CONDITION

Hurler disease

Hurler disease is a severe inherited condition that causes complex sugars to build up and damage many organs.

WHAT IT IS
Severe inherited form of mucopolysaccharidosis type I

BODY SYSTEM
Nervous system, bones, joints, eyes, heart, lungs, and liver

MAIN SYMPTOMS
Developmental slowing, joint stiffness, cloudy corneas, breathing problems

WHAT CAUSES IT
Inherited changes in the IDUA gene

HOW IT IS DIAGNOSED
Enzyme activity testing plus genetic testing

MAIN TREATMENT
Stem-cell transplant, enzyme replacement, and specialist supportive care

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

IS IT AN EMERGENCY?
Sometimes - severe breathing trouble or sudden neurologic symptoms

LONG-TERM OUTLOOK
Early treatment improves survival, but lifelong complications remain

Overview

Hurler disease, often called Hurler syndrome, is the severe form of mucopolysaccharidosis type I, or MPS I. It is a rare inherited condition that begins in early childhood and affects many parts of the body.

People with MPS I do not make enough of an enzyme called alpha-L-iduronidase. Enzymes are proteins that help cells carry out chemical processes. This enzyme normally breaks down large sugar molecules called glycosaminoglycans, or GAGs.

Without enough enzyme, GAGs collect inside structures in cells called lysosomes. The buildup gradually damages the brain, airways, heart, eyes, bones, joints, liver, spleen, and other tissues.

Babies with Hurler disease may appear healthy at birth. Signs often emerge during the first

years of life. Early diagnosis matters because treatment is most effective before significant brain, heart, airway, or skeletal damage has developed.

Hurler disease is not contagious. Nothing a parent did during pregnancy causes it.

Symptoms

The exact pattern and timing are different for each child. Early signs can resemble more common childhood problems, so the condition may not be recognised from one symptom alone.

Possible symptoms and signs include:

The spine may curve, and the chest, hips, legs, or skull can develop differently. A condition called dysostosis multiplex describes the characteristic pattern of bone changes seen on X-rays.

Pressure can also build around the brain, known as hydrocephalus. Some children develop pressure on the spinal cord, especially near the top of the neck. These problems can affect walking, strength, bladder control, or alertness.

- Frequent ear, sinus, or chest infections
- Noisy breathing, snoring, or pauses in breathing during sleep
- Umbilical or groin hernias
- A larger-than expected liver or spleen, causing a swollen abdomen
- Stiff joints, reduced movement, or claw-shaped hands
- Delayed walking or changes in posture
- Thickening of facial features over time
- Clouding of the clear front part of the eye, called the cornea
- Hearing loss
- Slowed development or loss of previously learned skills
- Short stature and abnormal bone growth
- Heart valve problems

Causes and risk factors

Hurler disease is caused by harmful changes in the IDUA gene. This gene provides the

instructions for making alpha-L-iduronidase.

The condition has an autosomal recessive inheritance pattern. This means a child usually inherits one altered copy of the gene from each parent. Parents who carry one altered copy generally do not have symptoms.

When both parents are carriers, each pregnancy has:

These chances are the same for each pregnancy. Having one affected or unaffected child does not change the chance for the next pregnancy.

MPS I covers a range of severity. Hurler disease is the severe end of that range. Other people have forms that progress more slowly and may be called attenuated MPS I. Genetic results can sometimes help predict severity, but they do not always show exactly how the condition will develop.

- A 1 in 4 chance of a child having MPS I
- A 1 in 2 chance of a child being an unaffected carrier
- A 1 in 4 chance of a child inheriting neither altered copy

Diagnosis

Some regions include MPS I in newborn screening. This screening usually measures alpha-L-iduronidase activity in a dried blood sample. An abnormal screening result does not by itself mean a baby has Hurler disease. Further testing is needed promptly.

Diagnosis usually involves:

Urine GAG testing can support the diagnosis, but it is not enough to confirm or exclude the condition on its own. Very low enzyme activity can also occur in harmless situations called pseudodeficiency, so enzyme, GAG, genetic, and clinical findings are considered together.

Once MPS I is confirmed, the care team assesses its likely severity and checks which organs are affected. Tests may include heart scans, hearing and eye examinations, sleep studies, breathing tests, developmental assessment, brain or spine imaging, and skeletal X-rays.

Brothers and sisters may be offered testing because early treatment can make a major difference. Genetic counselling can explain test results, inheritance, and options for future pregnancies.

- Measuring alpha-L-iduronidase activity in white blood cells or cultured skin cells
- Measuring GAGs in urine or blood

- Genetic testing for changes in both copies of the IDUA gene

Treatment and management

Care is usually coordinated through a specialist metabolic centre. Treatment aims to supply the missing enzyme, slow further damage, manage existing problems, and support development and daily life.

For many children with Hurler disease, early hematopoietic stem-cell transplantation is the main treatment. This may also be called a bone marrow or blood stem-cell transplant. Donor stem cells can produce cells that travel through the body and supply alpha-L-iduronidase.

A successful transplant can improve survival and help preserve thinking and developmental abilities, particularly when performed early. It may also reduce liver and spleen enlargement and improve some airway or heart problems. It cannot reliably reverse damage that has already occurred, and bone, joint, eye, hearing, and heart problems may continue.

Transplantation requires chemotherapy to prepare the bone marrow. It carries serious risks, including infection, organ complications, rejection, and graft-versus-host disease, in which donor immune cells attack the recipient's tissues. A transplant team explains these risks and the expected benefits for the individual child.

