CONDITION

Methylmalonic acidemia

Methylmalonic acidemia is an inherited condition in which the body cannot properly break down certain proteins and fats.

WHAT IT IS
Inherited disorder causing methylmalonic acid buildup

BODY SYSTEM
Metabolism, brain, kidneys, digestive system, and blood

MAIN SYMPTOMS
Poor feeding, vomiting, unusual sleepiness, weak muscle tone

WHAT CAUSES IT
Inherited changes affecting protein and vitamin B12 metabolism

HOW IT IS DIAGNOSED
Blood and urine metabolites, confirmed by genetic testing

MAIN TREATMENT
Specialist diet, medicines, illness plans, and sometimes transplantation

CAN IT BE CURED?
No - treatment controls but does not remove it

IS IT AN EMERGENCY?
Sometimes - vomiting, severe sleepiness, or breathing changes

LONG-TERM OUTLOOK
Better with early care; kidney and neurological problems may develop

Overview

Methylmalonic acidemia, often shortened to MMA, is a group of inherited metabolic conditions. Metabolism is the process your body uses to turn food into energy and other substances it needs.

In MMA, the body cannot properly break down certain protein building blocks, as well as parts of some fats and cholesterol. This causes methylmalonic acid and related substances to collect in the blood and tissues. High levels can disturb the body's acid balance and affect the brain, kidneys, digestive system, and other organs.

Some forms mainly cause methylmalonic acid to rise. These are called isolated MMA. Other forms also cause changes such as high homocysteine, an amino acid in the blood. These combined conditions can have different symptoms and treatment needs.

MMA often begins in infancy, but milder forms may first become clear later in childhood or adulthood. Symptoms may appear or worsen when the body is under stress, such as during an infection, vomiting illness, surgery, or a long period without food.

Early diagnosis matters because treatment can reduce toxic buildup and help prevent metabolic crises. A metabolic crisis is a sudden episode in which the body's chemical balance becomes unsafe.

Symptoms

Symptoms differ according to the type of MMA and how much enzyme activity remains. A newborn may appear well at first and then become unwell after feeding begins.

Early symptoms can include:

During a metabolic crisis, acids and ammonia may build up in the blood. A baby or child may become very sleepy, irritable, confused, or difficult to wake. Seizures or loss of consciousness can occur in a severe crisis.

People with a milder form may have less obvious problems. These can include slow growth, reduced stamina, learning or movement difficulties, repeated vomiting, or episodes of illness after fasting or infection.

Some forms of MMA associated with abnormal vitamin B12 processing may also cause vision problems, anemia, developmental changes, or blood clots. Anemia means there are too few healthy red blood cells.

These symptoms have many possible causes. Having one or more does not mean that you or your child has MMA.

- Poor feeding or difficulty finishing feeds
- Repeated vomiting
- Unusual sleepiness or reduced alertness
- Weak or floppy muscle tone
- Fast or deep breathing
- Dehydration and poor weight gain

Causes and risk factors

MMA is usually caused by a change in a gene needed to break down certain nutrients. The

affected gene may control the enzyme methylmalonyl-CoA mutase or help the body process vitamin B12, also called cobalamin.

Most forms are inherited in an autosomal recessive pattern. This means a child receives one altered copy of the same gene from each parent. The parents are usually healthy carriers. When both parents carry the same condition, each pregnancy has a 1 in 4 chance of being affected.

There are several genetic types. Some respond strongly to hydroxocobalamin, a form of vitamin B12, while others respond little or not at all. Testing is needed to identify the type; symptoms alone cannot do this reliably.

Illness, dehydration, fasting, surgery, and sudden reductions in food intake do not cause MMA. However, they can trigger symptoms because the body begins breaking down its own stores of protein and fat.

Vitamin B12 deficiency from diet or poor absorption can also raise methylmalonic acid. This acquired deficiency is different from inherited MMA and is treated differently.

Diagnosis

In many places, MMA is first suspected through newborn screening. A heel-prick blood sample may show a raised level of propionylcarnitine, known as C3. This screening result does not confirm MMA because other conditions, including vitamin B12 deficiency, can cause a similar result.

Follow-up testing usually examines:

Genetic testing can usually confirm the diagnosis and identify the type. In some cases, tests of enzyme activity or vitamin B12 processing in cultured cells are needed.

Doctors may also check kidney function, blood cell counts, growth, development, vision, hearing, and heart health. These tests establish a starting point and look for complications that may need treatment.

A person who becomes unwell before newborn screening results are available needs immediate assessment. Treatment may begin before all confirmatory results return if tests suggest a metabolic crisis.

- Methylmalonic acid and other organic acids in urine
- Methylmalonic acid, amino acids, and acylcarnitines in blood
- Blood gases, glucose, electrolytes, ammonia, and lactate

- Homocysteine, methionine, vitamin B12, and folate levels

Treatment and management

MMA is managed by a specialist metabolic team. Care is tailored to the genetic type, age, growth, kidney function, laboratory results, and response to treatment.

Some people need a controlled-protein eating plan. The goal is to provide enough protein for growth and health while limiting the amino acids the body cannot process. Special medical formulas may be used. Protein should not be restricted without specialist dietetic guidance because too little can cause poor growth, weakness, and nutritional deficiencies.

Hydroxocobalamin injections can improve metabolism in vitamin B12-responsive types. Specialists usually assess whether the condition responds before deciding on long-term treatment.

