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Nutrition and Dietetics

Women's and Children's Health

Fast Facts For Patients

Long-Chain Fatty Acid Oxidation Disorders

Karger

HEALTHCARE

First, the facts ...

1. Long-chain fatty acid oxidation disorders (LC-FAODs) are rare, inherited conditions.
2. With an LC-FAOD, the body has trouble breaking down fat for energy, which can lead to symptoms such as low blood sugars, muscle pain/weakness, and heart problems.
3. LC-FAODs are diagnosed by newborn screening or symptoms later in life.
4. Management includes a specialized nutrition plan, and prevention of fasting, especially during illness.
5. A person with an LC-FAOD can live a full, active and healthy life with lifestyle changes and close coordination with, and support from, an expert healthcare team.

This booklet aims to help you understand LC-FAODs so you can have a conversation with your dietitian, doctor and healthcare team, and with family and your wider support network (nurseries and schools, for example).

Contact details

Doctor:

Dietitian:

Genetic counselor:

Nurse practitioner/nurse:

In case of emergency, call:

Fats and fatty acids

You are probably reading this booklet because you or your child has been diagnosed with a long-chain fatty acid oxidation disorder (LC-FAOD) or this diagnosis is suspected.

With an LC-FAOD, the body is unable to properly break down fats in the diet.

Fat as an energy source

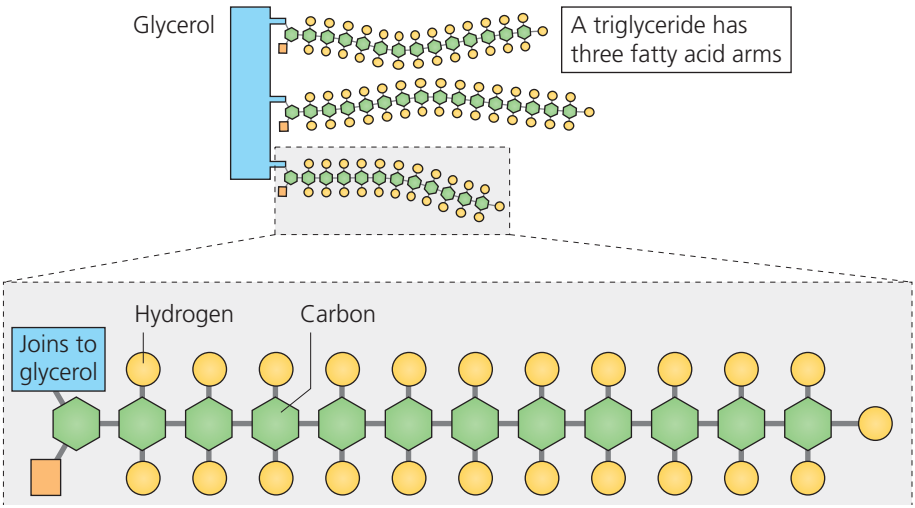
Our bodies need energy to keep muscles, organs and normal processes working.

The three types of food that provide energy are carbohydrates (in the form of sugars and starches), protein and fats.

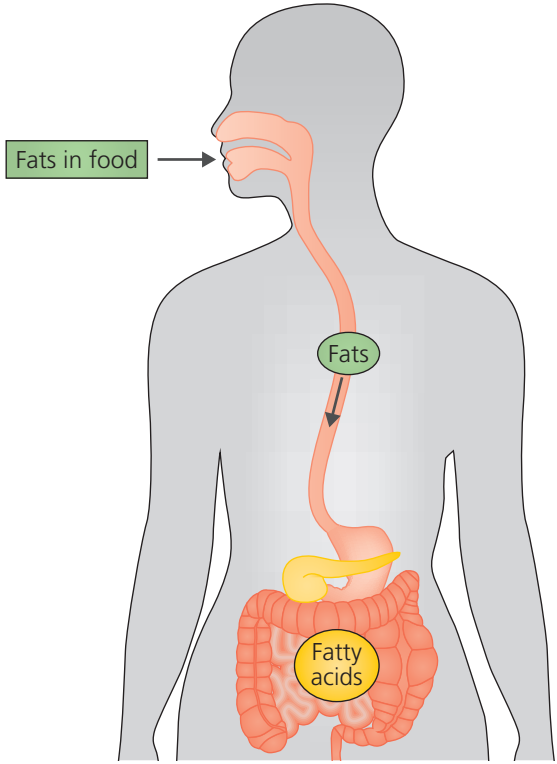
The body stores fat under the skin and around the organs so that it can be used to provide energy when needed.

