Genetic Fact Sheets for Parents

Fatty Acid Oxidation Disorders

Screening, Technology, and Research in Genetics is a multi-state project to improve information about the financial, ethical, legal, and social issues surrounding expanded newborn screening and genetic testing – http:// www.newbornscreening.info

Disorder name: Long chain 3-hydroxyacyl-CoA dehydrogenase deficiency
Acronym: LCHADD

- What is LCHADD?
- What causes LCHADD?
- If LCHADD is not treated, what problems occur?
- What is the treatment for LCHADD?
- What happens when LCHADD is treated?
- What causes the LCHAD enzyme to be absent or not working correctly?
- How is LCHADD inherited?
- Is there genetic testing available?
- What other testing is available?
- Can you test during a future pregnancy?
- Can other members of the family have LCHADD or be carriers?
- Can other family members be tested?
- How many people have LCHADD?
- Does LCHADD happen more often in a certain ethnic group?
- Does LCHADD go by any other names?
- Where can I find more information?

This fact sheet contains general information about LCHADD. Every child is different and some of this information may not apply to your child specifically. Certain treatments may be recommended for some children but not others. Children with LCHADD should be followed by a metabolic doctor in addition to their primary doctor.

What is LCHADD?

LCHADD stands for “long chain 3-hydroxyacyl-CoA dehydrogenase deficiency.” It is one type of **fatty acid oxidation disorder**. People with LCHADD have problems breaking down fat into energy for the body.

Fatty Acid Oxidation Disorders:

Fatty acid oxidation disorders (FAODs) are a group of rare inherited conditions. They are caused by enzymes that do not work properly.

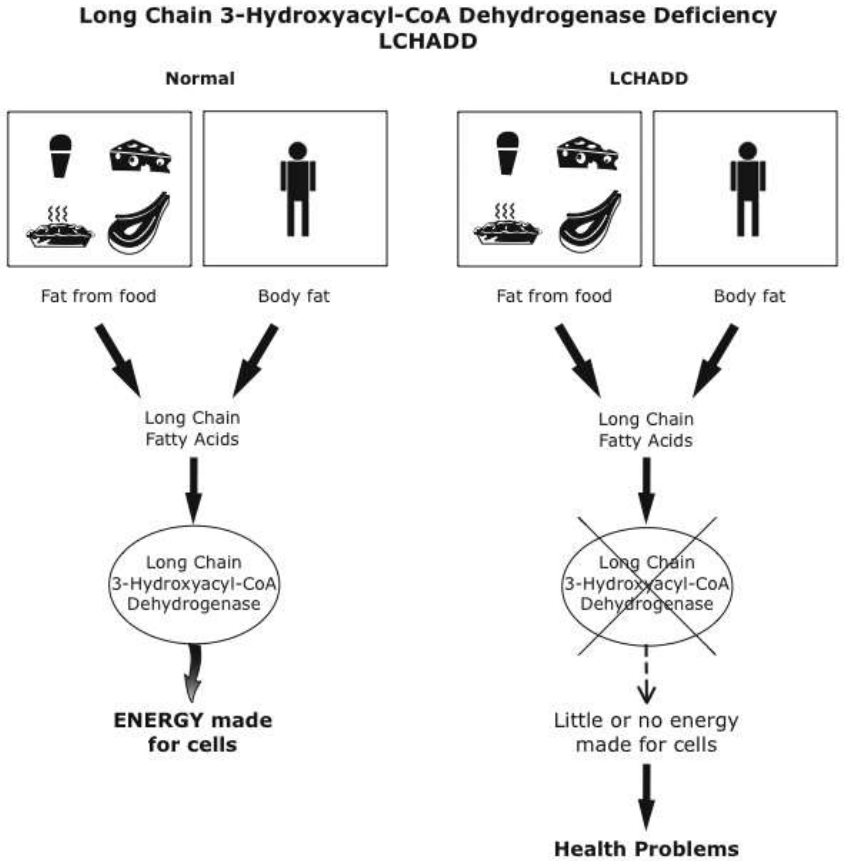
A number of enzymes are needed to break down fats in the body (a process called fatty acid oxidation). Problems with any of these enzymes can cause a fatty acid oxidation disorder. People with FAODs cannot properly break down fat from either the food they eat or from fat stored in their bodies.

