CONDITION

Mucopolysaccharidosis type IV

Mucopolysaccharidosis type IV is an inherited condition that mainly affects bone growth, joints, breathing, hearing, and the heart.

WHAT IT IS
Inherited lysosomal storage condition affecting bones and other organs

BODY SYSTEM
Bones, joints, breathing, heart, eyes, and hearing

MAIN SYMPTOMS
Short stature, skeletal differences, joint problems, breathing difficulties

WHAT CAUSES IT
Inherited GALNS or GLB1 gene changes

HOW IT IS DIAGNOSED
Enzyme activity testing and genetic testing

MAIN TREATMENT
Enzyme replacement for type A, plus multidisciplinary supportive care

CAN IT BE CURED?
No - treatment cannot correct the inherited cause

IS IT AN EMERGENCY?
Sometimes - breathing crisis or new spinal cord symptoms

LONG-TERM OUTLOOK
Lifelong condition with possible progressive mobility and breathing problems

Overview

Mucopolysaccharidosis type IV is a rare inherited condition that affects how the body breaks down certain complex sugars. These sugars are called glycosaminoglycans, or GAGs.

GAGs normally pass into lysosomes, which are recycling centres inside cells. In this condition, a needed enzyme is missing or does not work well. Partly broken-down GAGs collect in cells and tissues, especially in cartilage and bone.

There are two main forms:

Both forms can cause similar skeletal and physical changes. Severity differs widely, including among people with the same type.

The condition particularly affects growth, the spine, joints, chest, hips, and legs. It can also

affect breathing, hearing, eyesight, teeth, and heart valves. Intelligence is usually not affected, although hearing, vision, pain, fatigue, or long absences from school can affect learning and communication.

Early recognition matters because neck instability, breathing difficulties, and heart problems may need monitoring. Treatment cannot remove all established changes, but it can support mobility, comfort, breathing, and participation in daily life.

- Type IVA results from low activity of an enzyme called GALNS
- Type IVB results from low activity of an enzyme called beta-galactosidase

Symptoms

Signs may begin in early childhood, but milder forms may not become clear until later. Babies may appear unaffected at birth.

Skeletal growth is usually affected. A child may grow more slowly than expected or stop growing at a younger age. The breastbone may project forward, the ribs may flare, and the spine may curve. The knees may angle inward, while the hips can become unstable or painful.

The joints often behave differently from those in many other mucopolysaccharidosis conditions. The wrists and some other joints may be unusually flexible rather than stiff. Larger joints can become painful or have a limited range of movement as bone and cartilage changes progress.

Other possible features include:

The bones at the top of the neck may be small or unstable. This can narrow the space around the spinal cord. Pressure on the cord may cause weakness, numbness, poor balance, changes in walking, or loss of bladder or bowel control.

Breathing can be affected by a narrow airway, a small or unusually shaped chest, spinal curvature, enlarged tonsils or adenoids, and soft airway tissues. These effects may become more important over time.

- A short neck and relatively large head
- Weakness, fatigue, pain, or reduced walking endurance
- Flat feet, ankle instability, or an unusual walking pattern
- Clouding of the cornea, the clear front surface of the eye
- Hearing loss and repeated middle-ear problems

- Crowded or weak tooth enamel
- Frequent airway infections, snoring, or pauses in breathing during sleep
- Heart murmurs caused by thickened or leaky heart valves

Causes and risk factors

Mucopolysaccharidosis type IV is caused by changes in either the GALNS gene or the GLB1 gene. These genes provide instructions for enzymes that break down specific GAGs.

The condition follows an autosomal recessive inheritance pattern. This means a person has inherited one altered copy of the relevant gene from each biological parent.

Parents who each carry one altered copy usually do not have symptoms. For every pregnancy between two carriers of the same condition, there is:

These chances are the same for each pregnancy. They do not change according to the sex of the child or the outcomes of earlier pregnancies.

Having a sibling with the condition or parents who are known carriers increases the chance of being affected. It is not caused by diet, activity, parenting, or anything that happened during pregnancy.

- A 1 in 4 chance that the child will have the condition
- A 1 in 2 chance that the child will be a carrier
- A 1 in 4 chance that the child will inherit neither altered copy

Diagnosis

Diagnosis usually begins with the pattern of growth, skeletal changes, joint findings, breathing symptoms, and results from X-rays. X-rays may show a group of characteristic bone changes called dysostosis multiplex.

A urine test can measure GAGs or look for a pattern that includes keratan sulfate. However, urine levels may be low or missed, particularly in older people or those with milder features. A normal urine screening result therefore does not always exclude the condition.

Diagnosis is confirmed by measuring enzyme activity in blood cells or cultured skin cells. Low GALNS activity supports type IVA, while low beta-galactosidase activity can support type IVB. Laboratories may test other enzymes at the same time to avoid confusing the result with another storage condition.

Genetic testing can identify changes in GALNS or GLB1 . It can confirm the type, help test relatives, and support reproductive planning.

After diagnosis, assessments usually examine the spine and neck, hips, legs, breathing, sleep, hearing, eyesight, teeth, heart, walking ability, and daily function. These establish a baseline for future follow-up.

Treatment and management

Care is usually coordinated through a specialist metabolic team, with input from several other services. The plan is based on the type of mucopolysaccharidosis, age, symptoms, mobility, and test results.

For type IVA, enzyme replacement therapy with elosulfase alfa is available in some countries. It is given by intravenous infusion and replaces some of the missing GALNS enzyme. It may improve walking endurance and other measures of physical function, but responses differ. It does not reverse established skeletal changes or cure the inherited condition.

Infusion reactions can occur. These may include fever, rash, headache, nausea, breathing symptoms, or, rarely, a serious allergic reaction. Infusions are therefore given with clinical observation and a plan for managing reactions.

