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: 2-methylbutyryl CoA dehydrogenase deficiency
Acronym: 2MBCD deficiency / 2-MBADD

This fact sheet has general information about 2MBCD 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 symptoms of 2MBCD deficiency should be followed by a metabolic doctor in addition to their primary doctor.

What is 2MBCD deficiency?

2MBCD deficiency is one type of **organic acid disorder**. Some children with 2MBCD deficiency have problems breaking down an amino acid called isoleucine 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.

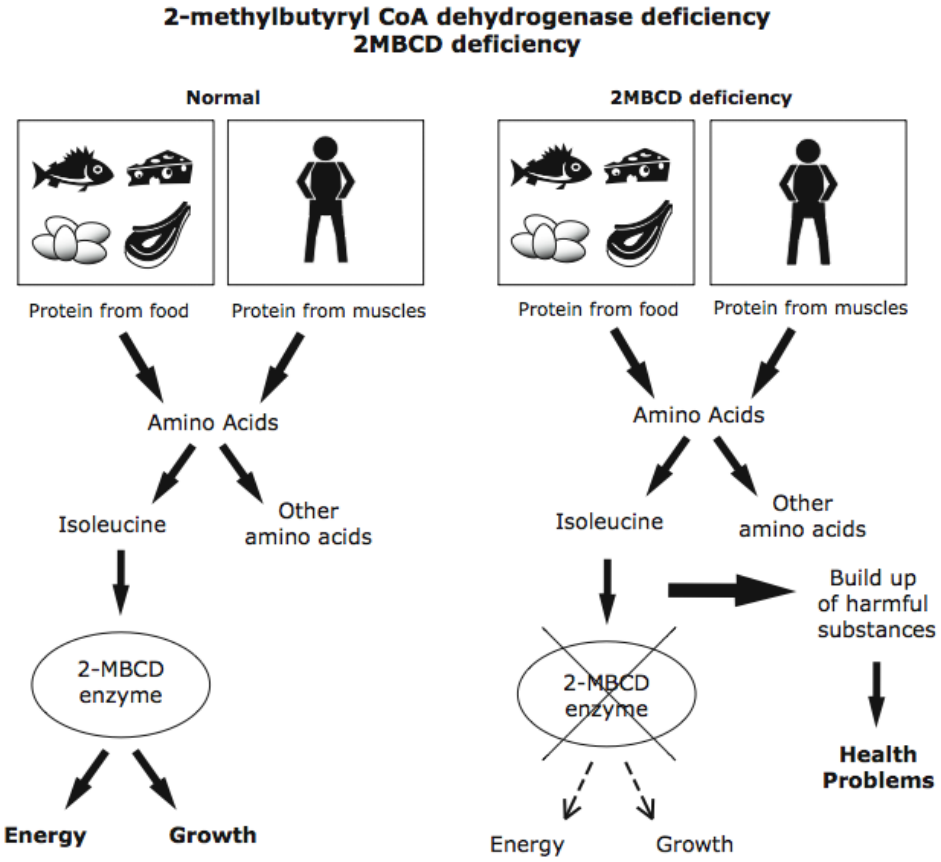
The symptoms and treatment vary between different organic acid disorders. They can also vary from person to person with the same organic acid disorder. See the fact sheets for each specific organic acid disorder.

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

What causes 2MBCD deficiency?

In order for the body to use protein from food, 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.

2MBCD deficiency is caused by problems with the enzyme “2-methylbutyryl-CoA dehydrogenase” (2MBCD). In people with 2MBCD deficiency, the 2MBCD enzyme is either missing or not working properly. This enzyme’s job is to help break down isoleucine. When a child with 2MBCD deficiency eats food containing isoleucine, harmful substances may build up in the blood. Isoleucine is found in all foods that contain protein.



If 2MBCD deficiency is not treated, what problems occur?

This condition is very rare. Only a small number of children with 2MBCD deficiency have been reported. The symptoms have been very severe in some children and mild or completely absent in others. It is likely that most babies found to have this condition through newborn screening will never develop symptoms.

Babies with 2MBCD deficiency have all been healthy at birth. A few babies started having symptoms just a few days after birth. Others had their first symptoms later in childhood. Some children have never had symptoms. Most infants with Hmong ancestry never develop symptoms.