Fatty acids are building blocks

Fats are made up of building blocks called fatty acids. Fatty acids are usually joined in groups of three (tri) to a glycerol backbone – this is called a triglyceride. Each fatty acid is made up of a chain of carbon atoms with hydrogen atoms attached.



Fats enter the body from our diet. Fatty acids are released from triglycerides. They are either stored as fat or used as a source of energy in the body.



The number of carbon atoms varies between different fatty acids; for example…

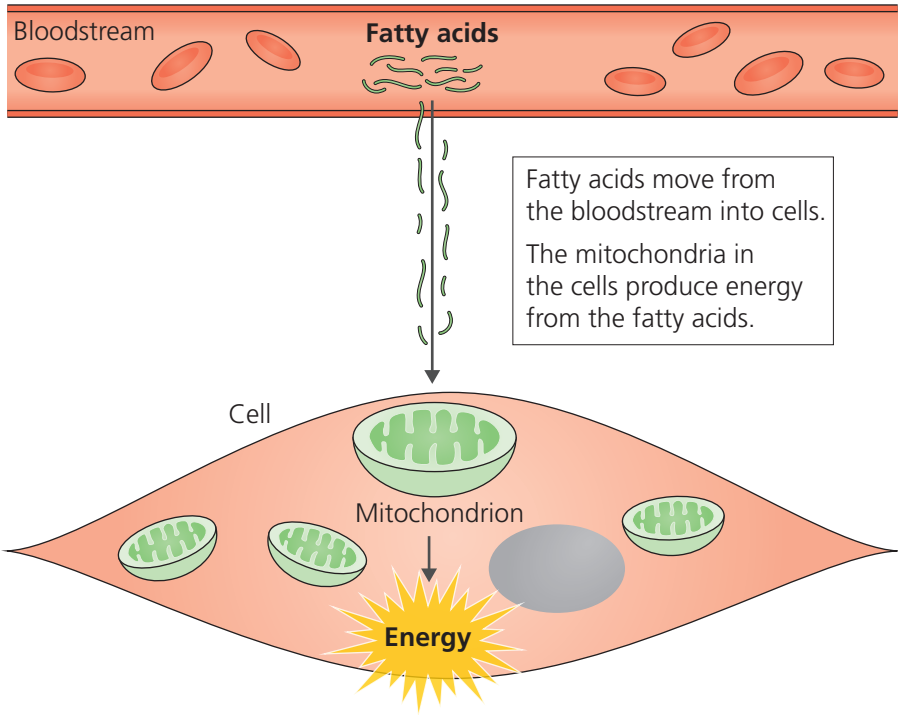
Palmitic acid has 16 carbons and is found in palm oil
Oleic acid has 18 carbons and is found in olive oil
Arachidonic acid has 20 carbons and is found in meat and dairy products

