CONDITION

# Mucopolysaccharidosis type III

An inherited condition that causes certain sugars to build up, mainly damaging the brain and nervous system.

**WHAT IT IS**
Inherited lysosomal storage condition mainly affecting brain function

**BODY SYSTEM**
Nervous system and multiple organs

**MAIN SYMPTOMS**
Developmental delay, behavior changes, sleep problems, loss of skills

**WHAT CAUSES IT**
Inherited enzyme deficiency

**HOW IT IS DIAGNOSED**
Enzyme activity testing and genetic testing

**MAIN TREATMENT**
Supportive care for symptoms and daily function

**CAN IT BE CURED?**
No - no treatment currently reverses it

**IS IT AN EMERGENCY?**
Sometimes - prolonged seizure or severe breathing difficulty

**LONG-TERM OUTLOOK**
Progressive loss of skills and shortened lifespan

## Overview

Mucopolysaccharidosis type III, often called Sanfilippo syndrome, is a rare inherited condition. It affects how the body breaks down a complex sugar called heparan sulfate.

Normally, enzymes break heparan sulfate into smaller parts inside cell structures called lysosomes. Lysosomes act as the cell's recycling centres. In MPS III, one of the needed enzymes is missing or does not work well. Heparan sulfate then builds up inside cells.

The buildup mainly damages the brain and nervous system. It can also affect hearing, breathing, digestion, joints and other organs. Physical changes may be less noticeable than in some other mucopolysaccharidosis conditions.

There are four subtypes: MPS IIIA, IIIB, IIIC and IIID. Each is caused by a problem with a

different enzyme. The subtypes have similar symptoms, although the age when symptoms begin and the speed of change can differ.

Children may develop as expected at first. Early signs often include delayed speech, difficult behavior or disrupted sleep. Over time, the condition causes loss of learned skills and an increasing need for care.

## Symptoms

Symptoms most often become noticeable in early childhood, but timing differs. People with a more slowly progressing form may not be identified until later childhood or adulthood.

Early symptoms can include:

Behavior can become hard to manage. A child may seem fearless, chew objects, have sudden emotional outbursts or wander away. These behaviors are caused by changes in brain function, not poor parenting.

Physical signs may include thick hair, more body hair than expected, coarse facial features, a larger head, stiff joints or a slightly enlarged liver and spleen. These signs can be mild.

As the condition progresses, a person may lose speech, learning, toileting and self-care skills. Walking can become unsteady. Swallowing may become difficult, and seizures can develop. Some people become less active and sleep more during later stages.

Symptoms and their timing are not identical for everyone. Even people with the same subtype, including siblings, can have different courses.

- Delayed speech or other developmental skills
- Very active, impulsive or restless behavior
- Difficulty concentrating
- Sleep problems, including frequent waking
- Frequent ear, sinus or chest infections
- Diarrhea or other bowel problems
- Reduced hearing

## Causes and risk factors

MPS III is caused by a change in one of four genes:

These genes provide instructions for enzymes involved in breaking down heparan sulfate.

MPS III follows an autosomal recessive inheritance pattern. This means a person must inherit one altered copy of the relevant gene from each biological parent. Parents usually carry one altered copy without having symptoms themselves.

When both parents carry an altered copy of the same gene, each pregnancy has:

These chances are the same for each pregnancy. MPS III is not caused by anything that happened during pregnancy, diet, behavior or parenting.

- SGSH causes MPS IIIA
- NAGLU causes MPS IIIB
- HGSNAT causes MPS IIIC
- GNS causes MPS IIID
- A 1 in 4 chance of a child having the condition
- A 1 in 2 chance of a child being an unaffected carrier
- A 1 in 4 chance of a child having neither altered copy

## Diagnosis

Diagnosis usually begins with a review of development, behavior, sleep, hearing and physical signs. Because early symptoms can resemble autism, attention-deficit hyperactivity disorder or a general developmental delay, MPS III may not be recognized immediately.

A urine test can look for increased glycosaminoglycans, the group of complex sugars that includes heparan sulfate. This is mainly a screening test. A normal urine result does not always exclude MPS III, especially with some testing methods or more slowly progressing forms.

Diagnosis is confirmed by measuring enzyme activity in blood cells or another suitable sample. Very low activity of a specific enzyme identifies the subtype.

Genetic testing can find changes in the related gene. It supports the diagnosis and may help with testing biological relatives, future pregnancy planning or eligibility for research studies.

Other assessments may check hearing, vision, heart function, breathing, swallowing, mobility and development. These tests show how the condition is affecting the person; they do not replace the enzyme or genetic tests that confirm it.

## Treatment and management

There is currently no cure that reverses MPS III or restores skills already lost. Care focuses on comfort, safety, communication and the symptoms affecting everyday life. Research into gene therapy, enzyme delivery and other approaches is continuing.

A coordinated care team may include specialists in metabolic conditions, child development, neurology, hearing, breathing, digestion, rehabilitation and palliative care. Palliative care can support comfort and quality of life at any stage; it is not limited to end-of-life care.

Management may include:

Behavior medicines may help selected symptoms but can also cause side effects. Treatment choices need regular review because communication, swallowing and movement change over time.

Procedures requiring sedation or a general anesthetic need careful planning. Airway shape, secretions, sleep-related breathing problems and joint stiffness can make anesthesia more complex. The anesthesia team should know about the MPS III diagnosis before any planned procedure.

