



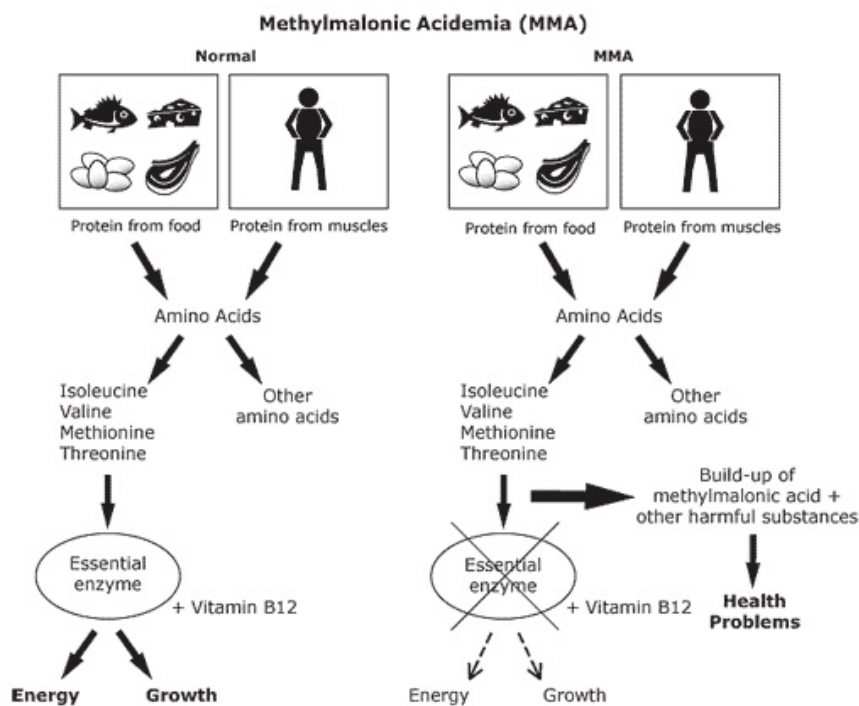
## METHYLMALONIC ACIDURIA

### A fact sheet for parents/carers

#### What is MMA?

MMA stands for "methylmalonic acidemia". It is one type of organic acid disorder. People with MMA have problems breaking down and using certain amino acids and fatty acids from the food they eat.

#### What causes MMA?



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. In the same way, fat from the food we eat is broken down by enzymes into fatty acids that the body can use for energy. MMA occurs when one of these special enzymes is either missing or not working properly. Without this enzyme, certain amino acids and fatty acids cannot be used correctly. This causes glycine, methylmalonic acid, and other harmful substances to build up in the blood and urine and cause health problems.

There are a number of different forms of MMA. Some forms can be treated with vitamin B12 injections. These types are called 'vitamin B12 responsive'. Two types of MMA that often can be treated with vitamin B12 are Cobalamin A (CblA) deficiency and Cobalamin B (CblB) deficiency.

There are other forms of MMA which cannot be treated with vitamin B12. These types are called 'vitamin B12 non-responsive'. One of these is called 'Mut 0'. It is caused by the absence of an enzyme called methylmalonyl-CoA mutase (MCM). Another type of MMA that does not respond to vitamin B12 treatment is called 'Mut -'. People with the 'Mut-' type of MMA have too little of the MCM enzyme.

Another form of MMA, called 'MMA with homocystinuria', is described in a separate fact sheet. See the fact sheet Homocystinuria for more information about this condition.



*Screening Today for a Safer Tomorrow*

Isoleucine, valine, methionine, and threonine are the four amino acids that cannot be used correctly by people with MMA. These amino acids are found in all foods that contain protein. Large amounts are found in meat, eggs, milk, and other dairy products. Smaller amounts are found in flour, cereal, and some vegetables and fruits.

**If MMA is not treated, what problems occur?**

Each child with MMA is likely to have somewhat different effects. Many babies with MMA start having symptoms in the first few days of life. Others begin to show symptoms sometime in infancy or childhood. Some people with MMA may never develop symptoms. MMA causes episodes of illness called metabolic crises. Some of the first symptoms of a metabolic crisis are:

- poor appetite
- vomiting
- extreme sleepiness or lack of energy
- low muscle tone (floppy muscles and joints)

**Common blood and urine findings are:**

- ketones in the urine
- high levels of acidic substances in the blood, called metabolic acidosis
- high blood ammonia levels
- high blood and urine levels of glycine
- high blood and urine levels of methylmalonic acid and propionic acid
- high levels of other harmful substances
- low platelets
- low white blood cells
- anemia

