



## Organic Acid 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: 3-methylcrotonyl CoA carboxylase deficiency**

**Acronym: 3MCC deficiency**

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This fact sheet has general information about 3MCC deficiency. Every child is different and some of these facts may not apply to your child specifically. Certain treatments may be recommended for some children but not others. Children with 3MCC deficiency should be followed by a metabolic doctor in addition to their primary doctor.

### What is 3MCC deficiency?

3MCC deficiency is one type of organic acid disorder. Some children with this condition have problems breaking down an amino acid called leucine from the food they eat.

### **Organic Acid Disorders:**

Organic acid disorders (OAs) are a group of rare inherited conditions. They are caused by enzymes that do not work properly. A number of enzymes are needed to process protein from the food we eat for use by the body. Problems with one or more of these enzymes can cause an organic acid disorder.

People with organic acid disorders cannot break down protein properly. This causes harmful substances to build up in their blood and urine. These substances can affect health, growth, and learning.

The symptoms and treatment vary between different organic acid disorders. They can also vary from person to person with the same organic acid disorder. See the fact sheets for each specific organic acid disorder.

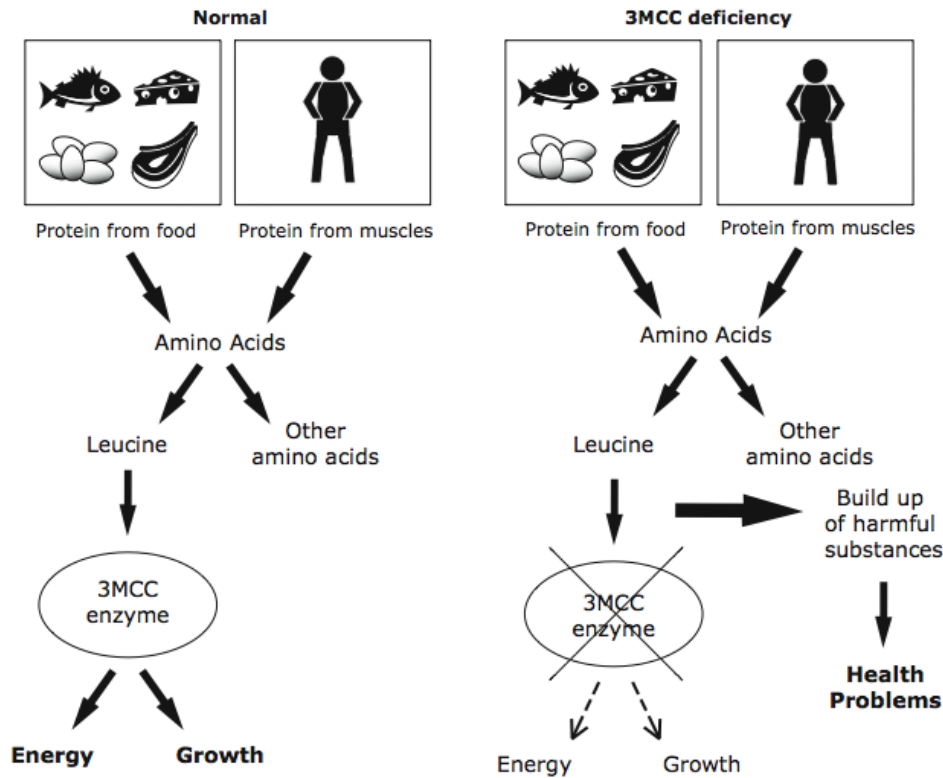
Organic acid disorders are inherited in an autosomal recessive manner and affect both males and females.

### **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 is caused by problems with the enzyme “3-methylcrotonyl CoA carboxylase” (3MCC). In people with 3MCC deficiency, the 3MCC enzyme 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.

### 3-methylcrotonyl CoA carboxylase deficiency 3MCC deficiency



### 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 start 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

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 intellectual disabilities.

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 low muscle tone or spasticity

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 to have 3MCC deficiency after a brother or sister is diagnosed, or they may be diagnosed through newborn screening.