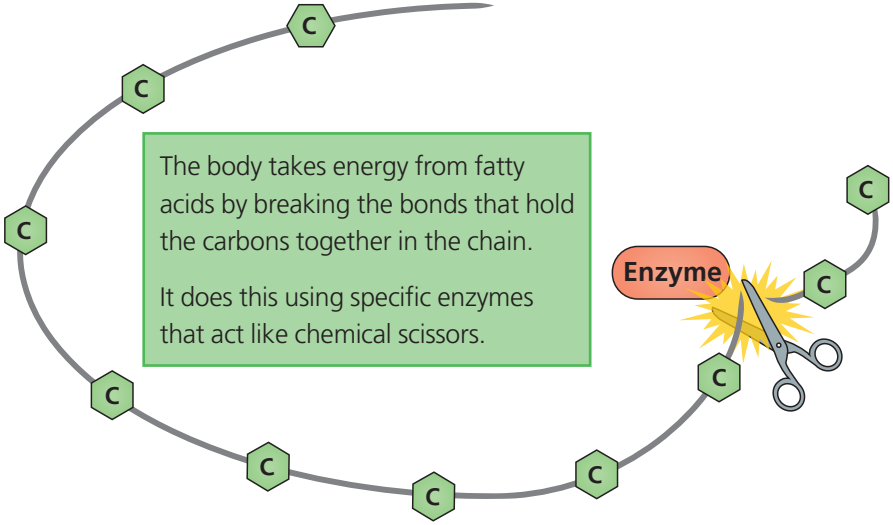
Fatty acids for energy

When the body needs to use fat as an energy source, it breaks down the triglyceride and releases fatty acids. These fatty acids then travel in the blood to the muscles and organs where they can be used for energy.

Introducing beta oxidation

Once the fatty acids are in the muscle or organ where they will be used for energy, they go through a complicated process called beta oxidation. This takes place in mitochondria, which are specialized areas in cells.



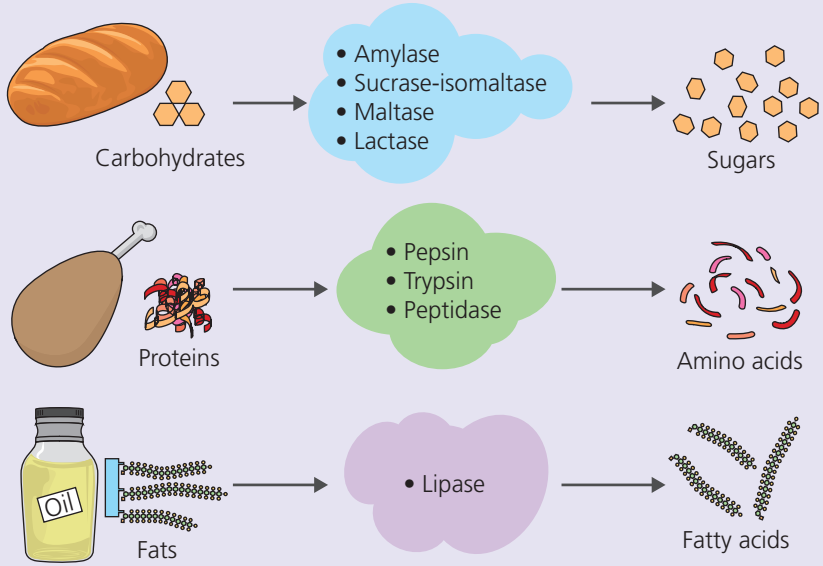


The body takes energy from fatty acids by breaking the bonds that hold the carbons together in the chain.

It does this using specific enzymes that act like chemical scissors.

What is an enzyme?

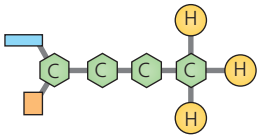
Enzymes are special proteins that help with a wide range of crucial tasks in the body. Each enzyme – and there are thousands in an average human cell – has a specific task. Examples of enzymes that help digest food are:



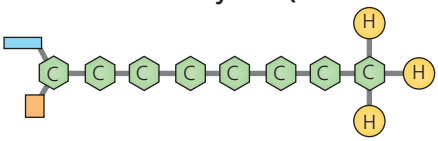
Long-chain fatty acid oxidation disorders

As shown on page 2, each fatty acid contains a chain of carbons. The length of this chain varies, with most fatty acids having between 4 and 24 carbons.

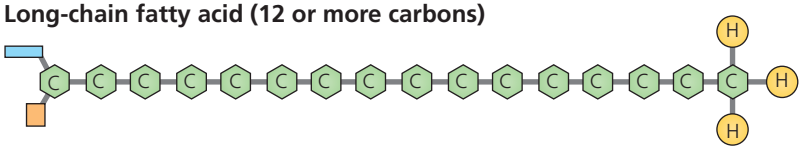
Short-chain fatty acid (fewer than 6 carbons)



Medium-chain fatty acid (6–10 carbons)



Long-chain fatty acid (12 or more carbons)



Enzymes are needed to move long-chain fatty acids into the mitochondria and process them for energy.

LC-FAODs happen when one of the enzymes involved in breaking down long-chain fatty acids for energy is not made or is not working properly.

