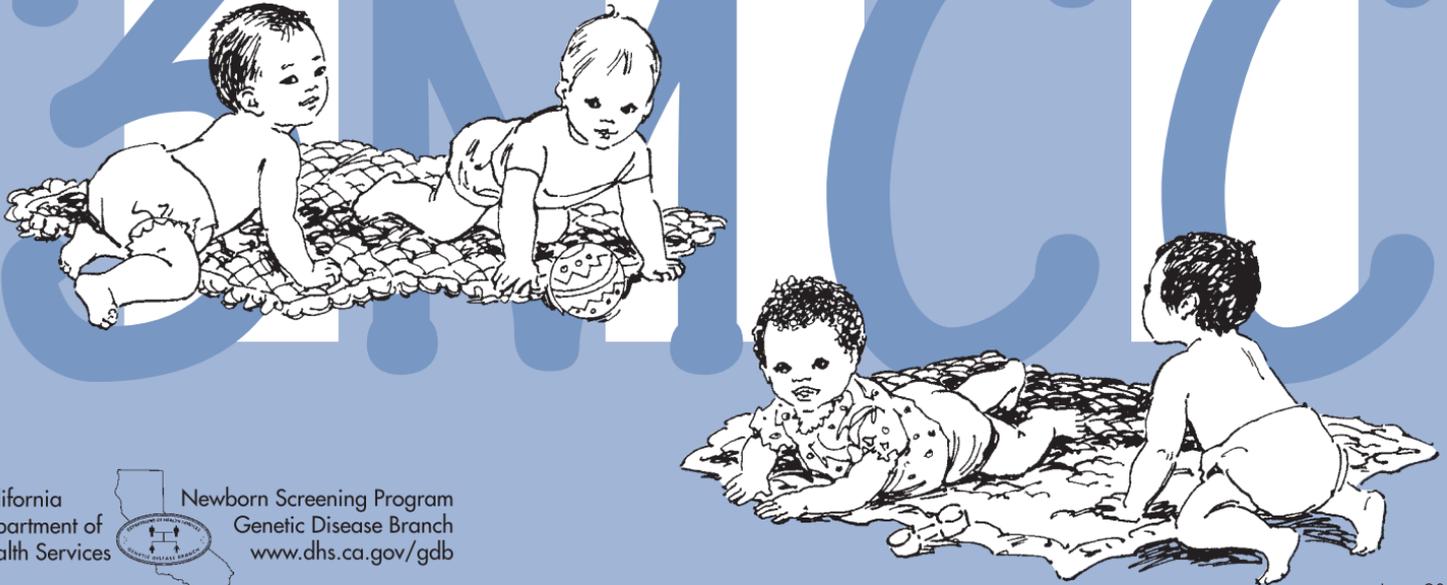


# Parents' Guide to 3MCC Deficiency

3-Methylcrotonyl-CoA Carboxylase Deficiency



California  
Department of  
Health Services



Newborn Screening Program  
Genetic Disease Branch  
[www.dhs.ca.gov/gdb](http://www.dhs.ca.gov/gdb)

