes-r-us.uthscsa.edu/) (NNSGRC) provides information and resources in the area of newborn screening and genetics to benefit health professionals, the public health community, consumers and government officials.

Treatment

Management of VLCAD deficiency depends on many factors, including the form of the condition and the specific signs and symptoms present. For example, people affected by the severe forms of the condition are typically placed on a low-fat, high-carbohydrate diet with frequent meals. Supplemental calories may be provided through medium-chain triglycerides

(MCT oil). If hospitalization is necessary for acute episodes of hypoglycemia and/or metabolic crisis (http://www.newbornscreening.info/GlossaryTerms/metabolicCrisis.html), intravenous glucose may be administered as an energy source. Periods of rhabdomyolysis (http://www.nlm.nih.gov/medlineplus/ency/article/000473.htm) may be treated with hydration and alkalization of the urine (decreasing the amount of acid you take in) to protect kidney function and to prevent acute kidney failure (http://www.nlm.nih.gov/medlineplus/ency/article/000501.htm). Affected people are generally advised to avoid fasting, dehydration, and a high-fat diet.[1][2]

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Management Guidelines

Orphanet Emergency Guidelines (https://www.orpha.net/data/patho/Pro/en/Emergency_BIMDG_LongChainFatOxidation-enPro8768.pdf) is an article which is expert-authored and peer-reviewed that is intended to guide health care professionals in emergency situations involving this condition.

Find a Specialist

If you need medical advice, you can look for doctors or other healthcare professionals who have experience with this disease. You may find these specialists through advocacy organizations, clinical trials, or articles published in medical journals. You may also want to contact a university or tertiary medical center in your area, because these centers tend to see more complex cases and have the latest technology and treatments.

If you can’t find a specialist in your local area, try contacting national or international specialists. They may be able to refer you to someone they know through conferences or research efforts. Some specialists may be willing to consult with you or your local doctors over the phone or by email if you can't travel to them for care.

You can find more tips in our guide, How to Find a Disease Specialist (/guides/pages/25/how-to-find-a-disease-specialist). We also encourage you to explore the rest of this page to find resources that can help you find specialists.

Healthcare Resources

To find a medical professional who specializes in genetics, you can ask your doctor for a referral or you can search for one yourself. Online directories are provided by the American College of Medical Genetics (https://www.acmg.net/ACMG/Find_Genetic_Services/ACMG/ISGweb/FindaGeneticService.aspx?hkey=720856ab-a827-42fb-a788-b618b15079f9) and the National Society of Genetic Counselors (https://www.findageneticcounselor.com/). If you need additional help, contact a GARD Information Specialist (https://rarediseases.info.nih.gov/about-gard/contact-gard). You can also learn more about genetic consultations (https://ghr.nlm.nih.gov/primer#consult) from Genetics Home Reference.

You can submit a question to Ask the Mito Doc℠ (http://www.askthemitodoc.org/site/c.cjINK3NLLgJ4E/b.8037069/k.5CF1/Ask_the_Mito_D

ocsmallsupSMsupsmall.htm), a service of the United Mitochondrial Diseases Foundation. Information contained in Ask the Mito Doc[SM] is for informational and educational purposes only.

Prognosis

The long-term outlook (prognosis) for people with VLCAD deficiency is hard to predict and can vary based on the severity of the condition.

For people with the severe, early-onset form, cardiomyopathy and arrhythmias (http://www.nhlbi.nih.gov/health/health-topics/topics/arr/) can be lethal. However, heart function can be improved with early treatment and specific diet modifications. Normal intellectual outcome has been reported in people with this form.[1]

For people with the hepatic (liver) or hypoketotic hypoglycemic form, hypoketotic hypoglycemia can cause a loss of consciousness or seizures.[1]

People with the later-onset episodic myopathic form may only have muscle-related symptoms. Some people with this form may not be diagnosed until adulthood. Since the later-onset form can have vague or intermittent symptoms, it is possible that some people may have no symptoms during their lifetime.[1]

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Do you have updated information on this disease? We want to hear from you. (/Feedback?diseaseId=5508)

Research

Research helps us better understand diseases and can lead to advances in diagnosis and treatment. This section provides resources to help you learn about medical research and ways to get involved.

