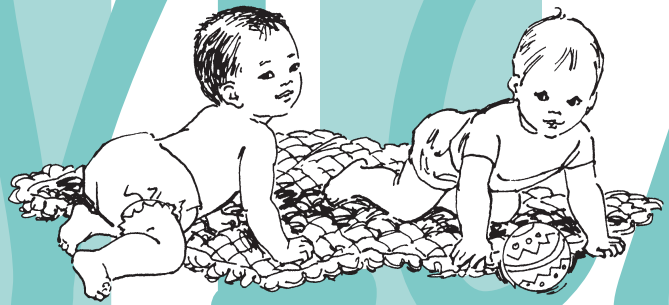
Parents' Guide to VLCADD

Very Long Chain Acyl-CoA Dehydrogenase Deficiency

VLCADD



California
Department of
Health Services

Newborn Screening Program
Genetic Disease Branch
www.dhs.ca.gov/gdb

June 2005

Table of Contents

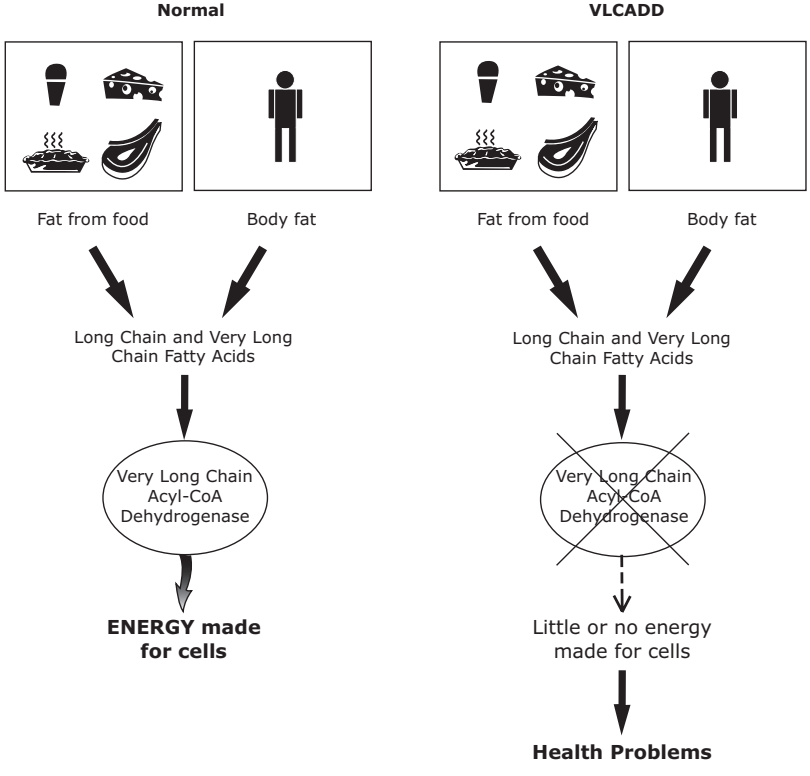
Contents	Page
What is VLCADD?	1-7
Treatment for VLCADD	7-13
Inheritance of VLCADD	14-15
Testing for VLCADD	15-18
Occurrence of VLCADD	18
Resources	19-20
Glossary	21-24*

*Underlined words in booklet are defined in the Glossary

The information in this booklet is general and is not meant to be specific to each child with VLCADD. Certain treatments may be recommended for some children but not others. Children with VLCADD should be followed by a physician specializing in metabolic diseases (metabolic specialist) in addition to their primary doctor. For a list of metabolic centers, see page 20 or visit our website at www.dhs.ca.gov/gdb.

What is VLCADD?

VLCADD stands for “very long chain acyl-CoA dehydrogenase deficiency”. It is one type of fatty acid oxidation disorder. People with VLCADD have problems breaking down certain types of fat into energy for the body.



What causes VLCADD?

VLCADD occurs when an enzyme, called “very long chain acyl-CoA dehydrogenase” (VLCAD), is either missing or not working properly. This enzyme’s job is to break down certain fats from the food we eat into energy. It also breaks down fat already stored in the body. Energy from fat keeps us going whenever our bodies run low of their main source of energy, a type of sugar called glucose. Our bodies rely on fat when we don’t eat for a while – such as when we miss a meal or when we sleep.

When the VLCADD enzyme is missing or not working, the body cannot break down fat for energy and must rely solely on glucose. Although glucose is a good source of energy, there is a limited amount available. Once the glucose has been used up, the body tries to use fat without success. This leads to low blood sugar, called hypoglycemia, and to the build up of harmful substances in the blood.