As a result, the body is unable to use these fatty acids for energy in the usual way. This can lead to problems with energy supplies.

Not being able to use energy from stored fat can cause harmful effects. Having partially digested fatty acids in the body may also cause problems.

LC-FAODs are named according to the enzyme that is affected. The most common types of LC-FAOD are:

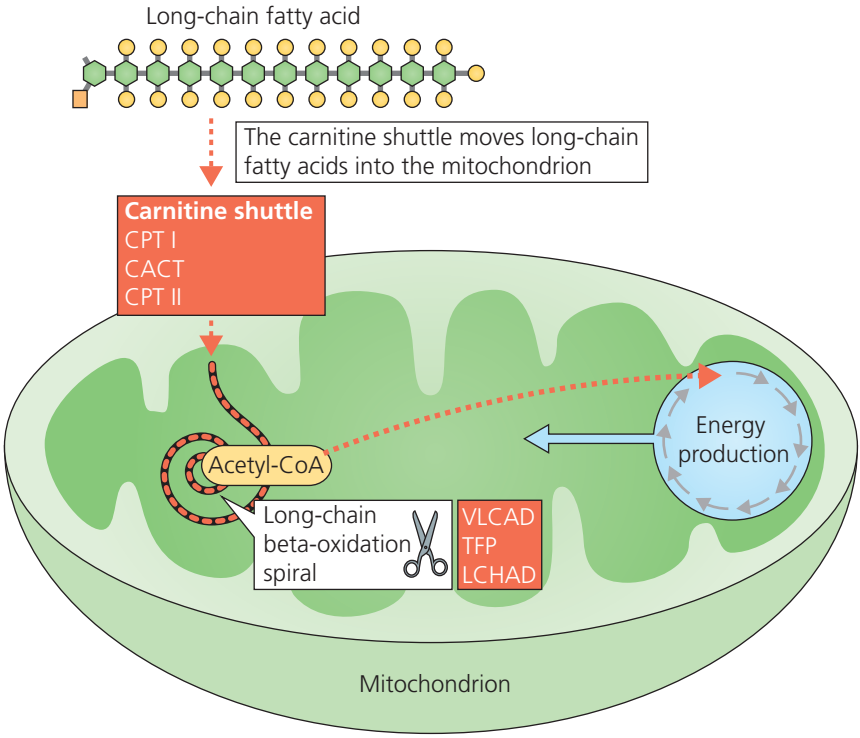
- Carnitine palmitoyltransferase 1 or CPT1 deficiency (sometimes written as CPT I)

- Carnitine acylcarnitine translocase or CACT deficiency
- Carnitine palmitoyltransferase 2 or CPT2 deficiency (sometimes written as CPT II)
- Very-long-chain acyl-CoA dehydrogenase or VLCAD deficiency
- Long-chain 3-hydroxy-acyl-CoA dehydrogenase or LCHAD deficiency
- Trifunctional protein or TFP deficiency.

The affected enzymes are important for either:

- the carnitine shuttle, which moves the long-chain fatty acids into the mitochondrion, or
- the long-chain beta-oxidation spiral, which breaks down long-chain fatty acids into shorter and shorter pieces, two carbons at a time.

The two carbons removed in each round of beta oxidation form a molecule called acetyl-CoA, which then enters another energy-producing cycle in the mitochondrion.



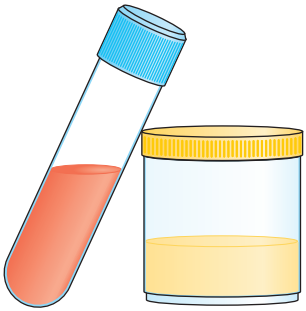
Diagnosis

'Newborn screening' describes the health tests that take place during the first few days of a newborn baby's life. Some countries include tests for LC-FAODs in newborn screening, but others do not.

If newborn screening was not carried out or the LC-FAOD was not identified at that time, it may be diagnosed when symptoms appear. This may be in infancy or later in life.