Other medicines or supplements may include carnitine, which helps the body remove certain waste products. Some people receive short courses or cycles of an antibiotic like amoxicillin or doxycycline to reduce production of propionate by gut bacteria. These treatments require monitoring and are not suitable in the same form for everyone.

Families are normally given a written illness or emergency plan. During fever, vomiting, or poor intake, this plan may advise extra carbohydrate and changes to normal feeding. Its purpose is to prevent the body from breaking down its own tissues. Follow the individual plan rather than making major dietary changes without advice.

A metabolic crisis is treated in hospital. Treatment may include glucose-containing fluids, correction of dehydration and chemical imbalances, and medicines to lower ammonia. Dialysis may be needed if ammonia or acids remain dangerously high.

Liver transplantation, or combined liver and kidney transplantation, may be considered in selected cases. Transplantation can improve metabolic stability and reduce crises, but it does not remove MMA from every tissue. Kidney and neurological problems can still continue, and transplantation has significant lifelong risks.

Complications

Repeated or severe metabolic crises can injure the brain and may affect learning, movement, coordination, or muscle tone. Neurological problems can sometimes develop even when major crises have been avoided.

Long-term kidney disease is common in some forms of isolated MMA. Kidney function may gradually decline over years, so regular blood, urine, and blood pressure checks are important.

Other possible complications include poor growth, pancreatitis, reduced bone strength, anemia or low blood cell counts, and damage to the optic nerve, which carries visual information from the eye to the brain. Heart problems are more closely associated with certain related cobalamin-processing conditions.

Not everyone develops these complications. Risk is influenced by the genetic type, remaining enzyme activity, past crises, kidney health, and consistency of metabolic care.

Prevention

Inherited MMA cannot currently be prevented through food choices, exercise, or care during pregnancy. Nothing a parent did caused the gene change.

For someone who has MMA, metabolic crises may sometimes be prevented or made less severe by avoiding prolonged fasting, following the prescribed nutrition plan, and using the emergency plan promptly during illness. Routine vaccinations and ordinary infection precautions may reduce some illness-related triggers.

Genetic counselling can explain inheritance and testing options. If the gene changes in a family are known, carrier testing, testing during pregnancy, and testing of embryos used in in vitro fertilisation may be available. These are personal choices rather than requirements.

Living with it and what to expect

MMA usually requires lifelong follow-up. Regular appointments may include blood and urine testing, nutrition reviews, kidney checks, and monitoring of growth, learning, movement, vision, and bone health.

Infancy and early childhood can involve frequent feeding plans and close attention during infections. As children grow, they can gradually learn why fasting matters, which foods or formulas they need, and how to describe early symptoms. Schools and other caregivers should have a copy of the emergency plan.

Some people have few crises once treatment begins. Others continue to have episodes during illness or develop kidney, developmental, or movement problems over time. Laboratory methylmalonic acid levels may remain high even with careful treatment, so care focuses on overall health rather than one result alone.

Many children attend school and take part in family and social activities, with planning for meals, medicines, travel, and illness. Adults may need support when moving from children's services to adult metabolic and kidney care.

Keep an emergency letter and current medicine list available. Medical identification jewellery may help emergency staff recognise the condition quickly. Before surgery or any procedure requiring fasting, the metabolic team should help arrange a safe plan.

When to get medical help

Contact the metabolic team promptly for fever, reduced appetite, diarrhea, repeated vomiting, or difficulty following the usual feeding plan. Early advice may prevent deterioration, even if the person is still alert and drinking.

Seek urgent medical assessment for:

Call emergency services for a seizure, collapse, loss of consciousness, or difficulty waking the person. Bring the emergency letter and tell staff that MMA can cause metabolic acidosis and high ammonia.

Routine concerns such as growth, food choices, school planning, medicine side effects, or slowly changing stamina belong in scheduled metabolic follow-up unless there is a sudden decline.

- Repeated vomiting or inability to keep emergency feeds down
- Unusual sleepiness, confusion, weakness, or floppiness
- Fast, deep, or laboured breathing
- Signs of dehydration, such as very little urine
- Sudden poor coordination or an abnormal change in behaviour

Common questions

Is methylmalonic acidemia the same as vitamin B12 deficiency?

No. Ordinary vitamin B12 deficiency can raise methylmalonic acid, but inherited MMA is caused by genetic problems with an enzyme or with vitamin B12 processing. Blood, urine, and genetic tests distinguish them.

Can vitamin B12 cure MMA?

Hydroxocobalamin can greatly improve control in some genetic types. Other types respond

only partly or not at all. Even with a good response, ongoing specialist monitoring is needed.

What foods should someone with MMA avoid?

There is no single food list that is safe for everyone. Some people need controlled amounts of natural protein and a special medical formula. A metabolic dietitian designs the plan so nutrition and growth are protected.

Can a person with MMA exercise?

Many people can be active, but prolonged or intense activity may increase energy needs. Regular food, fluids, and an individual plan can help reduce metabolic stress. New exercise plans should be discussed during routine metabolic care.

Does a liver transplant cure MMA?

No. A transplant may reduce metabolic crises and improve chemical control, but abnormal metabolism can continue in the kidneys, brain, and other tissues. Lifelong follow-up remains necessary.

Will my other children have MMA?

For most forms, if both parents carry an altered copy of the same gene, each pregnancy has a 1 in 4 chance of MMA. A genetic counsellor can explain the risk for the exact genetic type.

Sources

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