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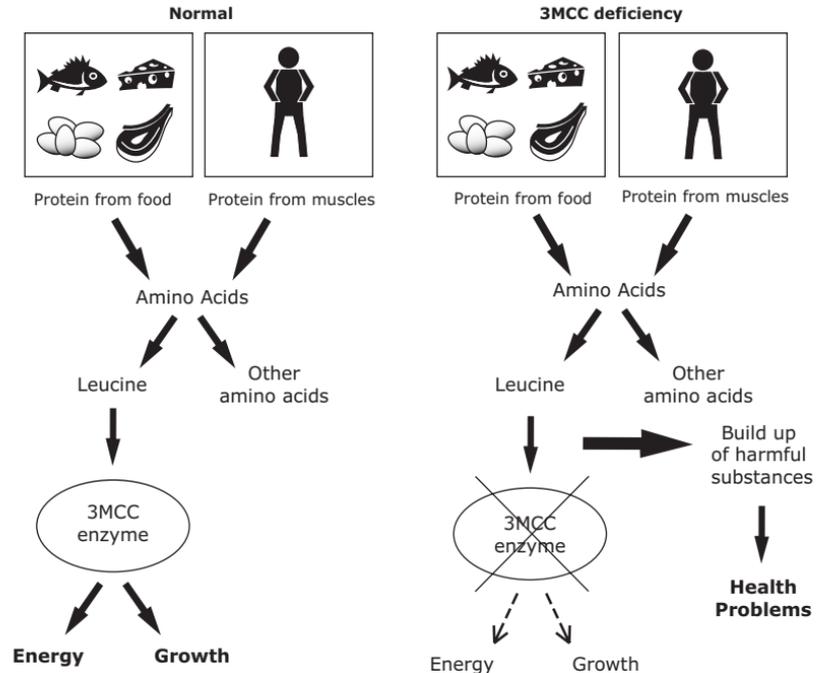
**The information in this booklet is general and is not meant to be specific to each child with 3MCC deficiency. Certain treatments may be recommended for some children but not others. Children with 3MCC deficiency should be followed by a physician specializing in metabolic diseases (metabolic specialist) in addition to their primary doctor. For a list of metabolic centers, see page 16 or visit our website at [www.dhs.ca.gov/gdb](http://www.dhs.ca.gov/gdb).**

\*Underlined words in booklet are defined in the Glossary

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## What is 3MCC deficiency?

3MCC deficiency is one type of organic acid disorder. People with these disorders have problems breaking down and using certain amino acids from the food they eat. With 3MCC deficiency, people have problems breaking down a specific amino acid called leucine.



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## What causes 3MCC deficiency?

In order for the body to use protein from the food we eat, it is broken down into smaller parts called amino acids. Special enzymes then make changes to the amino acids so the body can use them.

3MCC deficiency occurs when an enzyme, called “3-methylcrotonyl CoA carboxylase (3MCC)”, is either missing or not working properly. This enzyme’s job is to help break down leucine. When a child with 3MCC deficiency eats food containing leucine, harmful substances may build up in the blood and cause problems. Leucine is found in all foods with protein.

## What causes the 3MCC enzyme to be missing or not working correctly?

Genes tell the body to make various enzymes. People with 3MCC deficiency have a pair of genes that do not work correctly. Because of the changes in this pair of genes, the 3MCC enzyme either does not work properly or is not made at all.

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## If 3MCC deficiency is not treated, what problems occur?

Each child with 3MCC deficiency may have somewhat different effects. In fact, some children with this condition never have symptoms and may not ever need treatment.

Babies with 3MCC deficiency are healthy at birth. If symptoms occur, they often appear after 3 months of age. Some babies do not have their first symptoms until 6 months to 3 years of age. Others do not have symptoms until adulthood. Some people will never develop symptoms.

3MCC deficiency can cause episodes of illness called metabolic crises. Some of the first symptoms of a metabolic crisis are:

- poor appetite
- extreme sleepiness or lack of energy
- behavior changes
- irritable mood
- muscle weakness
- nausea
- vomiting

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Common blood and urine findings are:

- low blood sugar, called hypoglycemia
- increased levels of acidic substances in the blood, called metabolic acidosis
- high levels of ammonia in the blood
- low levels of carnitine in the blood
- increased ketones in the urine
- liver problems

If a metabolic crisis is not treated, a child with 3MCC deficiency can develop:

- breathing problems
- seizures
- liver failure
- coma, sometimes leading to death

If a metabolic crisis is not treated, it could result in death. In surviving babies and children, repeated episodes of metabolic crisis can cause brain damage. This can lead to life-long learning problems or mental retardation.

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Episodes of metabolic crisis can be triggered by:

- illness or infection
- going without food for long periods of time
- eating large amounts of protein

When a child is ill or goes without food for too long, the body breaks down its own protein and fat to use for energy. In some people with 3MCC deficiency, this can trigger a metabolic crisis.