What causes the VLCAD enzyme to be missing or not working correctly?

Genes tell the body to make various enzymes. People with VLCADD have a pair of genes that do not work correctly. Because of the changes in this pair of genes, the VLCAD enzyme either does not work properly or is not made at all.

If VLCADD is not treated, what problems occur?

VLCADD is variable and can cause mild effects in some people and more serious health problems in others. Symptoms may start in infancy or not until adulthood. There are three forms of VLCADD: “Early”, “Childhood” and “Adult”.

It is common for babies and children with the early and childhood types of VLCADD to have episodes of illness called metabolic crises. Some of the first symptoms of a metabolic crisis are

extreme sleepiness, behavior changes, irritable mood, and poor appetite. Crises are often set off by an infection so illness may start with symptoms of fever, nausea, diarrhea, and vomiting. Low blood sugar then follows. If a metabolic crisis is not treated, a child with VLCADD can develop breathing problems, seizures, and coma, sometimes leading to death.

Periods of low blood sugar can happen with or without the other symptoms. Low blood sugar can cause a child to feel weak, shaky, or dizzy with clammy, cold skin. If not treated, it can lead to coma, and possibly death.

Either low blood sugar or a full metabolic crisis can occur:

- after going too long without food
- during illness or infection
- after heavy exercise

Symptoms of early and childhood VLCADD often happen after a period of having nothing to eat for more than a few hours. Symptoms are also more likely when a child with VLCADD gets sick or has an infection.

Early VLCADD

About half of babies diagnosed with VLCADD have the “early” type. They usually start to show effects between birth and 4 months. In addition to metabolic crises, babies can also have:

- enlarged heart, irregular heartbeat and other heart problems
- enlarged liver and other liver problems
- muscle problems

If not treated, babies with early VLCADD usually die young.

Childhood VLCADD

About one third of people with VLCADD have the childhood type. They usually show symptoms in late infancy or early childhood. Episodes of low blood sugar or full metabolic crisis happen during illness or after long periods of not eating.

Other effects can include:

- enlarged liver
- other liver problems
- muscle weakness, especially after exercise

Heart problems are usually not seen in childhood VLCADD.

Some children with VLCADD have never had symptoms and are only found after a brother or sister has been diagnosed.

Adult VLCADD

About one fifth of people with VLCADD have the adult type. They usually show symptoms starting in the teen years or in adulthood. Periods of muscle weakness are common. Breakdown of muscle fibers can occur. This usually happens during heavy exercise or after going without food for a long period of time.

Signs of muscle breakdown are:

- muscle aches
- weakness
- cramps
- reddish-brown color to the urine

Adults with muscle symptoms who do not get treatment can develop kidney failure. People with the adult form of VLCADD usually do not have heart problems, low blood sugar or metabolic crises.

What happens when VLCADD is treated?

With prompt and careful treatment, people with the childhood and adult forms of VLCADD can often live healthy lives with typical growth and development.

Before diagnosis through newborn screening was available, the early form of VLCADD was fatal. Now, with immediate and ongoing treatment, many infants with VLCADD are surviving.

What is the treatment for VLCADD?

Your baby's primary doctor will work with a metabolic specialist to care for your child. Your doctor may also suggest that you meet with a dietician familiar with VLCADD.

Certain treatments may be advised for some children but not others. When necessary, treatment is usually needed throughout life. The following are treatments often recommended for children with VLCADD:

1. Avoid going a long time without food

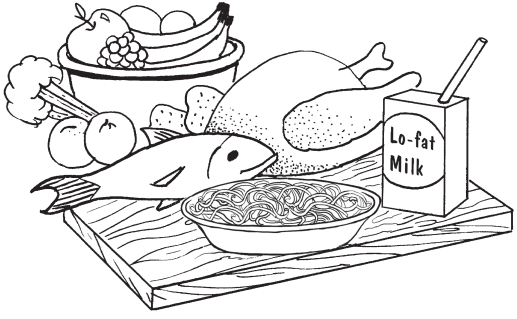
Babies and young children with VLCADD need to eat frequently to avoid low blood sugar or a metabolic crisis. These children should not go without food for more than 4 to 6 hours. Some babies may need to eat even more often than this. It is important that babies be fed during the night. You need to wake them up if they do not wake up on their own.

Children with VLCADD should have a starchy snack before bed and another during the night. They need another snack first thing in the morning. Raw cornstarch mixed with water, milk, or other drink is a good source of long-lasting energy. It is sometimes suggested for children older than one year of age. Your dietician can give you ideas for good snacks.