**If a metabolic crisis is not treated, a child with MMA can develop:**

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

**A metabolic crisis can be triggered by:**

- eating large amounts of protein
- illness or infection
- going too long without food
- stressful events such as surgery

Between episodes of metabolic crisis, children with MMA may be healthy. However, some continue to have problems with health and development. Some children have long-term problems even if they have never had a metabolic crisis. These can include:

- learning disabilities or mental retardation
- delays in walking and motor skills
- abnormal involuntary movements (dystonia and chorea)





## Screening Today for a Safer Tomorrow

- rigid muscle tone, called spasticity
- poor growth with short stature
- skin rashes and infections
- osteoporosis
- enlarged liver
- kidney disease or failure

Without treatment, brain and nerve damage can occur. This can cause mental retardation and problems with involuntary movements. Death is common in untreated babies and children. A small number of people with MMA never show symptoms.

### What is the treatment for MMA?

Your baby's primary doctor will work with a metabolic doctor and a dietician familiar with MMA to care for your child. Prompt treatment is needed to reduce the chance for mental retardation and serious medical problems. Children with 'vitamin B12 responsive' MMA are given vitamin B12. In addition, most children need to be on a low-protein diet and drink a special medical formula. You should start the treatments as soon as you know your child has MMA.

### The following are treatments often recommended for children with MMA:

#### 1. Medication

The main treatment for 'vitamin B12 responsive' MMA is vitamin B12 injections in the form of hydroxocobalamin (OH-cbl) or cyanocobalamin (CN-cbl). Vitamin B12 injections can prevent symptoms in children with this form of MMA. Over 90% of children with CblA deficiency respond to vitamin B12 injections. About 40% of children with CblB deficiency are helped by this treatment. Your doctors may need to treat your child with vitamin B12 for short period of time to determine whether this treatment is useful. Children with MMA may benefit by taking L-carnitine. This is a safe and natural substance that helps the body make energy. It also helps 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. Antibiotics taken by mouth can help lower the amount of methylmalonic acid made in the intestines. Your doctor will decide if your child needs antibiotics and, if so, what type. Children who are having symptoms of a metabolic crisis should be treated in the hospital. During a metabolic crisis, your child may be given medications such as bicarbonate through an IV to help reduce the acid levels in the blood. Glucose is given by IV to prevent the breakdown of protein and fat stored in the body. Do not use any medication without checking with your doctor.

#### 2. Low-protein diet, medical foods and medical formula Low-protein diet

A food plan low in the amino acids leucine, valine, methionine, and threonine with limited amounts of protein is often recommended. Most food in the diet will be carbohydrates (bread, cereal, pasta, fruit, vegetables, etc.). Carbohydrates give the body many types of



*Screening Today for a Safer Tomorrow*

sugar that can be used as energy. Eating a diet high in carbohydrates and low in protein and fat can help prevent 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 the diet. Children with MMA need a certain amount to grow properly. Your dietician can create a food plan that contains the right amount of protein, nutrients, and energy to keep your child healthy. It is likely your child will need to be on a special food plan throughout life.

### **Medical formula and foods**

In addition to a low-protein diet, your child may be given a special medical formula. This formula contains the correct amount of protein and nutrients your child needs for normal growth and development. Your metabolic doctor and dietician will tell you what type of formula is best and how much to use. There are also medical foods such as special low-protein flours, pastas, and rice that are made especially for people with organic acid disorders. Your dietician will tell you how to use these foods as part of your child's diet. Some states offer help with payment or require private insurance to pay for the formula and other special medical foods.

### **3. Avoid going a long time without food**

Infants and young children with MMA 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.

### **4. Regular blood and urine tests**

#### **Tracking of ketones**



*Screening Today for a Safer Tomorrow*

Periodic urine tests to check the level of ketones can be done at home or at the doctor's office. Ketones are substances formed when body fat is broken down for energy. This happens after going without food for long periods of time, during illness, and during periods of heavy exercise. Too many ketones in the urine may signal the start of a metabolic crisis.

**Blood tests**

Your child will have regular blood tests to measure the level of amino acids. Urine tests may also be done. Your child's diet and medication may need to be adjusted based on the results of these tests.