Blood and urine tests

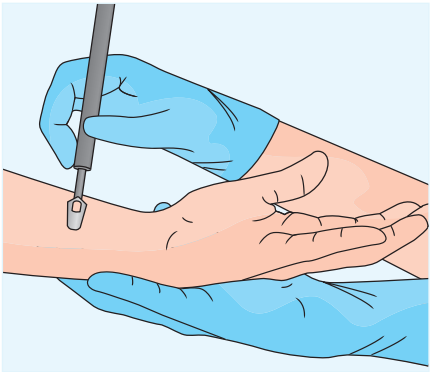
Blood and urine samples are tested in the laboratory to see if they have unusually high levels of partly digested fatty acids and other chemicals.



Although some LC-FAODs have a specific pattern of results, further tests may be needed.

Testing enzyme activity

Sometimes doctors need to test whether a particular enzyme is working. A small sample of skin is taken in a procedure called a skin biopsy.

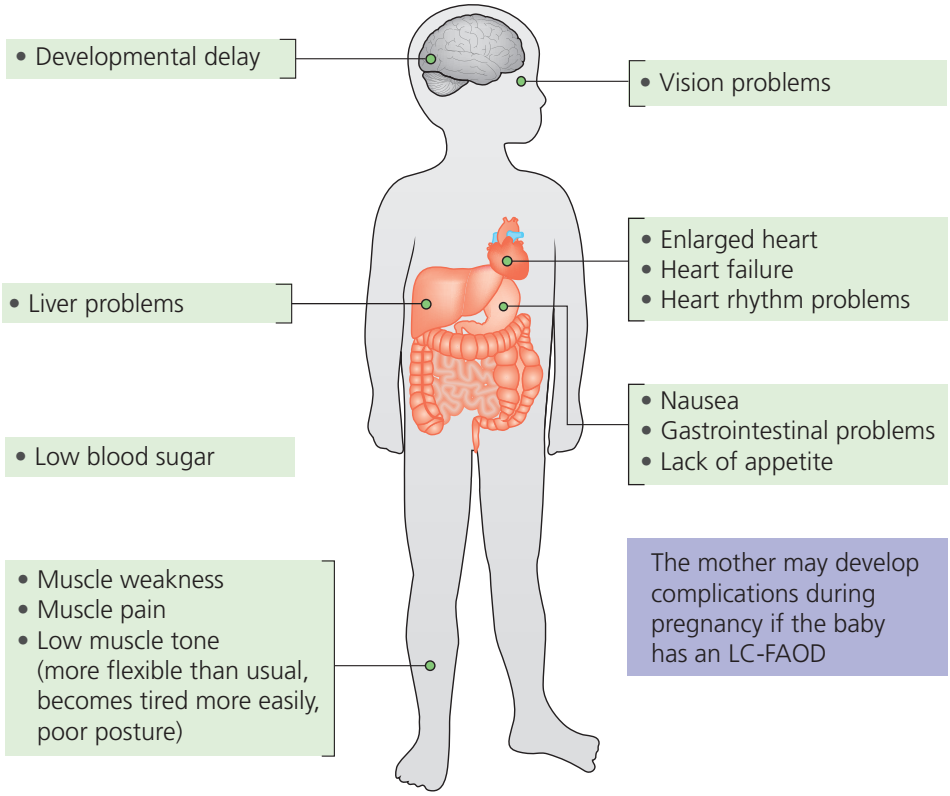


In the laboratory, cells called fibroblasts are taken from the skin sample and tested to see whether the enzyme is working normally.

Symptoms

Symptoms can range from mild to severe or life-threatening. Sometimes the symptoms are triggered by intense exercise or fasting. They can also happen following a viral infection or after surgery.

Most patients have only some of the symptoms shown, depending on the specific diagnosis.



Commonly used words

Cardiomyopathy: a description used when a disorder affects the heart muscle, causing heart symptoms

Myopathy: a description used when the disorder affects the muscles, causing them to become weak

Rhabdomyolysis: a serious complication in which muscles start to break down, releasing protein into the body. This causes severe muscle pain and cola-colored urine. It's important to seek immediate medical attention as rhabdomyolysis can lead to kidney damage

Genetic testing

LC-FAODs are inherited genetic disorders. They happen because the gene that carries the instructions for making the specific enzyme has a misprint or change. This means that not enough of the enzyme is made or it is made incorrectly and does not work properly.

What is a gene?