Clinical Research Resources

ClinicalTrials.gov (http://www.clinicaltrials.gov/ct2/results?cond=%22VLCAD+deficiency%22) lists trials that are related to VLCAD deficiency. Click on the link to go to ClinicalTrials.gov to read descriptions of these studies.

Please note: *Studies listed on the ClinicalTrials.gov website are listed for informational purposes only; being listed does not reflect an endorsement by GARD or the NIH. We strongly recommend that you talk with a trusted healthcare provider before choosing to participate in any clinical study.*

Organizations

Support and advocacy groups can help you connect with other patients and families, and they can provide valuable services. Many develop patient-centered information and are the driving force behind research for better treatments and possible cures. They can direct you to research, resources, and services. Many organizations also have experts who serve as medical advisors or provide lists of doctors/clinics. Visit the group's website or contact them to learn about the services they offer. Inclusion on this list is not an endorsement by GARD.

Organizations Supporting this Disease

FOD (Fatty Oxidation Disorder) Family Support Group (/organizations/175)
P.O. Box 54
Okemos, MI 48805-0054
Telephone: 517-381-1940
Fax: 866-290-5206
E-mail: deb@fodsupport.org (mailto:deb@fodsupport.org)
Website: http://www.fodsupport.org (http://www.fodsupport.org)

United Mitochondrial Disease Foundation (/organizations/176)
8085 Saltsburg Road, Suite 201
Pittsburgh, PA 15239
Toll-free: 888-317-8633
Telephone: 412-793-8077
Fax: 412-793-6477
E-mail: info@umdf.org (mailto:info@umdf.org)
Website: http://www.umdf.org (http://www.umdf.org)

Do you know of an organization? We want to hear from you. (/Feedback?diseaseId=5508)

Living With

Living with a genetic or rare disease can impact the daily lives of patients and families. These resources can help families navigate various aspects of living with a rare disease.

Education Resources

The Genetics Education Materials for School Success (GEMSS) (http://www.gemssforschools.org/conditions/vlcad/default) aims to assure that all children with genetic health conditions succeed in school-life. Their Web site offers general and condition-specific education resources to help teachers and parents better understand the needs of students who have genetic conditions.

Learn More

These resources provide more information about this condition or associated symptoms. The in-depth resources contain medical and scientific language that may be hard to understand. You may want to review these resources with a medical professional.

Where to Start

Genetics Home Reference (GHR) (http://www.ghr.nlm.nih.gov/condition=verylongchainacylcoenzymeadehydrogenasedeficiency) contains information on VLCAD deficiency. This website is maintained by the National Library of Medicine.

The National Organization for Rare Disorders (http://www.rarediseases.org/rare-disease-information/rare-diseases/byID/1053/viewAbstract) (NORD) has a report for patients and families about this condition. NORD is a patient advocacy organization for individuals with rare diseases and the organizations that serve them.

The Screening, Technology And Research in Genetics (STAR-G) Project (http://www.newbornscreening.info/Parents/fattyaciddisorders/VLCADD.html) has a fact sheet on this condition, which was written specifically for families that have received a diagnosis as a result of newborn screening. This fact sheet provides general information about the condition and answers questions that are of particular concern to parents.

In-Depth Information

GeneReviews (http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=gene&part=vlcad) provides current, expert-authored, peer-reviewed, full-text articles describing the application of genetic testing to the diagnosis, management, and genetic counseling of patients with specific inherited conditions.

The Monarch Initiative (https://monarchinitiative.org/disease/OMIM:201475) brings together data about this condition from humans and other species to help physicians and biomedical researchers. Monarch's tools are designed to make it easier to compare the signs and symptoms (phenotypes) of different diseases and discover common features. This initiative is a collaboration between several academic institutions across the world and is funded by the National Institutes of Health. Visit the website to explore the biology of this condition.