There is currently no approved enzyme replacement treatment specifically for type IVB. Supportive care remains important for both types.

Treatment may include:

Operations may be needed for neck instability, spinal cord compression, hip problems, or severe leg alignment changes. Surgery can be complex because the airway, neck, chest, and heart may all be affected.

Before any operation or sedation, the anaesthesia team needs to know about the condition. Airway narrowing and neck instability can make positioning and breathing support more difficult. Procedures are safest when planned by teams familiar with mucopolysaccharidosis.

- Physiotherapy and carefully selected activity to maintain strength and movement
- Mobility aids, braces, seating support, or adaptations at home and school
- Pain management suited to the cause and the person's needs
- Hearing aids, ear procedures, glasses, and dental care
- Treatment for sleep apnoea or other breathing problems
- Medicines or procedures for heart complications

- Orthopaedic or spinal surgery when instability, deformity, pain, or nerve pressure is significant

Complications

The most serious neurological complication is spinal cord compression. It may develop where the skull meets the upper spine or at another narrowed part of the spinal canal. Without treatment, it can lead to lasting weakness or paralysis.

Chest shape, spinal curvature, airway narrowing, and weak breathing muscles can reduce lung function. Obstructive sleep apnoea causes repeated airway blockage during sleep. Some people also develop restriction, meaning the lungs cannot fully expand.

Heart valves may thicken and become narrowed or leaky. The heart muscle and the main blood vessel leaving the heart can also be affected. Regular assessment can identify changes before they cause marked symptoms.

Other possible complications include progressive hearing loss, corneal clouding, dental enamel problems, chronic pain, fatigue, reduced mobility, and early joint wear.

These complications do not affect everyone in the same way. Regular follow-up is intended to find changes early and plan treatment rather than wait for a crisis.

Prevention

Mucopolysaccharidosis type IV cannot be prevented through lifestyle choices because it is inherited.

When the gene changes in a family are known, carrier testing can help relatives understand their chance of passing on the condition. A genetics service can explain options such as testing during pregnancy or testing embryos created through in vitro fertilisation. These are personal reproductive choices, not requirements.

Early diagnosis and planned monitoring cannot prevent the genetic cause. They may, however, reduce avoidable harm from complications such as unrecognised neck instability, sleep apnoea, hearing loss, or anaesthetic risk.

Living with it and what to expect

Mucopolysaccharidosis type IV is lifelong. Skeletal changes often progress during growth and

may continue to affect mobility in adulthood. Some people walk independently throughout life. Others use walking aids or a wheelchair for longer distances or regular mobility.

Physical ability can change gradually. Pain, fatigue, breathing limitations, hip problems, or spinal cord pressure may reduce endurance. Treatment, surgery, rehabilitation, and practical equipment can preserve function or make everyday activities safer, but no single course applies to everyone.

Children usually have typical intellectual ability and can attend mainstream education. Adjustments may be needed for hearing or vision difficulties, reduced stamina, short stature, missed appointments, or physical access. Adults may work, study, form relationships, and live independently or with practical support.

Follow-up generally continues throughout life. It may include heart imaging, breathing and sleep tests, hearing and eye checks, dental care, neurological examinations, and imaging of the neck or spine. The timing is tailored to age, previous findings, and symptoms.

Emotional support can be as important as physical treatment. Changes in mobility, repeated procedures, pain, and being visibly different can affect confidence and mental health. Peer groups, counselling, accessible recreation, and suitable school or workplace adjustments may help.

When to get medical help

Call emergency services for:

Seek urgent medical assessment for new or worsening arm or leg weakness, numbness, frequent falls, loss of balance, or a clear change in walking. These may be signs of spinal cord pressure.

Prompt assessment is also appropriate for rapidly worsening breathlessness, repeated choking, unusually long pauses in breathing during sleep, or chest pain.

Routine follow-up should address gradual changes such as increasing pain, reduced walking distance, louder snoring, hearing difficulty, vision changes, dental problems, or trouble with daily activities. These are not usually emergencies, but they may show that monitoring or support needs to change.

- Severe difficulty breathing, blue or grey lips, collapse, or inability to speak
- A serious infusion reaction with breathing difficulty, facial swelling, or fainting
- Sudden weakness, loss of movement, or major loss of sensation

- New loss of bladder or bowel control with weakness or back or neck symptoms

Common questions

Is mucopolysaccharidosis type IV the same as Morquio syndrome?

Yes. Morquio syndrome is the commonly used name for mucopolysaccharidosis type IV. Type A is caused by changes in GALNS , while type B is caused by changes in GLB1 .

Does it affect intelligence?

Intelligence is usually typical. Hearing loss, vision problems, fatigue, pain, or time away from school can still affect communication and learning. These barriers should not be mistaken for an intellectual disability.

Can someone with this condition walk?

Many people can walk, especially during childhood, but endurance and mobility differ. Some later use braces, walking aids, scooters, or wheelchairs because of pain, fatigue, joint problems, breathing limits, or spinal complications.

Can enzyme replacement therapy cure type IVA?

No. Elosulfase alfa replaces some missing enzyme activity but does not change the underlying genes. It may improve physical endurance or other functions, but it cannot reverse all bone and joint changes.

Why is the neck checked so often?

The bones and ligaments at the top of the neck may not fully protect the spinal cord. Imaging and neurological examinations help identify instability or narrowing before it causes permanent nerve damage.

Can adults have a milder form that was missed in childhood?

Yes. Some people have slower progression and less obvious skeletal changes. Diagnosis may occur in adolescence or adulthood after investigations for short stature, hip or spine problems, joint flexibility, hearing loss, or breathing difficulties.

Sources

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