CONDITION

# Maple syrup urine disease

Maple syrup urine disease is an inherited condition that prevents the body from properly breaking down certain amino acids.

**WHAT IT IS**
Inherited disorder of branched-chain amino acid breakdown

**BODY SYSTEM**
Brain, nervous system, and metabolism

**MAIN SYMPTOMS**
Poor feeding, vomiting, sleepiness, maple-syrup body odor

**WHAT CAUSES IT**
Inherited gene changes affecting amino acid breakdown

**HOW IT IS DIAGNOSED**
Plasma amino acids, urine organic acids, genetic testing

**MAIN TREATMENT**
Controlled protein diet, medical formula, emergency metabolic care

**CAN IT BE CURED?**
Sometimes - liver transplant largely corrects metabolism

**IS IT AN EMERGENCY?**
Sometimes - new lethargy, confusion, or poor feeding

**LONG-TERM OUTLOOK**
Often good with early, lifelong specialist treatment

## Overview

Maple syrup urine disease, often shortened to MSUD, is an inherited metabolic condition. "Metabolic" means it affects how the body processes nutrients and turns them into energy or other substances.

In MSUD, the body cannot properly break down three amino acids: leucine, isoleucine, and valine. Amino acids are building blocks of protein. These three are called branched-chain amino acids.

Without treatment, these amino acids and their by-products can build up in the blood. Leucine is especially harmful at high levels because it can affect the brain. A severe rise can cause swelling in the brain, reduced consciousness, seizures, and lasting brain injury.

The name comes from the sweet smell that may develop in urine, sweat, or earwax. The odor can resemble maple syrup or burnt sugar. It is an important clue, but it may be absent and should not be used to rule the condition in or out.

The most severe form, called classic MSUD, usually appears during the first days of life. Intermediate and intermittent forms may cause milder symptoms or episodes triggered by illness, fasting, surgery, or other physical stress.

Early detection and lifelong specialist care greatly reduce the risk of serious complications.

## Symptoms

Babies with classic MSUD often seem healthy at birth. Symptoms can then appear as amino acids build up, sometimes within the first few days.

Early symptoms may include:

Without prompt treatment, a baby may develop abnormal breathing, seizures, reduced consciousness, or coma.

Intermediate MSUD may cause ongoing problems with feeding, growth, movement, learning, or development. Symptoms can be less obvious than in classic MSUD.

People with intermittent MSUD may grow and develop as expected between episodes. Symptoms can appear during an infection, prolonged fasting, surgery, or another stress on the body. An episode may cause vomiting, poor balance, confusion, extreme tiredness, unusual behavior, or reduced consciousness.

Symptoms alone cannot confirm MSUD. Other conditions can cause similar problems, and some people with MSUD do not have the characteristic odor.

- Poor feeding or difficulty sucking
- Vomiting
- Unusual sleepiness or difficulty waking
- Irritability
- Changes in muscle tone, such as stiffness or floppiness
- Repeated abnormal movements
- A sweet, maple-syrup-like smell in urine, sweat, or earwax

## Causes and risk factors

MSUD is caused by changes in genes that help make the branched-chain alpha-ketoacid dehydrogenase complex. This group of enzymes is needed to break down leucine, isoleucine, and valine.

Most cases involve changes in the `BCKDHA`, `BCKDHB`, or `DBT` gene. Changes in `DLD` can cause a related form with additional metabolic problems.

MSUD is usually inherited in an autosomal recessive pattern. This means a child must inherit one altered gene copy from each biological parent. Parents who each carry one altered copy usually do not have symptoms.

When both parents are carriers, each pregnancy has:

These chances are the same for each pregnancy. A family history of MSUD or having parents who are related by blood increases the chance of carrying the same gene change.

Diet, parenting, and anything done during pregnancy do not cause MSUD.

- A 1 in 4 chance that the child will have MSUD
- A 1 in 2 chance that the child will be an unaffected carrier
- A 1 in 4 chance that the child will inherit neither altered copy

## Diagnosis

In many places, MSUD is included in newborn blood spot screening. A small blood sample is tested shortly after birth for patterns that may suggest certain inherited conditions.

Screening is not a final diagnosis. An abnormal result needs urgent follow-up because amino acid levels can rise before a baby looks seriously unwell.

Tests used to confirm MSUD include:

Enzyme testing may occasionally be used when other results are unclear.

If symptoms strongly suggest MSUD, treatment may begin while confirmatory results are pending. The medical team may also check blood sugar, acid levels, salts, kidney function, and signs that the brain is being affected.

Brothers and sisters may be offered testing if one child is diagnosed. Genetic counseling can help families understand test results and inheritance.

- Plasma amino acid testing: measures amino acids in the blood, including leucine, isoleucine, and valine

- Alloisoleucine testing: checks for an unusual amino acid that strongly supports an MSUD diagnosis
- Urine organic acid testing: looks for characteristic breakdown products in urine
- Genetic testing: identifies the gene changes causing the condition

## Treatment and management

MSUD needs lifelong care from a specialist metabolic team. Treatment aims to keep branched-chain amino acids within a safe range while providing enough protein and calories for growth, repair, and general health.

The main treatment is a carefully managed diet. Natural protein is limited rather than completely removed. Foods such as meat, fish, eggs, dairy products, nuts, beans, and some grains contain substantial amounts of branched-chain amino acids.

Many people use a special medical formula or medical foods. These provide protein components without leucine, isoleucine, and valine. Small, measured amounts of these amino acids are still needed because the body cannot make them. A metabolic dietitian helps balance these needs.

Regular blood tests guide dietary adjustments. Treatment plans change with age, growth, activity, pregnancy, illness, and test results.