**5. Call your doctor at the start of any illness**

For children with MMA, even minor illness could lead to a metabolic crisis. To prevent serious health problems, call your doctor right away when your child has any of the following:

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

When ill, your child needs extra fluids and carbohydrates in order to prevent a metabolic crisis. During an illness, you should restrict protein and give your child starchy foods and fluids. Children with MMA may need to be treated in the hospital during illness to avoid serious health problems. Ask your metabolic doctor if you should carry a special travel letter with medical instructions for your child's care.

**6. Organ transplantation**

Some children with MMA are given liver or kidney transplants, or both. This may reduce some of the symptoms. However, transplant surgery has serious risks and may or may not be right for your child. Talk with your doctor or metabolic specialist if you have questions about the risks and benefits of transplantation.

**What happens when MMA is treated?**

Babies and children who have prompt and ongoing treatment may be able to live healthy lives with normal growth and development. In general, the earlier treatment is started, the better the outcome. Children who respond to vitamin B12 treatment tend to do very well as long as treatment is continued. Children who are not treated until after they have symptoms may have lasting health and learning problems. Even with treatment, some children develop life-long learning disabilities or mental retardation. In addition, despite treatment, seizures, involuntary movement disorders, and kidney failure have occurred in some children.

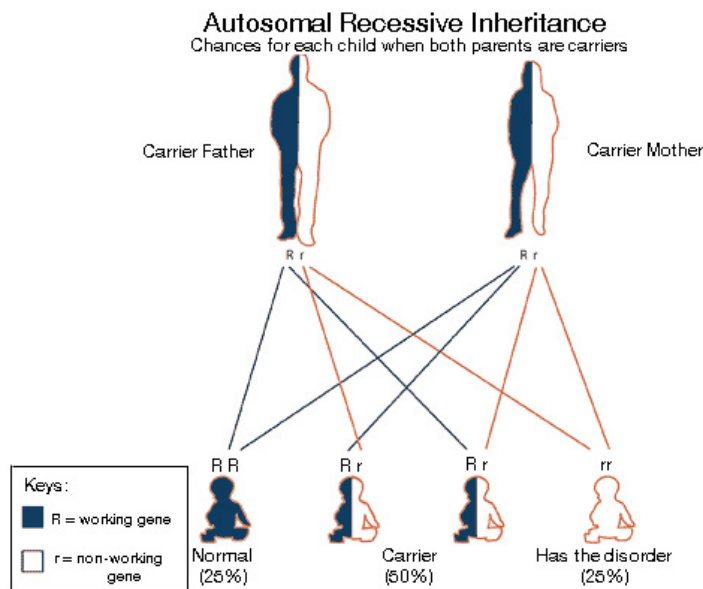
What causes the enzyme to be absent or not working correctly?





Genes tell the body to make various enzymes. People with MMA have a pair of genes that do not work correctly. Because of these gene changes, an enzyme needed by the body does not work properly or is not made at all.

### How is MMA inherited?



MMA is inherited in an autosomal recessive manner. It affects both boys and girls equally. Everyone has a pair of genes that make the needed enzyme. In children with MMA, neither of these genes works correctly. These children inherit one non-working gene for the condition from each parent.

Parents of children with MMA rarely have the disorder. Instead, each parent has a single non-working gene for MMA. They are called carriers. Carriers do not have MMA because the 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 MMA.

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 MMA. Genetic counselors can answer your questions about how MMA 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 is available for some types of MMA. Genetic testing, also called DNA testing, looks for changes in the pair of genes that cause MMA. 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, 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 help confirm MMA. Talk to your metabolic doctor or genetic counselor if you have questions about testing for MMA.

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





## Having MMA

If they are healthy and growing normally, older brothers and sisters of a baby with MMA are unlikely to have the condition. However, finding out if other children in the family have this condition is important because early treatment can prevent serious health problems. Ask your metabolic doctor whether your other children should be tested.

## MMA carriers

Brothers and sisters who do not have MMA still have a chance to be carriers like their parents. Except in special cases, carrier testing should only be done on people over 18 years of age. Each of the parents' brothers and sisters has a 50% chance to be an MMA 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 MMA. Some states do not provide newborn screening for MMA. However, expanded newborn screening through private labs is available for babies born in states that do not screen for MMA. To learn more about expanded newborn screening, see How to obtain MS/MS. When both parents are MMA 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 MMA can have special tests on blood, urine, or skin samples. Talk to your doctor or genetic counselor if you have questions about testing for MMA.

## How many people have MMA?

About one in 80,000 babies is born with MMA.

## Does MMA happen more frequently in a certain ethnic group?

MMA occurs in all ethnic groups around the world. It does not occur more often in any specific race, ethnic group, geographical area, or country.