A gene is a section of DNA that tells the body how to make a specific protein – in the case of LC-FAODs, the protein is an enzyme

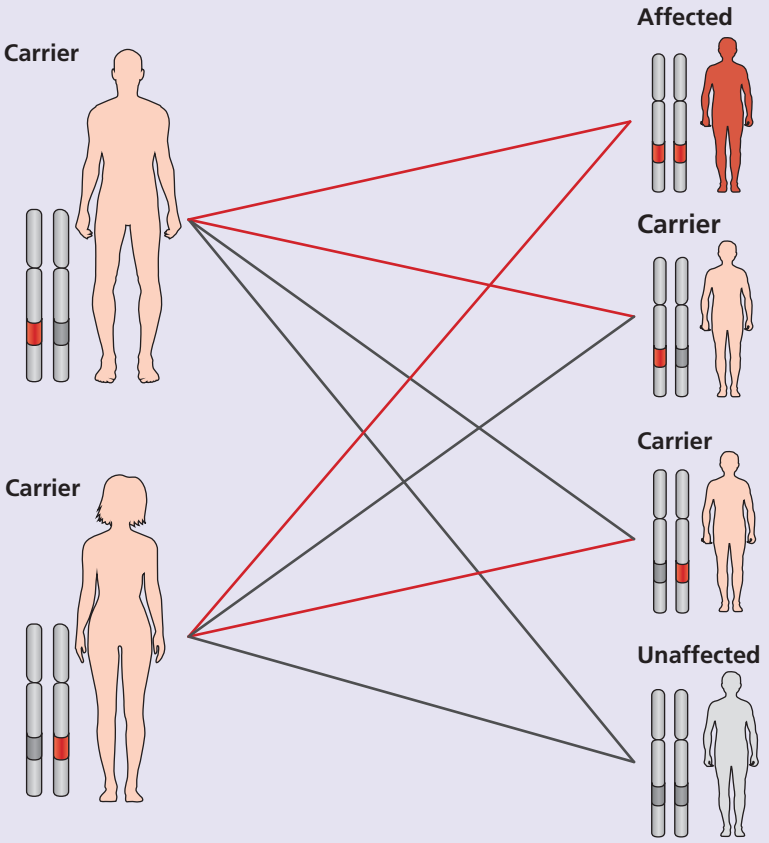
Your doctor may suggest genetic testing to identify the genetic changes that are present. The test is carried out on a blood sample.

There are many different genetic changes that can lead to LC-FAODs. The name of the gene that is altered or changed in each of the LC-FAODs is shown in the table below.

We have two copies of most of our genes – one copy from each of our biological parents. A person will have an LC-FAOD only if both copies of the gene passed on from their parents have the genetic

Disorder	Gene affected
CPT1 deficiency	*CPT1A*
CACT deficiency	*CACT*, which is also known as *SLC25A20*
CPT2 deficiency	*CPT2*
Carnitine transporter deficiency*	*OCTN2*, also known as *SLC22A5*
LCHAD deficiency	*HADHA*, sometimes also called *LCHAD*
VLCAD deficiency	*ACADVL*, sometimes also called *VLCAD*
TFP deficiency	*HADHA* or *HADHB*
*Also called carnitine uptake disorder	

change. If only one parent passes on a copy with a change, the other copy of the gene may be able to make a working enzyme. If this happens, the person will not have an LC-FAOD but is said to be a carrier. A carrier can pass the genetic change on to their child. The illustration below shows the different combinations – the pattern is called recessive inheritance.



The gene with the change is shown here in **red**. If a person inherits two copies with the change – one from both parents – they have the disorder.

If they inherit only one copy, they are a carrier. If they inherit both copies of the unaffected gene, shown in **gray**, they do not have the condition, are not a carrier and cannot pass the genetic change on to a child.

Living with an LC-FAOD

Diet

LC-FAODs are managed with a special individualized diet (nutrition plan) – your healthcare team will talk to you about this.

Depending on the severity of the condition, your baby may need a special formula that is very low in long-chain fats. These formulas contain all the vitamins and minerals needed to allow normal growth. They also contain medium-chain fats, which a person with an LC-FAOD can break down into energy.

As your child starts to take solid food, your dietitian will give you advice on suitable foods to offer and introduce you to medium-chain fats that can be substituted for normal fats.