Between episodes of metabolic crisis, children with 3MCC deficiency are usually healthy.

Some children do not ever have metabolic crises. However, they may have other symptoms. These can include:

- poor growth and development
- either poor muscle tone (floppy muscles and joints) or spasticity

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Some people do not have any symptoms until adulthood. Some of the symptoms seen in adults are:

- weakness
- fatigue

Some people with 3MCC deficiency never have symptoms and are only found after a brother or sister is diagnosed.

### **What happens when 3MCC deficiency is treated?**

With prompt and careful treatment, children who have shown symptoms of 3MCC deficiency have a good chance to live healthy lives with typical growth and development.

Even with treatment, some children still have repeated bouts of metabolic crisis. This can cause brain damage and may lead to life-long learning problems or mental retardation.



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## What is the treatment for 3MCC deficiency?

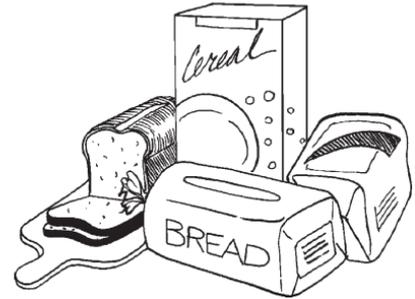
Your baby's primary doctor may work with a metabolic doctor and a dietician to care for your child.

In some children, prompt treatment is needed to prevent metabolic crises and the health effects that follow. Certain treatments may be advised for some children but not others. Children who do not show symptoms may not need treatment.

The following are treatments that are used for some babies and children with 3MCC deficiency:

### 1. Low-leucine diet, including medical foods and formula

A food plan low in leucine with limited amounts of protein is sometimes needed. Most food in the diet will be carbohydrates (bread, cereal, pasta, fruit, vegetables, etc.). Carbohydrates give the body many types of sugar that can be used as energy. Eating a diet high in carbohydrates and low in protein can help prevent low blood sugar and metabolic crises.



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Foods high in protein (which contain leucine) that may need to be avoided or limited include:

- milk and dairy products
- meat and poultry
- fish
- eggs
- dried beans and legumes
- nuts and peanut butter

Do not remove all protein from the diet. Children with 3MCC deficiency need small amounts of protein to grow properly. Many vegetables and fruits have only small amounts of protein and can be eaten in carefully measured amounts.

If needed, your dietician will create a food plan that contains the right amount of protein, nutrients, and energy for your child. Some children may be on a special food plan throughout life.



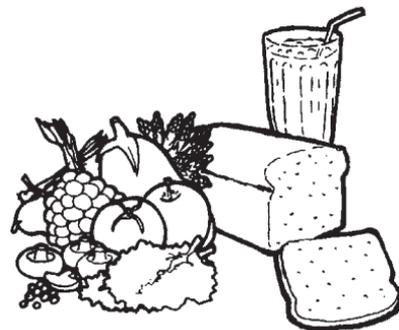
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There are medical foods such as special low-protein flours, pastas, and rice that are made especially for people with organic acid disorders. If necessary for your child, your dietician will tell you how to use these foods.

In addition to a low-protein diet, some children are given a special leucine-free medical formula. Your metabolic specialist and dietician will decide whether your child needs this formula.

## 2. Medications

Some children may benefit by taking 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 or not your child needs L-carnitine. Do not use any medication without checking with your doctor.



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### 3. Call your doctor immediately if your child has signs of illness

In some children, even minor illnesses such as a cold or the flu can lead to a metabolic crisis. In order to prevent problems, you may be told to call your doctor right away when your child has any of the following symptoms:

- loss of appetite
- vomiting
- diarrhea
- infection or illness
- fever

Some children need to eat more carbohydrates and drink more fluids when they are ill – even if they're not hungry – or they could have a metabolic crisis. They should also avoid eating protein during any illness.