Some people respond partly to thiamine, also called vitamin B1. This is assessed and managed by a metabolic specialist. Thiamine does not replace dietary treatment unless the specialist team confirms that the person's condition responds to it.

Illness can cause the body to break down its own protein, rapidly raising leucine levels. Each person should have a written emergency or "sick day" plan. It may include special feeds and instructions about when to contact the metabolic team or attend hospital.

Hospital treatment for a metabolic crisis may involve:

A liver transplant can provide enough working enzyme to prevent most future metabolic crises and often allows a much less restricted diet. It does not reverse brain injury that happened before surgery. Transplantation also brings lifelong risks, including rejection, infection, and the need for medicines that suppress the immune system.

- Calories given through a vein or feeding tube to stop tissue breakdown
- Specialized amino acid mixtures
- Careful correction of fluids and body salts

- Frequent blood tests
- Treatment of the infection or other trigger
- Dialysis or a similar filtering treatment when leucine is dangerously high

## Complications

The main serious complication is metabolic decompensation. This means amino acids and toxic by-products rise because the body is under stress or treatment is not meeting its needs.

A severe crisis can cause swelling in the brain, seizures, coma, and permanent brain injury. Prompt treatment lowers these risks.

Possible longer-term complications include difficulties with learning, attention, memory, speech, movement, coordination, or mental health. Some people develop these problems despite treatment, while others do not.

Poorly balanced dietary treatment can affect growth, bone health, and nutrition. This is why protein should not be restricted without specialist guidance.

Liver transplantation prevents most metabolic crises but has its own possible complications. These include rejection, infection, medication side effects, and surgical problems.

## Prevention

MSUD itself cannot be prevented because it is inherited.

Newborn screening can identify the condition before clear symptoms develop. Early treatment can prevent or reduce many complications, but it cannot guarantee that every problem will be avoided.

For someone who already has MSUD, the risk of a crisis can often be reduced by:

Genetic counseling can explain reproductive options to carriers and affected adults. These may include testing during pregnancy or testing embryos created through in vitro fertilization. These are personal choices rather than ways to prevent an inherited gene change.

- Following the individual food and medical formula plan
- Keeping scheduled blood tests and metabolic appointments
- Avoiding prolonged fasting
- Using the emergency plan during illness

- Planning ahead for surgery, pregnancy, travel, and other physical stress

## Living with it and what to expect

MSUD is lifelong unless liver transplantation largely corrects the metabolic problem. Even after transplant, follow-up remains important.

During infancy and childhood, families often measure foods, prepare medical formula, arrange blood tests, and watch closely for signs of illness. Dietary needs change as a child grows, so regular review with a metabolic dietitian is essential.

Many children diagnosed early and treated consistently attend school, take part in activities, and grow into independent adults. Some need support for learning, attention, movement, or emotional health. Existing neurological injury may remain stable, improve with rehabilitation, or become more noticeable as tasks become harder with age.

A stable period does not mean the condition has disappeared. Infection, vomiting, fasting, surgery, injury, or childbirth can still trigger a rise in leucine. Adults need an up-to-date emergency plan as well as children.

Routine follow-up usually includes blood amino acid testing, nutrition and growth checks, and review of development or neurological symptoms. Care may involve a metabolic doctor, dietitian, primary care professional, psychologist, and other specialists.

School staff, employers, and travel companions may need simple information about meals and emergency symptoms. Carrying an emergency letter or medical identification can help unfamiliar healthcare teams respond quickly.

## When to get medical help

Contact the metabolic team promptly during fever, infection, reduced appetite, vomiting, diarrhea, or difficulty taking the usual formula. Follow the personal emergency plan rather than making major dietary changes without guidance.

Seek emergency care if a person with known or possible MSUD has:

Tell emergency staff about MSUD immediately and provide the emergency letter if available. A metabolic crisis can progress even when early symptoms seem mild.

Routine concerns, such as food planning, stable test results, development, or preparation for travel and surgery, belong in scheduled follow-up with the metabolic team.

- New extreme sleepiness or difficulty waking
- Confusion, unusual behavior, or poor coordination
- Repeated vomiting or inability to keep emergency feeds down
- Poor feeding in a newborn
- Abnormal breathing
- A seizure
- Loss of consciousness

## Common questions

Why does MSUD cause a maple-syrup smell?

The smell comes from chemical by-products that build up when branched-chain amino acids are not broken down normally. The odor may be noticed in urine, sweat, or earwax. Not everyone has an obvious smell.

Can a baby with MSUD breastfeed?

Breast milk contains protein and branched-chain amino acids, so feeding must be carefully measured. Some babies can receive a planned amount of breast milk alongside special formula. A metabolic team should create and monitor the feeding plan.

Can someone with MSUD eat protein?

Yes. The body needs protein, including small amounts of leucine, isoleucine, and valine. The safe amount is individual and can change over time. Treatment combines controlled natural protein with medical formula or foods.

Can adults be diagnosed with MSUD?

Yes. Intermediate or intermittent forms may not be recognized in infancy. Symptoms may first become clear during a severe illness, surgery, fasting, or another metabolic stress. Blood amino acid and genetic tests can investigate the possibility.

Does a liver transplant cure MSUD?

A successful transplant usually prevents metabolic crises and may remove most dietary restrictions because the donor liver supplies working enzyme. The genetic change remains elsewhere in the body, and the transplant cannot undo earlier brain injury.

Could another child in the family have MSUD?

If both biological parents are carriers, each pregnancy has a 1 in 4 chance of being affected.

Genetic testing can clarify carrier status and identify which relatives may benefit from testing.

## Sources

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