Enzyme replacement therapy uses manufactured alpha-L-iduronidase, called laronidase, given through a vein. It can improve some physical features, such as breathing capacity, mobility, and liver or spleen enlargement. It does not reach the brain well because of the blood-brain barrier, the protective boundary around the brain. It therefore cannot replace transplant's effect on neurologic decline in severe MPS I.

Laronidase may be used before or around transplantation, or when transplantation is not possible. Infusion reactions can occur, so treatment is given with monitoring.

Supportive care may include:

Anaesthesia can be more complicated because of narrowed airways, heart problems, and differences in the neck and spine. Planned procedures should involve teams familiar with MPS I.

- Hearing aids, ear tubes, or treatment for ear infections
- Breathing support for sleep apnea
- Physical and occupational therapy
- Educational and communication support

- Treatment for heart, eye, dental, or digestive problems
- Surgery for hernias, spinal pressure, hydrocephalus, or severe joint problems

Complications

GAG buildup can continue to affect several organs, even after successful treatment. Regular monitoring is important because some complications develop before they cause obvious symptoms.

Possible long-term complications include:

The response to treatment is not the same in every organ. For example, transplant may protect brain development more effectively than it corrects abnormal bone growth. This is why follow-up continues even when treatment has gone well.

- Obstructive sleep apnea and narrowed airways
- Recurrent respiratory infections
- Hearing loss and reduced vision
- Heart valve thickening or heart muscle disease
- Joint stiffness, pain, and reduced mobility
- Hip, spine, and leg abnormalities
- Spinal cord compression
- Hydrocephalus
- Dental crowding and gum problems
- Developmental disability or neurologic decline

Prevention

Hurler disease cannot be prevented through diet, exercise, medicines, or actions during pregnancy. It is caused by inherited gene changes.

If MPS I is present in a family, genetic counselling can explain carrier testing and reproductive options. These may include testing during pregnancy or testing embryos created through in vitro fertilisation. These are personal choices, and counselling should provide information without pressure.

Newborn screening does not prevent the condition, but it can identify it before symptoms

become clear. This may allow treatment to begin earlier.

Living with it and what to expect

The months around diagnosis and transplantation can involve frequent appointments, tests, hospital stays, and protection from infection while the immune system recovers. Families may need practical support with travel, work, childcare, and schooling.

After initial treatment, most children still need lifelong follow-up. Care commonly involves metabolic, transplant, heart, breathing, ear, eye, bone, rehabilitation, dental, and developmental specialists. Monitoring is intended to find treatable changes early, not because a new problem is expected at every visit.

Early successful transplantation has improved survival and can preserve learning and development. However, it does not remove the altered gene from every tissue or correct all established damage. Short stature, joint stiffness, spinal or hip problems, corneal clouding, hearing loss, and heart valve changes may persist or progress over years.

Some children attend mainstream school with support, while others need more extensive educational and daily-living assistance. Physical ability may change as skeletal problems develop. Therapy, mobility equipment, hearing support, and adjustments at school or home can help maintain independence.

The long-term course is influenced by how early treatment begins, whether transplantation is successful, the amount of damage present at diagnosis, and later complications. The care plan will change as the child grows.

When to get medical help

Contact the specialist team promptly for a new change in walking, strength, coordination, bladder control, hearing, vision, sleep, breathing, or development. Increasing snoring, repeated pauses in breathing, frequent falls, persistent pain, or reduced ability to move a joint also need assessment.

During transplant recovery, follow the transplant team's instructions about fever, exposure to infection, vomiting, diarrhoea, rashes, or missed medicines. A fever during this period often needs urgent assessment even if the child otherwise seems well.

Seek emergency help for:

Routine concerns, such as gradually worsening stiffness or hearing, are usually handled

through the specialist team rather than an emergency department.

- Severe difficulty breathing, blue or grey lips, or long breathing pauses
- A seizure, collapse, or difficulty waking
- Sudden weakness, inability to walk, or loss of bladder or bowel control
- A severe headache with repeated vomiting or marked drowsiness
- A serious allergic reaction during or after an infusion

Common questions

Is Hurler disease the same as MPS I?

Hurler disease is the severe form of MPS I. MPS I also includes less severe, or attenuated, forms. These forms are caused by changes in the same gene but differ in their speed of progression and effect on the brain and other organs.

Can Hurler disease be cured with a stem-cell transplant?

A successful transplant can supply the missing enzyme, improve survival, and protect development when performed early. It is not a complete cure because it cannot reverse all existing damage, and some bone, joint, eye, heart, and hearing problems may continue.

Does Hurler disease affect intelligence?

Without effective early treatment, GAG buildup in the brain can cause developmental slowing and loss of skills. Early transplantation can preserve cognitive development in many children, but outcomes are influenced by age and developmental status at treatment.

Why is enzyme replacement not enough by itself?

Laronidase can reach many organs through the bloodstream, but very little crosses the blood-brain barrier. It can improve several physical features but does not adequately protect the brain in severe MPS I.

Can another child in the family have it?

If both parents are carriers, each pregnancy has a 1 in 4 chance of MPS I. Siblings may be offered testing even when they have no symptoms because the condition can be difficult to recognise early.

Is Hurler disease painful?

Joint stiffness, abnormal bone growth, nerve pressure, headaches, or surgery can cause pain. Pain should not be assumed to be unavoidable. Assessment can identify treatable causes and guide safe pain management.

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