## 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 hypoglycemia and metabolic crises.

Foods high in protein 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

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

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.

### Medical foods and formula

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 doctor and dietician will decide whether your child needs this formula. Some states offer help with payment for this formula, and others require private insurance to pay for the formula and other special medical foods.

## **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. Unless you are advised otherwise, use only L-carnitine prescribed by your doctor.

Your doctor may suggest other medications or supplements that may be helpful in preventing some of the symptoms of 3MCC deficiency. Do not use any medication without checking with your doctor.

## **3. Call your doctor at the start of any 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:

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

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

Many children found to have 3MCC deficiency during newborn screening will never need treatment.

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 intellectual disabilities.

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

Genes tell the body how to make enzymes. 3MCC deficiency is caused by changes in either the MCCC1 or MCCC2 genes. Both the MCCC1 and MCCC2 genes instruct the body to make the 3MCC enzyme. Everyone has two copies of both the MCCC1 and MCCC2 genes. People with 3MCC deficiency have changes, also called variants, in both copies of either their MCCC1 genes or their MCCC2 genes. Because of the variants in either the MCCC1 or MCCC2 genes, the 3MCC enzyme either does not work properly or is not made at all.

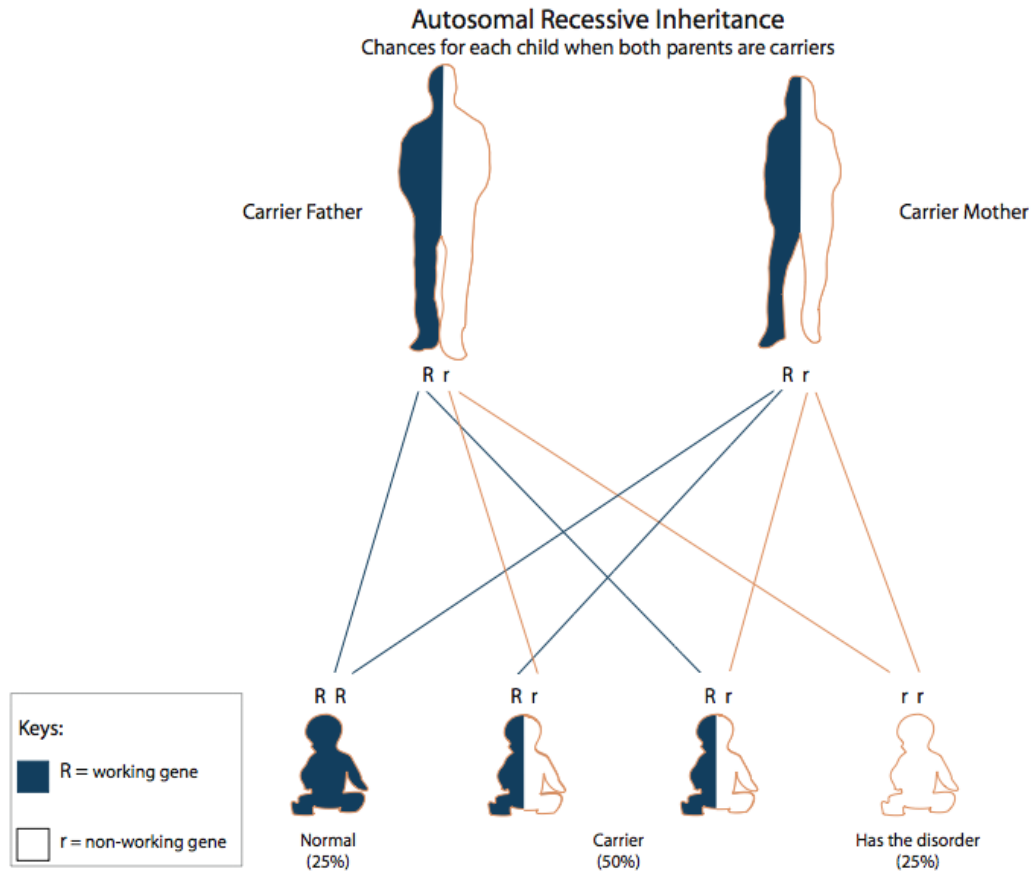
## How is 3MCC deficiency inherited?