The symptoms and treatment vary between different FAODs. They can also vary from person to person with the same FAOD. See the fact sheets for each specific FAOD.

FAODs are inherited in an autosomal recessive manner and affect both males and females.

What causes LCHADD?

LCHADD is caused by problems with the enzyme "long chain 3-hydroxyacyl-CoA dehydrogenase" (LCHAD). In people with LCHADD, the LCHAD enzyme 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 stretch of time – like when we miss a meal or when we sleep.

When the LCHAD enzyme is missing or not working well, the body cannot break down fat for energy. Instead, it 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.

If LCHADD is not treated, what problems occur?

LCHADD can cause mild effects in some people and more serious health problems in others. Babies and children with LCHADD usually begin to show symptoms sometime from birth through age two. LCHADD causes episodes of hypoglycemia. The first symptoms of hypoglycemia are:

- extreme sleepiness or fatigue
- weakness
- nausea
- vomiting
- irritability or jitteriness
- behavior changes

If hypoglycemia is not treated, a child with LCHADD can develop:

- breathing problems
- swelling of the brain
- seizures
- coma, sometimes leading to death

Symptoms often happen after having nothing to eat for more than a few hours. Symptoms are also more likely to occur when a person with LCHADD gets sick or has an infection.

Between episodes of hypoglycemia, people with LCHADD are usually healthy. However, repeated episodes can cause brain damage. This can result in learning problems or intellectual disabilities.

Babies and children who are not treated may have:

- poor weight gain
- delays in learning
- delays in walking and other motor skills
- enlarged liver and other liver problems
- enlarged heart and other heart problems

- vision loss due to build-up of pigment in the retina
- anemia
- nerve problems
- bouts of muscle weakness and pain, especially after heavy exercise or illness

Some children with LCHADD have never had symptoms and are only found to be affected after a brother or sister is diagnosed.

What is the treatment for LCHADD?

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

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 LCHADD:

1. Avoid going a long time without food
Infants and young children with LCHADD need to eat frequently to prevent a metabolic crisis. Your metabolic doctor will tell you how often your child needs to be fed. In general, it is often suggested that infants be fed every four to six hours. Some babies need to eat even more frequently than this. It is important that infants be fed during the night. They may need to be woken up to eat if they do not wake up on their own. Your metabolic doctor and dietician will give you an appropriate feeding plan for your infant. Your doctor will also give you a 'sick day' plan tailored to your child's needs for you to follow during illnesses or other times when your child will not eat.

Your metabolic doctor will continue to advise you on how often your child should eat as he or she gets older. When they are well, many teens and adults with LCHADD can go without food for up to 12 hours without problems. The other treatments usually need to be continued throughout life.

2. Diet
Sometimes a diet low in fat and high in carbohydrates is recommended. Carbohydrates give the body many types of sugar that can be used as energy. In fact, for children needing this treatment, most foods in the diet should be carbohydrates (bread, pasta, fruit, vegetables, etc.) and protein (lean meat and low-fat dairy foods). Any diet changes should be made under the guidance of a dietician familiar with LCHADD.

People with LCHADD 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 the fat in the diet will likely be in the form of medium chain fatty acids.

Ask your doctor if your child needs to have any changes in his or her diet.

3. MCT oil, L-carnitine, and other supplements

Medium Chain Triglyceride oil (MCT oil) is often used as part of the food plan for people with LCHADD. This special oil has medium chain fatty acids that can be used in small amounts for energy. Your metabolic doctor 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 L-carnitine. This is a safe and natural substance that helps body cells make energy. It also helps the body get rid of harmful wastes. Your doctor will decide whether your child needs L-carnitine. Unless you are advised otherwise, use only L-carnitine prescribed by your doctor.

In addition to the above supplements, some doctors suggest taking DHA (docosahexanoic acid) which may help prevent loss of eyesight. Ask your doctor whether your child should use this supplement.

Do not use any supplements or medications without checking with your doctor.