Bone marrow or stem cell transplantation has not been shown to stop the neurological decline of MPS III and carries significant risks. Families considering an experimental treatment should receive a clear explanation of its goals, uncertainties, burdens and possible harms.

- Communication therapy and picture, sign or device-based communication
- Hearing aids or treatment for recurring ear problems
- Structured routines and environmental changes for behavior
- Sleep assessment and symptom-based sleep treatment
- Physiotherapy and equipment to support movement and positioning
- Seizure treatment when seizures occur
- Swallowing assessment and nutrition support
- Dental care and treatment for pain, constipation or diarrhea
- School or community support matched to changing abilities

## Complications

Progressive changes in the brain can lead to loss of language, mobility and independence. Seizures may occur, particularly later in the condition.

Poor coordination and reduced awareness of danger can increase the risk of falls and injuries. Swallowing difficulty can allow food, drink or saliva to enter the lungs. This is called aspiration

and can cause chest infections.

Other complications can include hearing loss, sleep-related breathing problems, constipation, dental problems, joint stiffness and reduced movement. Pain may be shown through behavior, sleep changes or reduced activity when a person cannot describe it.

In later stages, repeated respiratory infections and difficulty clearing airway secretions can become serious.

## Prevention

MPS III cannot be prevented in a person who has inherited two altered gene copies. Lifestyle, diet and pregnancy care do not cause or prevent the condition.

After a diagnosis, genetic counseling can explain the inheritance pattern and testing options. Biological siblings may be offered testing, including those without symptoms, because early signs can be subtle.

If the family gene changes are known, carrier testing may be available to adult relatives. Prenatal testing and testing embryos created through in vitro fertilization may also be possible. These are personal choices, and availability differs by location.

Early diagnosis does not prevent the underlying condition. It can, however, reduce delays in hearing, sleep, communication and safety support.

## Living with it and what to expect

MPS III changes over years. Early childhood may be marked by delayed speech, high activity and poor sleep. During the following years, learning and behavior often become more difficult, and previously gained skills may be lost.

Later, many people need help with eating, washing, dressing, toileting and movement. Speech may become limited or disappear. Mobility may decline from independent walking to needing a wheelchair or full assistance. These changes do not happen at the same age or speed for everyone.

People with more slowly progressing forms may retain skills longer and may survive into later adulthood. In more typical forms, lifespan is often shortened, with many people living into their teenage years or early adulthood. An individual's lifespan cannot be predicted from the subtype alone.

Even as abilities change, people may continue to respond to familiar voices, music, touch and

routines. Care usually shifts toward maintaining comfort, preserving safe movement and supporting meaningful interaction.

Families often need increasing practical help. Respite care, disability services, home adaptations and plans for school or adult care can reduce pressure. It can be useful to discuss future feeding, breathing and emergency care before a crisis occurs, while allowing plans to be reviewed as circumstances change.

## When to get medical help

Arrange routine medical review for new or worsening symptoms such as:

Prompt assessment is important after repeated choking or chest infections because these can indicate swallowing or airway problems.

Seek urgent or emergency help for:

Follow an existing seizure or emergency plan if one has been provided.

- Changes in sleep, behavior or alertness
- Possible hearing loss
- New staring spells, shaking or unexplained falls
- Coughing during meals or taking much longer to eat
- Weight loss, constipation or ongoing diarrhea
- Reduced walking, stiffness or signs of pain
- Increasing snoring or pauses in breathing during sleep
- Severe difficulty breathing, blue or grey lips, or inability to clear the airway
- Choking that does not resolve
- A seizure lasting longer than five minutes
- Repeated seizures without recovery between them
- Unresponsiveness or a major sudden change in awareness
- A serious injury, especially involving the head

## Common questions

Is Sanfilippo syndrome the same as MPS III?

Yes. Sanfilippo syndrome is another name for mucopolysaccharidosis type III. The condition is divided into types A, B, C and D according to which enzyme and gene are affected.

Can MPS III be mistaken for autism or ADHD?

Early features can overlap with autism or attention-deficit hyperactivity disorder. These may include delayed speech, high activity, impulsive behavior and sleep problems. Loss of previously learned skills, recurring infections, bowel symptoms or physical signs may lead to metabolic testing. Some people can also meet criteria for a separate developmental or behavioral diagnosis.

Is there a cure for MPS III?

There is no established cure that stops or reverses the neurological changes. Current care treats symptoms and supports communication, mobility, sleep, nutrition and comfort. Experimental treatments are being studied, but participation does not guarantee benefit.

Will another child in the family have MPS III?

If both biological parents carry an altered copy of the same MPS III gene, each pregnancy has a 1 in 4 chance of being affected. Genetic testing can confirm the family gene changes and allow more specific counseling.

How long can someone with MPS III live?

Life expectancy is often shortened, but there is a broad range. Many people with a typical course live into their teenage years or early adulthood. Some people with a slower course live considerably longer. Breathing problems, swallowing safety, infections, seizures and the form of the condition all influence outlook.

Does MPS III cause pain?

MPS III does not always cause obvious pain, but ear infections, dental problems, constipation, joint stiffness, injuries and muscle positioning can be painful. Someone who has limited speech may show pain through agitation, poor sleep, facial expressions, guarding or reduced activity.

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