Fasting times and regular meals

Every child will have a different fasting time. This is the length of time that the body can provide energy safely without having to use fat stores. The way this is tested will depend on where you live. Your hospital or metabolic team will give you advice on a safe fasting time for your child. Some children need overnight feeding (sometimes using a tube) if they have very short fasting times.

It is also important to avoid long periods without food – again, your healthcare team will give you specific information and advice.

Exercise and sport

Exercising makes extra demands on the body's energy reserves. Your healthcare team will advise on how to make adjustments for this.

Illness and the emergency/sick day plan

Illness (high temperature, vomiting, diarrhea) disrupts the body's metabolism and the body needs more energy. A person with an LC-FAOD will need to use their emergency or sick day plan. This involves taking a high-sugar drink that will have been prescribed for you.

Metabolic crisis

A metabolic crisis happens in response to a trigger, such as illness with high fever or a long interval between meals.

During a metabolic crisis, the person has little energy and becomes ill as the harmful semi-digested fatty acids build up in the body.

The advice that your healthcare team gives you about diet, mealtimes and illness will help avoid metabolic crisis.

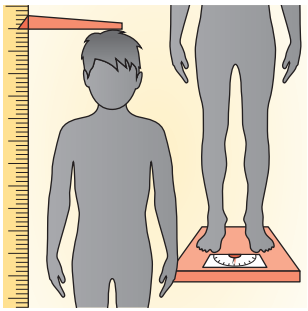
Immunizations

It is very important to have the recommended immunizations, to avoid infections, which may cause a high temperature.

Write your notes here

It may be helpful to write down the specific instructions given to you by your healthcare team in this area

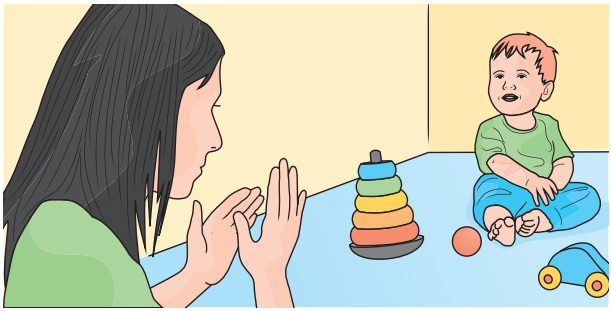
Monitoring



Keeping a check on your child's height and weight will be important as they grow. As well as checking that growth is normal, the information can also be used to make adjustments to the advice on diet, fasting, illness and exercise.

If you are an adult, monitoring weight is important to make sure that your dietary regimen is providing appropriate calories.

Regular blood tests will be used to check your metabolic health or that of your child.



Your child will have the usual regular monitoring that all children have to check they are meeting their developmental targets (milestones), such as smiling, crawling, walking and talking. In this way, your healthcare team will be able to see whether your child's learning, coordination or sensory development (seeing and hearing) is being affected by the LC-FAOD.

Questions you might want to ask

How often should weight and height be checked?

What can I do to help my child?

The best way to lead a healthy active life or to help your child do this is to follow the specific advice of your healthcare team. Some general tips are:

- have plenty of in-date emergency drink/food supplement at home and plan ahead
- have medications that help reduce a high temperature at home
- buy and use a thermometer
- use the full amounts of prescribed or advised special food
- if your child will not take the emergency drink/food supplement or you are concerned, go to your hospital
- keep contact numbers for your healthcare team in an easy-to-reach place (it is a good idea to have them written down as well as stored in your phone contacts)
- keep your emergency protocol in a safe and accessible place and make copies for those who care for your child
- ring your metabolic team for advice or go to the hospital
- inform childcare providers, nurseries, schools and clubs about your child's condition and what to do if your child appears unwell

Information to share with care providers, schools and clubs

- A **meal or eating schedule**
- A list of **supplements, formulas and/or medications**
- A list that explains **details of foods** that you or your child can and cannot have, preferences and favorites
- A list that explains **limitations regarding certain activities**
- **Warning signs/symptoms** to watch out for and what to do if they occur
- **Key phone numbers** (family, doctors, nearby hospitals)
- **Letter from your LC-FAOD healthcare team** to share with other medical providers

Genetic counseling

Genetic counseling involves discussing the likelihood that the genetic change that you carry would be passed on to your children.