Online Mendelian Inheritance in Man (OMIM) (http://www.omim.org/609575) is a catalog of human genes and genetic disorders. Each entry has a summary of related medical articles. It is meant for health care professionals and researchers. OMIM is maintained by Johns Hopkins University School of Medicine.

Orphanet (http://www.orpha.net/consor/cgi-bin/OC_Exp.php?lng=en&Expert=26793) is a European reference portal for information on rare diseases and orphan drugs. Access to this database is free of charge.

PubMed (http://www.ncbi.nlm.nih.gov/pubmed?term=Very%20long-chain%20acyl-CoA%20dehydrogenase%20deficiency%5BTitle%5D%20OR%20VLCAD%5BTitle%5D%20AND%20hasabstract%5Btext%5D&cmd=DetailsSearch) is a searchable database of medical literature and lists journal articles that discuss VLCAD deficiency. Click on the link to view a

sample search on this topic.

News & Events

News

National DNA Day Reddit "Ask Me Anything" (AMA) Series (/news/615)
April 11, 2018

Other Conferences

The International Network for Fatty Acid Oxidation Research and Management (http://www.informnetwork2014.org/) (INFORM) has been formed in order to promote research and discussion into the cause, diagnosis, and management of inborn errors of fatty acid oxidation. INFORM will sponsor an inaugural symposium to be held on September 6, 2014 in Innsbruck, Austria following SSIEM, with annual meetings thereafter. The Network will provide a collaborative framework for ongoing communication and research between the members.

GARD Answers

Questions sent to GARD may be posted here if the information could be helpful to others. We remove all identifying information when posting a question to protect your privacy. If you do not want your question posted, please let us know. Submit a new question (/about-gard/contact-gard)

My husband and I were recently told we are carriers, and our first baby girl died at about 40 hrs old from VLCAD. I am now pregnant with another little girl and we worry about this baby having VLCAD. What are the chances that she comes out and has the condition and dies? And if she does have it, is there any treatment I can do before she's born? Can she survive having the mutated gene and live a healthy life? See answer (/diseases/5508/vlcad-deficiency/cases/42731)

What is the life expectancy of a child with VLCAD deficiency? Who are the best doctors in the United States for this condition? I was told that my child has one mutated gene and one with significant variables. Does that mean she has the condition?
See answer (/diseases/5508/vlcad-deficiency/cases/21792)

Have a question? Contact a GARD Information Specialist. (/about-gard/contact-gard)

References

1. Nancy D Leslie, MD, C Alexander Valencia, PhD, Arnold W Strauss, MD, Jessica Connor,

MS, and Kejian Zhang, MD, MBA. Very Long-Chain Acyl-Coenzyme A Dehydrogenase Deficiency. *GeneReviews*. September 2014; http://www.ncbi.nlm.nih.gov/books/NBK6816/ (http://www.ncbi.nlm.nih.gov/books/NBK6816/).

2. Very Long Chain Acyl CoA Dehydrogenase Deficiency (LCAD). *NORD*. 2013; http://rarediseases.org/rare-diseases/very-long-chain-acyl-coa-dehydrogenase-deficiency-lcad/ (http://rarediseases.org/rare-diseases/very-long-chain-acyl-coa-dehydrogenase-deficiency-lcad/).
3. VLCAD deficiency. *Genetics Home Reference Web site*. 11/2009; http://ghr.nlm.nih.gov/condition/very-long-chain-acyl-coa-dehydrogenase-deficiency (http://ghr.nlm.nih.gov/condition/very-long-chain-acyl-coa-dehydrogenase-deficiency).
4. Very long chain acyl-CoA dehydrogenase. *STAR-G*. July 2013; http://www.newbornscreening.info/Parents/fattyaciddisorders/VLCADD.html#3 (http://www.newbornscreening.info/Parents/fattyaciddisorders/VLCADD.html#3).

Do you know of a review article? We want to hear from you. (/Feedback?diseaseId=5508)