4. Call your doctor at the start of any illness

Always call your health care provider when your child has any of the following:

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

Children with LCHADD need to eat extra starchy food and drink more fluids during any illness - even if they may not feel hungry – or they could develop hypoglycemia. Children who are sick often don't want to eat. If they won't or can't eat, children with LCHADD may need to be treated in the hospital to prevent problems.

Ask your metabolic doctor if you should carry a special travel letter with medical instructions for your child's care.

5. Avoid prolonged exercise or exertion

Long periods of heavy exercise can also trigger symptoms. Effects of exercise may include:

- muscle aches
- cramps

- weakness
- reddish-brown color to the urine (caused by breakdown of muscle fibers)

If muscle symptoms occur, prompt treatment is needed to prevent kidney damage. Children or adults with 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

What happens when LCHADD is treated?

With prompt and careful treatment, children with LCHADD can often live healthy lives with typical growth and development.

Even with treatment, some people with LCHADD continue to have episodes of hypoglycemia. This can lead to learning problems or intellectual disabilities. And, even with treatment, some people still develop vision, muscle, liver, or heart problems.

What causes the LCHAD enzyme to be absent or not working correctly?

Genes tell the body to make various enzymes. The HADHA gene instructs the body to make the LCHAD enzyme. Everyone has two copies of the HADHA gene. People with LCHADD have changes, also called variants in both copies of their HADHA genes that cause them to not work correctly. Because of the changes in this pair of genes, the LCHAD enzyme either does not work properly or is not made at all.

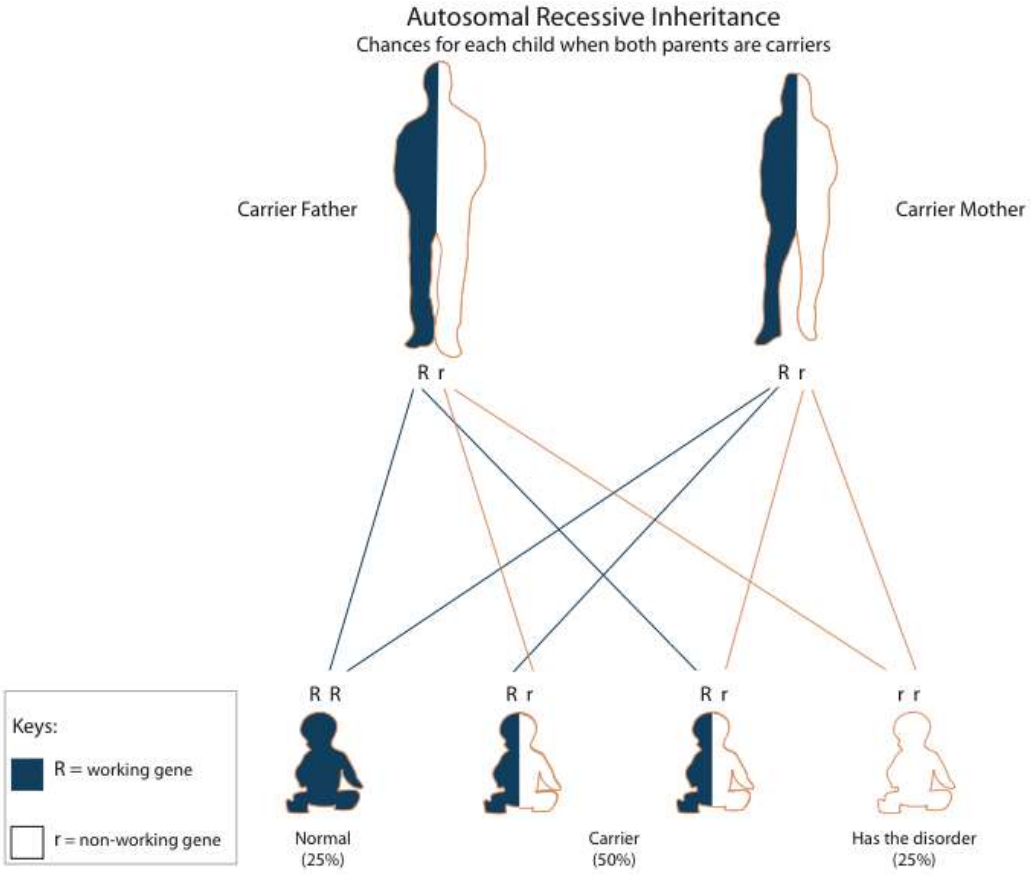
How is LCHADD inherited?

