CONDITION

Mucopolysaccharidoses

Mucopolysaccharidoses are inherited conditions that cause complex sugars to build up and damage different parts of the body.

WHAT IT IS
Group of inherited lysosomal storage conditions

BODY SYSTEM
Bones, joints, airways, heart, eyes, ears, and brain

MAIN SYMPTOMS
Joint stiffness, unusual bone growth, hearing loss, breathing problems

WHAT CAUSES IT
Inherited deficiency of a GAG-breaking enzyme

HOW IT IS DIAGNOSED
Urine GAGs, enzyme activity testing, and genetic testing

MAIN TREATMENT
Enzyme replacement, specialist monitoring, surgery, and supportive therapies

CAN IT BE CURED?
No - treatment cannot reverse all established damage

IS IT AN EMERGENCY?
Sometimes - sudden breathing trouble, weakness, or lost movement

LONG-TERM OUTLOOK
Ranges from near-normal lifespan to serious progressive illness

Overview

Mucopolysaccharidoses, often shortened to MPS, are a group of rare inherited conditions. They affect how the body breaks down substances called glycosaminoglycans, or GAGs. These are long sugar molecules used to build cartilage, bone, skin, and other tissues.

GAGs are normally recycled inside structures in cells called lysosomes. Lysosomes act like recycling centres. In MPS, the body is missing or has too little of an enzyme needed for this process. Partly broken-down GAGs then collect inside cells and can gradually damage tissues and organs.

There are several MPS types. They include MPS I, II, III, IV, VI, VII, and the extremely rare MPS IX. Some have older names, such as Hurler syndrome for severe MPS I, Hunter syndrome for MPS II, Sanfilippo syndrome for MPS III, and Morquio syndrome for MPS IV.

The body systems affected and the rate of change differ greatly between types. Some mainly affect bones, joints, breathing, and the heart. Others, especially MPS III and some forms of MPS I and II, can affect learning, behaviour, and brain function.

Early recognition matters because some treatments work best before permanent organ damage develops. Care is usually coordinated through a specialist metabolic or genetics centre.

Symptoms

Babies with MPS may appear healthy at birth. Symptoms often develop gradually during infancy or childhood, although milder forms may not be recognised until adolescence or adulthood.

Possible physical features include:

Frequent ear infections, hearing loss, persistent nasal discharge, noisy breathing, and sleep apnoea are common. Sleep apnoea means breathing repeatedly pauses or becomes shallow during sleep. Enlarged tonsils, narrowed airways, and changes in chest shape may contribute.

Some people develop cloudy corneas, which are the clear front surfaces of the eyes. Others have glaucoma, retinal damage, or problems with the optic nerve. Vision problems differ by MPS type.

Heart complications may include thickened or leaky heart valves, heart muscle changes, and narrowed blood vessels. These may not cause early symptoms, so regular heart checks are important.

Effects on development also differ. Intelligence is often unaffected in MPS IV and VI. Developmental slowing, loss of previously learned skills, seizures, or behavioural changes can occur in MPS III and in more severe forms of MPS I and II.

No single symptom confirms MPS. Many of these features have more common causes.

- Stiff joints or, in some types, unusually loose joints
- Short stature or slowed growth
- Abnormal development of the spine, chest, hips, knees, or hands
- A larger head, prominent forehead, or thickened facial features
- A swollen-looking abdomen from an enlarged liver or spleen
- A belly-button or groin hernia

Causes and risk factors

Each MPS type is caused by a change in a specific gene. The gene change reduces the activity of an enzyme needed to break down a particular GAG.

Most MPS types are inherited in an autosomal recessive pattern. This means a child must inherit one altered copy of the gene from each parent. The parents are usually healthy carriers. With each pregnancy, two carrier parents have a chance of having an affected child, but the outcome cannot be predicted from previous pregnancies.

MPS II is usually inherited through the X chromosome. It therefore affects boys and men much more often. Females can carry the gene change and, rarely, may develop symptoms.