In a few children, 2MBCD deficiency causes episodes of illness called metabolic crises. Some of the first symptoms of a metabolic crisis are:

- poor appetite
- extreme sleepiness or lack of energy
- irritable mood
- difficulty keeping warm

Other symptoms then follow:

- fever
- nausea
- vomiting
- low blood sugar, called hypoglycemia
- increased levels of acidic substances in the blood, called metabolic acidosis

If a metabolic crisis is not treated, a child with 2MBCD deficiency can develop:

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

If not treated, 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 children with 2MBCD deficiency, this can trigger a metabolic crisis.

Between episodes of metabolic crisis, children with 2MBCD deficiency are likely to be healthy.

Some children never have metabolic crises. Some may have other symptoms, though. These can include:

- poor growth
- tight, rigid muscles, called spasticity
- involuntary movements, called choreoathetosis
- vision problems
- muscle weakness
- smaller head than normal (microcephaly)
- delays in walking and other motor skills
- learning problems or intellectual disabilities

Some people with 2MBCD deficiency never have any symptoms and are only found to have the condition after a brother or sister is diagnosed, or they may be diagnosed through newborn screening.

What is the treatment for 2MBCD deficiency?

Some children diagnosed with 2MBCD deficiency through newborn screening will never have symptoms. These children may not need treatment.

Babies that do have symptoms may need lifelong treatment. If this is the case, your baby's primary doctor may work with a metabolic doctor and a dietician to care for your child.

Prompt treatment may be needed to prevent metabolic crises and the health effects that follow. Certain treatments may be advised for some children but not others. Your doctor and metabolic doctor will decide whether your child needs treatment.

The following are treatments recommended for some babies and children with 2MBCD deficiency:

1. Avoid going a long time without food
Some infants and young children with 2MBCD deficiency 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.

2. Low-protein diet, including medical foods and formula
A food plan low in protein is sometimes advised. 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. It is important not to remove all protein from the

diet. Children with 2MBCD deficiency need a certain amount 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. It is important to follow the advice of your dietician and metabolic doctor.

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 needed, your dietician will tell you how to use these foods as part of your child's diet.

In addition to a low-protein diet, some children are given a special medical formula that does not contain isoleucine. 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.

3. 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. Do not use any medication without checking with your doctor.

4. Call your doctor at the start of any illness

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

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

Some children may 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 may also need to 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 2MBCD deficiency is treated?

With prompt and careful treatment, children with symptoms of 2MBCD deficiency have a good chance to live healthy lives with typical growth and development.

Despite treatment, some children may have repeated bouts of hypoglycemia or metabolic crises. This can cause brain damage and may lead to life-long learning problems or intellectual disabilities.

What causes the 2MBCD enzyme to be absent or not working correctly?

Genes tell the body how to make enzymes. The ACADSB gene instructs the body to make the 2MBCD enzyme. Everyone has two copies of the ACADSB gene. People with 2MBCD deficiency have changes, also called variants, in both copies of their ACADSB genes. Because of the variants in the ACADSB genes, the 2MBCD enzyme either does not work properly or is not made at all.