When they are well, most teens and adults with VLCADD can go without food for up to 12 hours without problems. They do need to continue the other treatments throughout life.

2. Diet

Sometimes a low fat, high carbohydrate diet is recommended. Carbohydrates give the body many types of sugar that can be used as energy. In fact, for children needing this treatment, most food in the diet should be carbohydrates (bread, pasta, fruit, etc.) and protein (lean meat and low-fat dairy foods).



People with VLCADD cannot use certain building blocks of fat called long chain fatty acids. Your dietician can help create a food plan low in these fats. Much of the rest of fat in the diet may be in the form of medium chain fatty acids.

Ask your doctor whether your child needs to have any changes in his or her diet. Any diet changes should be made under the guidance of a dietician.

3. MCT oil and L-carnitine

Medium Chain Triglyceride oil (MCT oil) is often used as part of the food plan for people with VLCADD. This special oil has medium chain fatty acids that can be used in small amounts for energy. Your metabolic specialist or dietician can guide you in how to use this supplement. You will need to get a prescription from your doctor to get MCT oil.

Some children may be helped by taking L-carnitine. This is a safe and natural substance that helps the body make energy. It also helps the body get rid of harmful wastes. Your doctor will decide whether your child needs L-carnitine.

Do not use any medication without checking with your doctor.

4. Call your doctor immediately at the sign of any of these symptoms in your child:

- poor appetite
- low energy or excessive sleepiness
- vomiting
- diarrhea
- an infection
- a fever
- persistent muscle pain, weakness, or reddish-brown color to the urine

Children with VLCADD need to eat extra starchy food and drink more fluids during any illness – even if they may not feel hungry – or they could develop low blood sugar or a metabolic crisis. When they become sick, children with VLCADD need to be treated in the hospital with intravenous (IV) glucose to prevent serious health problems.

5. Avoid prolonged exercise or exertion

Long periods of exercise can also trigger symptoms. Problems occurring during or after exercise can include the following symptoms of muscle breakdown:

- muscle aches
- weakness
- cramps
- reddish-brown color to the urine

If a person with VLCADD is having these symptoms, prompt treatment is needed to prevent kidney damage. Children and adults with these muscle symptoms should:

- drink fluids right away
- eat something starchy or sugary
- get to a hospital for treatment

To help prevent muscle symptoms:

- avoid prolonged or heavy exercise
- keep the body warm
- eat carbohydrates before and during periods of moderate exercise

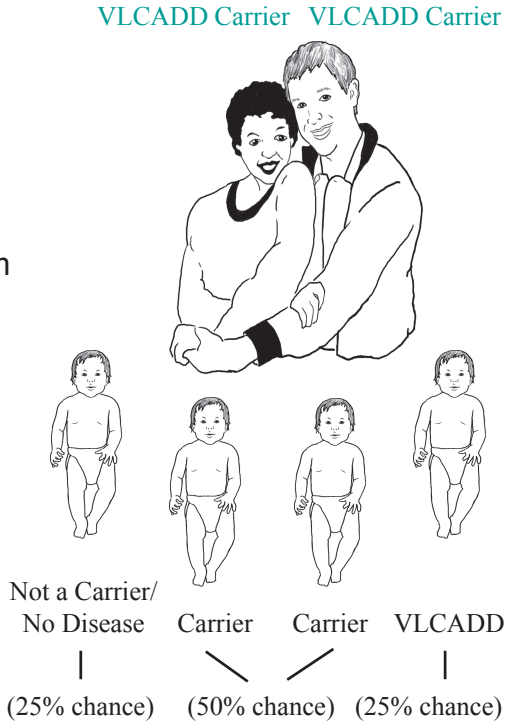
How is VLCADD inherited?

VLCADD affects both boys and girls equally.

Everyone has a pair of genes that make the VLCAD enzyme. In children with VLCADD, neither of these genes works correctly. These children inherit one non-working gene for the condition from each parent. This is called autosomal recessive inheritance.

Parents of children with VLCADD are rarely affected with the disorder. Instead, each parent has a single non-working gene for VLCADD. They are called carriers. Carriers are not affected because their other gene of this pair is working correctly.

When both parents are carriers, there is a 25% chance in each pregnancy for the child to have two working genes. This means the child is not a carrier and does not have the disease. There is a 50% chance for the child to be a carrier, just like the parents. There is a 25% chance for the child to have VLCADD.