Having a relative with MPS or being part of a family known to carry an MPS-related gene change increases the chance of the condition. It is not caused by anything a parent did during pregnancy, and it cannot be caught from another person.

Different changes in the same gene can leave different amounts of working enzyme. This helps explain why two people with the same MPS type may have different symptoms and rates of progression.

Diagnosis

A clinician may suspect MPS from a pattern of skeletal changes, joint problems, hearing loss, airway symptoms, hernias, heart valve changes, or developmental concerns. X-rays may show a characteristic group of bone changes called dysostosis multiplex.

A urine test can measure GAG levels or identify unusual GAG patterns. This is generally a screening test rather than final confirmation. A normal result does not reliably exclude every MPS type.

Diagnosis is confirmed by measuring the activity of the relevant enzyme in blood cells, skin cells, or another validated sample. Very low enzyme activity supports a specific MPS type. Genetic testing can identify the responsible gene changes, support the diagnosis, and help with family testing.

Other tests assess which organs are affected. These may include hearing and eye examinations, heart ultrasound, breathing and sleep studies, developmental assessment, and imaging of the brain, spine, hips, or other bones.

Some newborn screening programmes test for particular MPS types. Availability differs by location. An abnormal newborn screening result is not itself a diagnosis and requires prompt confirmatory testing.

Treatment and management

There is no treatment that reverses every effect of MPS. Management aims to replace the missing enzyme when possible, protect organ function, support development and mobility, and treat complications early.

Enzyme replacement therapy is available for certain forms of MPS I, II, IVA, VI, and VII, although approval and access differ by country. The replacement enzyme is given into a vein at regular intervals.

Enzyme replacement can improve some problems, such as reduced stamina, enlarged liver or spleen, and parts of airway or heart involvement. Its effects on bone and joint changes are limited. Standard intravenous treatment does not readily enter the brain, so it is not expected to prevent all neurological changes.

Haematopoietic stem cell transplantation replaces blood-forming cells with donor cells that can produce the missing enzyme. It is an established treatment for selected children with severe MPS I, particularly when performed early. Its role in other MPS types is more limited. Transplantation has significant risks and requires assessment at an experienced centre.

Supportive care may include:

Anaesthesia can be more complicated because of narrowed airways, limited neck movement, heart problems, or spinal instability. Any planned procedure should involve a team familiar with the person's MPS type and current medical findings.

- Physiotherapy and occupational therapy to support movement and daily activities
- Hearing aids, glasses, or other hearing and vision care
- Treatment for sleep apnoea and airway obstruction
- Heart monitoring and treatment of heart complications
- Educational, communication, and behavioural support
- Surgery for hernias, carpal tunnel syndrome, bone problems, or spinal compression

Complications

GAG buildup can affect several organs at the same time. Possible complications include progressive hearing or sight loss, reduced mobility, chronic pain, sleep apnoea, repeated chest infections, and heart valve problems.

Narrowing around the spinal cord can cause spinal cord compression. This is especially

important when the upper neck bones are unstable or poorly formed. Warning signs include new weakness, numbness, reduced hand control, balance problems, or changes in bladder or bowel control.

Fluid can sometimes collect around the brain, causing hydrocephalus. Possible signs include worsening headaches, vomiting, unusual sleepiness, changes in walking, or loss of skills.

In MPS types that affect the brain, a child may learn more slowly and later lose abilities such as speech, walking, or independent self-care. Behaviour and sleep may also change.

The chance and timing of these complications differ by MPS type and severity. Regular checks are intended to find changes before they cause major symptoms.

Prevention

MPS cannot be prevented through diet, exercise, vaccination, or changes during pregnancy. It results from an inherited gene change.

People with an MPS-related gene change can speak with a genetics professional before or during pregnancy. Carrier testing may be available for relatives when the family's gene change is known. Prenatal testing and testing of embryos created through in vitro fertilisation may also be options.