Children who are ill often don't want to eat. If they can't eat, or if they show signs of a metabolic crisis, they may need to be treated in the hospital.



## How is 3MCC deficiency inherited?

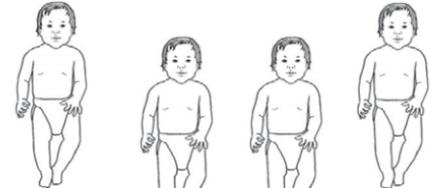
3MCC deficiency affects both boys and girls equally.

Everyone has a pair of genes that make the 3MCC enzyme. In children with 3MCC deficiency, 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 3MCC deficiency rarely have the disorder. Instead, each parent has a single non-working gene for 3MCC deficiency. 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 3MCC deficiency.

3MCC Deficiency Carriers



Not a Carrier/ No Disease	Carrier	Carrier	3MCC Deficiency
	↘	↗	
(25% chance)	(50% chance)		(25% chance)

*Chances apply to each pregnancy*

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Genetic counseling is available to families who have children with 3MCC deficiency. Genetic counselors can answer your questions about how the condition 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 3MCC deficiency.

### Is genetic testing available?

Genetic testing, also called DNA testing, looks for changes in the pair of genes that cause 3MCC deficiency. Talk with your genetic counselor or metabolic specialist if you have questions about DNA testing.

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?

Special tests on blood, urine, or skin samples can be done to confirm 3MCC deficiency. Talk to your metabolic specialist if you



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have questions about testing for this condition.

### Can you test during pregnancy?

If both gene changes are known in the child with 3MCC deficiency, DNA testing can be done during future pregnancies to determine if the sibling also has 3MCC deficiency. The sample needed for this test is obtained by either CVS or amniocentesis.

It may also be possible to test for 3MCC deficiency using an enzyme test on cells from the fetus. 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 questions about prenatal testing or testing your baby after birth.



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## Can other family members have 3MCC deficiency or be carriers?

The brothers and sisters of a baby with 3MCC deficiency have a chance of being affected even if they haven't had symptoms. Finding out whether other children in the family have this condition may be important because early treatment may prevent serious health problems. Ask your metabolic specialist whether your other children should be tested.

Brothers and sisters who do not have 3MCC deficiency 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 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 3MCC deficiency.

When both parents are known carriers for 3MCC deficiency or have had a baby with 3MCC deficiency, subsequent newborns should have special diagnostic testing in addition to the newborn screen to

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test for 3MCC deficiency.

### **How many people have 3MCC deficiency?**

About one in every 50,000 babies in the United States is born with 3MCC deficiency. This condition does not happen more often in any specific race, ethnic group, geographical area or country.

### **RESOURCES**

Organic Acidemia Association  
13210 35<sup>th</sup> Avenue North  
Plymouth, MN 55441  
(763) 559-1797  
[www.oaanews.org](http://www.oaanews.org)

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

Save Babies Through Screening Foundation  
4 Manor View Circle  
Malvern, PA 19355-1622  
(888) 454-3383  
[www.savebabies.org](http://www.savebabies.org)

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## 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 and  
Health Center of San Diego  
(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

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## 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 causes 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

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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 passes 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

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enzyme can participate in many chemical reactions without changing or being used up.

**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.

**Metabolic Crisis (Metabolic Crises = plural)** - 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. If not treated, breathing problems, seizures, coma, and sometimes even death can occur. Metabolic crises happen more often in people with certain metabolic disorders (some fatty acid oxidation disorders, amino acid disorders, and organic acid disorders). They are often

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triggered by things like illness or infection, going without food for a long time, and, in some cases, heavy exercise.

**Seizure** - Also called “convulsions” or “fits”. During a seizure, a person may lose 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.

**Spasticity** - Rigidity of the muscles and increased reflexes. It is caused by increased muscle tone. It results in abnormal tightness or stiffness of the muscles and joints.

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- Parents of children with 3MCC Deficiency