Chances apply to each pregnancy

Genetic counseling is available to families who have children with VLCADD. Genetic counselors can answer your questions about how VLCADD is inherited, options during future pregnancies, and how to test other family members. Other family members can also ask about genetic counseling and testing for VLCADD.

Is genetic testing available?

Genetic testing, also called DNA testing, looks for changes in the pair of genes that cause VLCADD. Talk with your metabolic specialist or genetic counselor about DNA testing for VLCADD.

DNA testing may not be necessary to diagnose your child. However, it can be helpful for carrier testing or prenatal diagnosis.

What other testing is available?

VLCADD can be confirmed by a special test called a “fatty acid oxidation probe” using a skin sample. Talk to your doctor or genetic counselor if you have questions about testing for VLCADD.

Can you test during pregnancy?

Yes, it is possible to test for VLCADD during pregnancy. The sample needed for this test is obtained by either CVS or amniocentesis.

Parents may either choose to have testing during pregnancy or wait until birth to have the baby tested. A genetic counselor can talk to you about your choices and answer other questions you may have about prenatal testing or testing your baby after birth.

Can other members of the family have VLCADD or be carriers?

The brothers and sisters 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. Talk to your doctor or genetic counselor about testing your other children for VLCADD.

Brothers and sisters who do not have VLCADD still have a chance to be carriers like their parents. Carriers do not have the disorder and will never develop it.

Each of the parents' brothers and sisters has a chance to be a VLCADD carrier. It is important for other family members to be told that they could be carriers. There is a small chance they are also at risk to have children with VLCADD.

When both parents are carriers or have had a baby with VLCADD, subsequent newborns should have special diagnostic testing in addition to the newborn screen to test for VLCADD.

During pregnancy, women carrying fetuses with VLCADD may be at increased risk to develop serious medical problems.

A small number of women are known to have developed:

- excessive vomiting
- abdominal pain
- high blood pressure
- jaundice
- abnormal fat storage in the liver
- severe bleeding

All women with a family history of VLCADD should share this information with their obstetricians and other health care providers before and during any future pregnancies. Knowing about these risks allows early treatment.

How many people have VLCADD?

VLCADD is thought to be a rare disorder. The actual incidence is unknown. VLCADD does not happen more often in any specific race, ethnic group, geographical area or country.

Does VLCADD go by any other names?

VLCADD is sometimes also called:

- VLCAD deficiency
- ACADVL deficiency

RESOURCES

Fatty Oxidation Disorders (FOD)
Family Support Group
1559 New Garden Road, 2E
Greensboro, NC 27410
(336) 547-8682
www.fodsupport.org

United Mitochondrial Disease Foundation
8085 Saltsburg Road, Suite 201
Pittsburgh, PA 15239
(412) 793-8077
www.umdf.org

Children Living with Inherited Metabolic Diseases
CLIMB Building
176 Nantwich Road
Crewe, CW2 6BG
United Kingdom
www.climb.org.uk

Genetic Alliance
4301 Connecticut Ave. NW, Suite 404
Washington, DC 20008-2369
(202) 966-5557
www.geneticalliance.org

CALIFORNIA METABOLIC CENTERS

Cedars-Sinai Medical Center, Los Angeles
(310) 423-9914

Children's Hospital Central California, Madera
(559) 353-6400

Children's Hospital & Research Center, Oakland
(510) 428-3550

Children's Hospital Los Angeles
(323) 660-2450

Children's Hospital of Orange County, Orange
(714) 532-8852

Children's Hospital San Diego Health Center, La Jolla
(619) 543-7800

Harbor/UCLA Medical Center Torrance
(310) 222-3756

Kaiser Permanente - No. Cal.
(510) 752-7703

Kaiser Permanente - So. Cal.
(323) 783-6970

LAC/USC Medical Center Los Angeles
(323) 226-3816

Lucile Salter Packard Children's Hospital at Stanford
(650) 723-6858

Sutter Medical Center Sacramento
(916) 733-6023

UC Davis Medical Center
(916) 734-3112

UC San Francisco Medical Center
(415) 476-2757

UCLA Medical Center
(310) 206-6581

UCI Medical Center, Orange
(714) 456-8513

GLOSSARY

Amniocentesis - Test done during pregnancy (usually between 16 and 20 weeks). A needle is used to remove a small sample of fluid from the sac around the fetus. The sample can be used to test for certain genetic disorders in the fetus.