These are personal choices. Genetic counselling can explain what each test can and cannot show without directing a family toward a particular decision.

Living with it and what to expect

MPS is lifelong. Its course is shaped mainly by the MPS type, the amount of working enzyme, which organs are involved, and how early treatment begins.

Some people have slowly progressive physical symptoms and typical learning ability. They may attend school, work, form relationships, and live independently, although mobility, hearing, fatigue, or medical appointments may affect daily life.

People with more severe forms may develop major breathing, heart, skeletal, or neurological problems during childhood. They may need increasing help with communication, movement, and personal care. Life expectancy can be shortened in severe forms, while people with milder forms may live well into adulthood.

Treatment may slow or reduce some complications, but existing bone, eye, or nervous system damage may remain. New concerns can also appear despite treatment. Follow-up commonly

includes metabolic, heart, breathing, hearing, eye, dental, bone, neurological, and developmental care.

Plans at school or work may need to account for hearing loss, reduced stamina, short stature, pain, frequent appointments, or learning needs. Mental health support and contact with an MPS patient organisation can also help individuals and families manage the practical and emotional effects of a rare condition.

When to get medical help

Arrange routine medical review if there are new or gradually worsening problems such as reduced stamina, joint pain, changes in walking, snoring, daytime sleepiness, hearing or vision changes, headaches, or loss of previously learned skills. These changes do not always represent an emergency, but they should not wait until the next annual assessment.

Seek urgent medical advice for:

Call emergency services for severe breathing difficulty, blue or grey lips, collapse, a seizure lasting longer than expected under an existing care plan, or sudden inability to move an arm or leg.

After a significant fall or neck injury, urgent assessment may be needed, especially if the person has known spinal instability or develops pain, weakness, or altered sensation.

- Increasing breathing difficulty or repeated pauses in breathing during sleep
- New weakness, numbness, clumsiness, or balance problems
- A sudden decline in walking or hand control
- Persistent severe headache, repeated vomiting, or unusual drowsiness
- New bladder or bowel control problems with back or neck symptoms

Common questions

Is MPS contagious?

No. MPS is caused by an inherited gene change. It cannot spread through touch, coughing, shared food, blood, or sexual contact.

Is MPS the same as Hunter or Hurler syndrome?

Hunter syndrome is MPS II. Hurler syndrome is the older name for the severe end of the MPS I spectrum. These are individual types within the larger MPS group.

Can someone have MPS without learning difficulties?

Yes. Many people with MPS IV or VI have typical intelligence. Milder forms of other MPS types may also have little or no effect on thinking. Neurological effects are more prominent in MPS III and some forms of MPS I and II.

Can enzyme replacement therapy cure MPS?

No. It supplies some of the missing enzyme and may improve or stabilise certain organ problems. It does not correct the gene change, reliably reach the brain, or reverse all established bone and tissue damage.

Can two children in the same family be affected differently?

Yes. Siblings with the same gene changes can still have differences in symptoms and complications. However, their overall MPS type and expected pattern are often similar.

Will a person with MPS pass it to their children?

The possibility depends on the MPS type, the affected person's chromosomes, and whether their partner carries a change in the same gene. Genetic counselling and carrier testing can clarify the chance for a particular family.

Sources

- National Institute of Neurological Disorders and Stroke. Mucopolysaccharidoses
- Clarke LA. Mucopolysaccharidosis Type I . GeneReviews, University of Washington, Seattle
- Scarpa M, et al. Mucopolysaccharidosis Type II . GeneReviews, University of Washington, Seattle
- Fedele AO. Sanfilippo Syndrome: Causes, Consequences, and Treatments . The Application of Clinical Genetics . 2015;8:269-281
- Hendriksz CJ, et al. International Guidelines for the Management and Treatment of Morquio A Syndrome . Journal of Inherited Metabolic Disease . 2015;38:11-52
- Giugliani R, et al. Management Guidelines for Mucopolysaccharidosis VI . Pediatrics . 2007;120:405-418