3MCC deficiency is inherited in an autosomal recessive manner. It affects both boys and girls equally.

Everyone has two copies of the MCCC1 and MCCC2 genes that make the 3MCC enzyme. In children with 3MCC deficiency, one set of these genes is not working correctly. These children inherit one non-working MCCC1 or MCCC2 gene from each parent.

Parents of children with 3MCC deficiency rarely have the disorder. Instead, each parent has a single non-working MCCC1 or MCCC2 gene for 3MCC deficiency. They are called carriers. Carriers do not have the condition because their other gene is working correctly.

When both parents are carriers, there is a 25% chance in each pregnancy for the child to have 3MCC deficiency. 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 3MCC deficiency. Genetic counselors can answer your questions about how the condition 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 3MCC deficiency can be done on a blood sample. Genetic testing, also called DNA testing, looks for changes (variants) in both copies of the MCCC1 or MCCC2 genes that causes 3MCC deficiency. Talk with your genetic counselor or metabolic doctor if you have questions about DNA testing.

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

### What other testing is available?

Special tests on blood, urine, or skin samples can be done to confirm 3MCC deficiency. Talk to your metabolic doctor if you have questions about testing for this condition.



## Can you test during a future pregnancy?

If both gene changes have been found in the child with 3MCC deficiency, DNA testing can be done during future pregnancies. The sample needed for this test is obtained by either CVS or amniocentesis.

Parents may 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 3MCC deficiency. 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 3MCC deficiency or be carriers?

### Having 3MCC deficiency

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 doctor whether your other children should be tested.

### 3MCC deficiency carriers

Brothers and sisters who do not have 3MCC deficiency 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 3MCC deficiency, your brothers and sisters have a 50% 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.

All states offer newborn screening for 3MCC deficiency. However, when both parents are carriers for 3MCC deficiency, newborn screening results are not sufficient to rule out the condition in a newborn baby. In this case, special diagnostic testing should be done in addition to newborn screening.

## Can other family members be tested?

### Diagnostic testing

Brothers and sisters of a child with 3MCC deficiency can be tested using blood, urine, or skin samples.

### **Carrier testing**

If both gene changes (variants) have been found in your child with 3MCC deficiency, other family members can have DNA testing to see if they are carriers.

If DNA testing is not possible or is not helpful, other methods of carrier testing may be available. Your metabolic doctor or genetic counselor can answer your questions about carrier testing.

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

About one in every 40,000 to 50,000 babies in the United States is born with 3MCC deficiency.

### **Does 3MCC deficiency happen more often in a certain ethnic group?**

No, this condition does not happen more often in any specific race, ethnic group, geographical area, or country.

### **Does 3MCC deficiency go by any other names?**

3MCC deficiency is sometimes also called:

- 3-methylcrotonylglycinuria
- Methylcrotonyl-CoA carboxylase deficiency
- 3-methylcrotonylglycinuria
- Methylcrotonyl-CoA carboxylase deficiency

The adult form of 3MCC deficiency is also called:

- Late-onset 3-methylcrotonyl CoA carboxylase deficiency

### **Where can I find more information?**

Organic Acidemia Association

<http://www.oaanews.org>

Save Babies Through Screening Foundation

<http://www.savebabies.org/>

Metabolic Support UK

<https://www.metabolicsupportuk.org>

MedlinePlus

<https://medlineplus.gov/genetics/condition/3-methylcrotonyl-coa-carboxylase-deficiency/>

Baby's First Test

<http://www.babysfirsttest.org>

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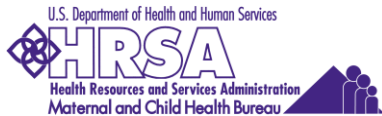
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