Autosomal recessive - Autosomal recessive conditions affect both boys and girls equally. How autosomal recessive inheritance works: Everyone has a pair of genes responsible for making each enzyme in the body. A person with a metabolic disorder has one enzyme that is either missing or not working properly. The problem is caused by a pair of "recessive" genes that are not working correctly. They do not make the needed enzyme. A person has to have two non-working "recessive" genes in order to have an autosomal recessive metabolic disorder. A person with an autosomal recessive disorder inherits one non-working gene from their mother and the other from their father.

Carrier - A person who has a gene mutation in one of their genes that cause a disease, but does not have any symptoms of the disease. The mutation is often recessive, which means that both copies of the gene have to be mutated in order for disease symptoms to develop. Carriers are able to pass the mutation onto their children and therefore have an increased chance of having a child with the disease.

CVS - Chorionic Villus Sampling (CVS) is a special test done during early pregnancy (usually between 10 and 12 weeks). A small sample of the placenta is removed for testing. This sample can be used to test for certain genetic disorders in the fetus.

DNA - Deoxyribonucleic acid (DNA) is a molecule that makes up chromosomes. It is composed of four units (called bases) that are designated A, T, G, and C. The sequence of the bases spell out instructions for making all of the proteins in an organism. The instructions set for each individual protein is a gene. A change in one of the DNA letters making up a gene is a mutation. In some cases, these mutations can alter the protein instructions and lead to disease. Each individual passes their chromosomes on to their children, and therefore pass down the DNA instructions. It is these instructions that cause certain traits, such as eye or hair color, to be inherited.

Enzyme - A molecule that helps chemical reactions take place. For example, enzymes in the stomach speed up the process of breaking down food. Each enzyme can participate in many chemical reactions without changing or being used up.

Fatty Acid Oxidation Disorders (FAODs) - A group of rare inherited conditions. FAODs are caused by missing or non-working enzymes. Normally, many enzymes are used by the body to break down fat into energy. In people with FAODs, one of these enzymes is not working and fat connot be used for energy. If these conditions are not treated, they can lead to serious health problems.

Gene - A segment of DNA that contains the instructions to make a specific protein (or part of a protein). Genes are contained on chromosomes. Chromosomes, and the genes on those chromosomes, are passed on from parent to child. Errors in the DNA that make up a gene are called mutations and can lead to diseases.

Genetic Counseling - Genetic counseling gives patients and their families education and information about genetic-related conditions and helps them make informed decisions. It is often provided by Genetic Counselors or Medical Geneticists who have special training in inherited disorders.

Jaundice - A yellow color to the skin and whites of the eyes. It is often a sign of liver damage or dysfunction (ie., not working properly).

Long chain fatty acids - One of many types of fatty acids, the building blocks of fat. Long-chain fatty acids are made up of chains of 12 or more carbon atoms.

Medium chain fatty acids - One of many types of fatty acids, the building blocks of fat. Medium-chain fatty acids are made up of chains of 4 to 12 carbon atoms.

Medium Chain Triglyceride (MCT) oil - A special type of oil made up of medium chain triglycerides - a type of fatty acid. MCT oil can be used for energy by people with long chain fatty acid oxidation disorders. A doctor's prescription is needed to get MCT oil. It should be used only under the guidance of a registered dietician.

Metabolic Crisis - A serious health condition caused by low blood sugar and the build-up of toxic substances in the blood. Symptoms of a metabolic crisis are: poor appetite, nausea, vomiting, diarrhea, extreme sleepiness, irritable mood and behavior changes. Metabolic crises happen more often in people with certain metabolic disorders (some fatty acid oxidation disorders, amino acid disorders, and organic acid disorders). If not treated, breathing problems, seizures, coma, and sometimes even death can occur. They are often triggered by things like illness or infection, going without food for a long time, and, in some cases, heavy exercise.

Seizures - These are also called "convulsions" or "fits". During a seizure, a person loses consciousness and control of their muscles. It may also cause involuntary movements. Seizures can happen for many reasons. Some causes are metabolic disorders, a metabolic crisis, brain injury, and infection.

This booklet has been adapted from the materials developed by STAR-G Project – a multi-state collaborative project including representatives from California DHS, Newborn Screening Program, and funded by a federal grant from the MCH Bureau, Project #1 H46 MC 00189-02.

Acknowledgements

We would like to thank the following people for their help in reviewing and providing input into this booklet:

- Metabolic Specialists and Dieticians at California Children's Services (CCS) Approved Metabolic Centers
- California Newborn Screening Area Service Center staff
- Parents of children with VLCADD

© CA Department of Health Services, Genetic Disease Branch, Newborn Screening Section, June 2005