LCHADD is inherited in an autosomal recessive manner. It affects both boys and girls equally.

Everyone has two copies of the HADHA gene that make the LCHAD enzyme. In children with LCHADD, neither of their HADHA genes works correctly. These children inherit one non-working HADHA gene for the condition from each parent.

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

When both parents are carriers, there is a 25% chance in each pregnancy for the child to have LCHADD. There is a 50% chance for the child to be a carrier, just like the parents. And, there is a 25% chance for the child to have two working genes.



Genetic counseling is available to families who have children with LCHADD. Genetic counselors can answer your questions about how LCHADD is inherited, choices during future pregnancies, and how to test other family members. Ask your doctor about a referral to a genetic counselor.

Is genetic testing available?

Genetic testing for LCHADD can be done on a blood sample. Genetic testing, also called DNA testing, looks for changes (variants) in the pair of genes that

causes LCHADD. About 70% of children with LCHADD have one particular change in both genes of this pair.

DNA testing is not necessary to diagnose your child. It can be helpful for carrier testing or prenatal diagnosis, discussed below.

What other testing is available?

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

Can you test during a future pregnancy?

If both gene changes (variants) have been found in your child with LCHADD, DNA testing can be done during future pregnancies. The sample needed for this test is obtained by either CVS or amniocentesis.

If DNA testing would not be helpful, testing during pregnancy can be done by a special test called a "fatty acid oxidation probe" using cells from the fetus. Again, 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. Parents may also choose to use assisted reproductive techniques to decrease the chance that their future children would have LCHADD. A genetic counselor can talk to you about your choices and answer questions about prenatal testing or testing your baby after birth.

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

Having LCHADD

The brothers and sisters of a baby with LCHADD have a chance of being affected, even if they haven't had symptoms. Finding out whether other children in the family have LCHADD is important because early treatment may prevent serious health problems. Talk to your doctor or genetic counselor about testing your other children for LCHADD.

LCHADD Carriers

Brothers and sisters who do not have LCHADD still have a chance to be carriers like their parents. Except in special cases, carrier testing should only be done in people over 18 years of age.

If you are a parent of a child with LCHADD, your brothers and sisters have a 50% chance to be an LCHADD 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 LCHADD.

All states offer newborn screening for LCHADD. However, when both parents are carriers, newborn screening results are not sufficient to rule out LCHADD in a newborn baby. In this case, special diagnostic testing should be done in addition to newborn screening.

During pregnancy, women carrying fetuses with LCHADD are at risk to develop serious medical problems. Some of these women develop:

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

All women with a family history of LCHADD 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.

Can other family members be tested?

Diagnostic testing

Brothers and sisters can be tested for LCHADD by DNA testing or other special tests to determine if they also have LCHADD.

Carrier testing

If both gene changes in the HADHA gene have been found in the child with LCHADD, other family members can have DNA testing to see if they are carriers.

How many people have LCHADD?

LCHADD is a rare disorder. The actual incidence is unknown.

Does LCHADD happen more often in a certain ethnic group?

Although LCHADD happens in every ethnic group, it happens more often in people who have ancestors from Finland.

Does LCHADD go by any other names?

LCHADD is also called:

- LCHAD deficiency
- 3hydroxyacyl-CoA dehydrogenase, long chain, deficiency
- Trifunctional protein deficiency, type 1

A variant of LCHADD is called Trifunctional Protein Deficiency (TFP). Please see the TFP fact sheet for information on this condition.

Where can I find more information?

Fatty Oxidation Disorders (FOD) Family Support Group
http://www.fodsupport.org

Organic Acidemia Association
http://www.oaanews.org

United Mitochondrial Disease Foundation
http://www.umdf.org

Metabolic Support UK
https://www.metabolicsupportuk.org/

Baby's First Test
http://www.babysfirsttest.org

Genetic Home Reference
https://ghr.nlm.nih.gov/condition/long-chain-3-hydroxyacyl-coa-dehydrogenase-deficiency

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