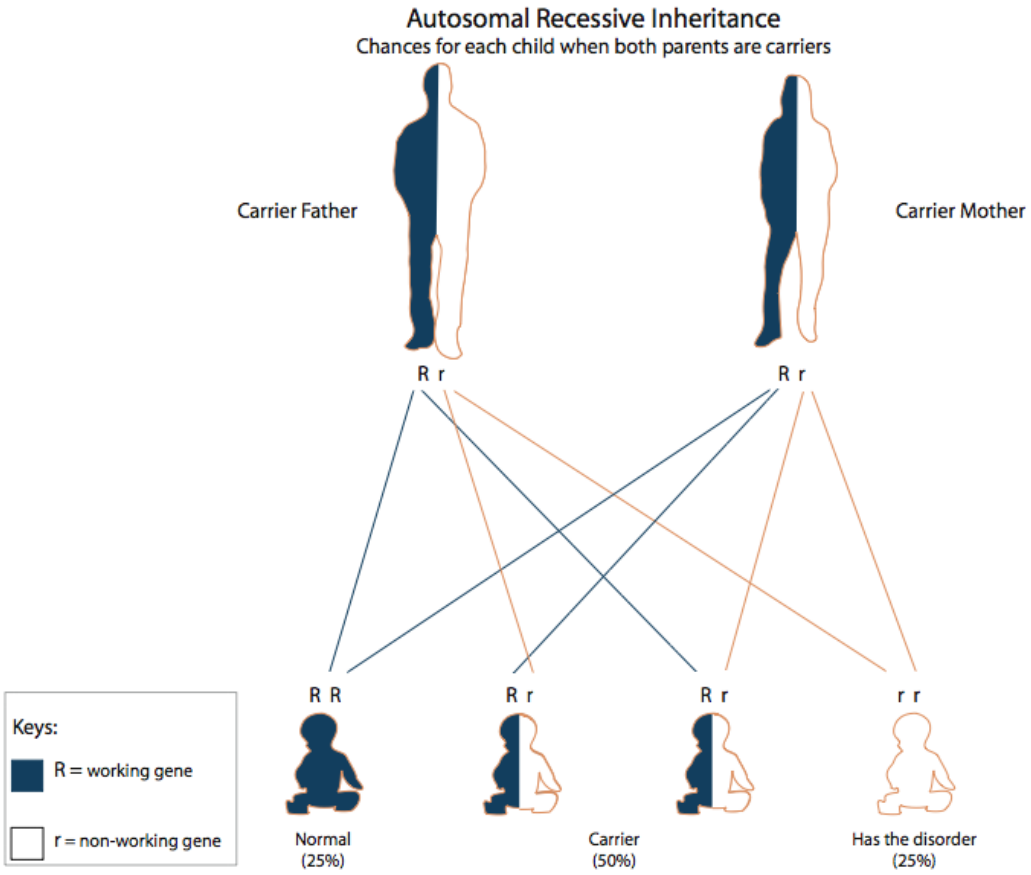
How is 2MBCD deficiency inherited?

2MBCD deficiency is inherited in an autosomal recessive manner. It affects both boys and girls equally.

Everyone has two copies of the ACADSB genes that make the 2MBCD enzyme. In children with 2MBCD deficiency, neither of these ACADSB genes works correctly. These children inherit one non-working ACADSB gene from each parent.

Parents of children with 2MBCD deficiency rarely have the disorder. Instead, each parent has a single non-working ACADSB gene for 2MBCD 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 2MBCD 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 2MBCD 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 2MBCD deficiency is available. Genetic testing, also called DNA testing, looks for changes, also called variants, in the ACADSB genes that causes 2MBCD 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. If available, 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 2MBCD 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 (variants) have been found in your child with 2MBCD 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 2MBCD 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 2MBCD deficiency or be carriers?

Having 2MBCD deficiency

The brothers and sisters of a baby with 2MBCD deficiency have a chance of being affected, even if they haven't had symptoms. Finding out whether other children in the family have the condition may be important. Early treatment may prevent serious health problems. Talk to your metabolic doctor or genetic counselor about whether your other children should be tested.

2MBCD deficiency carriers

Brothers and sisters who do not have 2MBCD 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 2MBCD 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 2MBCD deficiency.

Some states do not provide newborn screening for 2MBCD deficiency. However, expanded newborn screening through private labs is available for babies born in states that do not screen for this condition. Your healthcare provider or genetic counselor can help you obtain expanded newborn screening.

When both parents are carriers, 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 2MBCD deficiency can be tested using blood, urine, or skin samples.

Carrier testing

If both gene changes (variants) have been found in the child with 2MBCD 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 2MBCD deficiency?

2MBCD deficiency is very rare. The actual incidence is unknown.

Does 2MBCD deficiency happen more often in a certain ethnic group?

2MBCD deficiency is more common in the Hmong population from Southeast Asia and in Hmong-Americans. One in every 500 babies of Hmong ancestry is born with this condition.

Does 2MBCD deficiency go by any other names?

2MBCD deficiency is sometimes also called:

- 2-methylbutyrylglycinuria
- Short/branched chain acyl-CoA dehydrogenase deficiency (SBCAD)
- 2MBCD deficiency
- 2MBAD deficiency
- SBCDD
- Short/branched-chain acyl-CoA dehydrogenase deficiency

Where can I find more information?

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

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

MedlinePlus
https://medlineplus.gov/genetics/condition/short-branched-chain-acyl-coa-dehydrogenase-deficiency/

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

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