If you are a parent of a child with an LC-FAOD, you most likely were not aware that you carried the genetic change. A health professional or geneticist will talk to you about the likelihood of other or future children being affected.

You and your partner may also be offered carrier testing. Blood samples will be sent to the laboratory, and the gene will be checked to see if it has the same genetic change as your child has.

Prenatal diagnosis

Prenatal diagnosis is a way of checking during pregnancy whether a baby carries two copies of the genetic change. Your doctor or geneticist will talk to you about what is involved and the information that the test will provide.

In vitro fertilization so that the genetic make-up of the embryo can be checked before implantation may also be a possibility. Again, this is something to discuss with your healthcare team.

Pregnancy

If you are a woman with an LC-FAOD and you become pregnant, you may require closer monitoring during the pregnancy. There may be changes in your dietary recommendations or supplements.

You should notify your metabolic care team if you are planning a pregnancy and as soon as you know that you are pregnant.

Questions you might want to ask

What is the specific condition that I have or that my child has?

How many people are affected?

LC-FAODs are very rare. Overall, it is estimated that 1 newborn is identified with a fatty acid oxidation disorder in every 9300 babies.

The conditions tend to be more common in European countries and populations with European ancestry. In contrast, they are much less common in Asian countries.

Some disorders are particularly common in specific groups: for example, CPT1 deficiency seems to occur more often in Inuit people living in northern Canada.

VLCAD deficiency is the most common LC-FAOD. It is identified in 1 in 30 000 to 1 in 100 000 newborns, depending on the population.

Questions you might want to ask

What health changes should I watch for?

What will happen as I get older or my child gets older?

Note your own questions here

Who's who?

Advanced practice clinician: a person trained as either a nurse practitioner or physician assistant. Advanced practice clinicians provide care under the supervision of the doctor, but they can see patients and prescribe medications independently.

Geneticist: a doctor or scientist who diagnoses and advises on the care of people with genetic conditions.

Metabolic biochemist: a scientist with specialist knowledge of the chemical reactions that happen in the body.

Nurse: a person trained to assess individuals and provide education on treatment and symptom management. Nurses work closely with doctors to coordinate care.

Nutritionist or Dietitian: a health professional who is qualified and trained to provide guidance on how and what to eat to improve the diet to help manage symptoms.

Patient navigator: a person, who may also be a nurse, who helps with scheduling, obtaining materials for appointments and coordinating care.

Pediatrician: a doctor specializing in treating children with medical conditions.

Guide to words and phrases

Enzyme: a type of protein that helps with specific tasks in the body's cells.

Gene: a section of DNA that carries the instructions for making a protein.

Metabolism: the chemical reactions that take place in the body.

Proteins: large molecules with many different functions in the body; the instructions for making proteins are carried by genes.

Genetic change or mutation: a change in the gene that changes the instructions for making the protein. In some instances, the protein is not made, while in other cases the protein will behave differently.

Useful resources

These organizations may be of interest to, and offer support for, people affected by LC-FAODs.*

International

INFORM Families
informnetwork.org/inform-families

USA

FOD Family Support Group
www.fodsupport.org

MitoAction
www.mitoaction.org

National Organization for Rare Disorders (NORD)
rarediseases.org

Global Genes
globalgenes.org

Everylife Foundation for Rare Diseases
everylifefoundation.org

Save Babies Through Screening Foundation
www.savebabies.org

Canada

Canadian Organization for Rare Disorders
www.raredisorders.ca

MitoCanada
mitocanada.org

UK

Metabolic Support UK
www.metabolicsupportuk.org

*The inclusion of an organization's name and URL does not imply endorsement of this publication. Nor does it imply an association with the publisher or any pharmaceutical company that has, through an educational grant, supported the independent development of this resource.

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Questions for the Editor

What have you found most useful about this book? What is missing? Do you still have unanswered questions? Please send your questions, or any other comments, to fastfacts@karger.com and help the readers of future editions. Thank you!

With sincere thanks to those who have reviewed this publication for all their help and guidance

HEALTHCARE

Nutrition and Dietetics

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Women's and Children's Health

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