CONDITION

Multiple sulfatase deficiency

Multiple sulfatase deficiency is an inherited condition in which low enzyme activity causes harmful materials to build up in several body systems.

WHAT IT IS
An inherited condition affecting multiple waste-clearing enzymes

BODY SYSTEM
Nervous system, skin, bones, eyes, and internal organs

MAIN SYMPTOMS
Developmental loss, muscle stiffness, scaly skin, skeletal changes

WHAT CAUSES IT
Inherited SUMF1 gene changes

HOW IT IS DIAGNOSED
Sulfatase enzyme tests and SUMF1 genetic testing

MAIN TREATMENT
Supportive, symptom-based multidisciplinary care

CAN IT BE CURED?
No - no established disease-modifying treatment

IS IT AN EMERGENCY?
Sometimes - breathing difficulty, choking, or prolonged seizure

LONG-TERM OUTLOOK
Progressive disability, often with shortened lifespan

Overview

Multiple sulfatase deficiency is a very rare inherited condition. It affects several enzymes called sulfatases, which help cells break down complex fats and sugars. When these enzymes do not work properly, substances that should be recycled build up inside cells.

This buildup can damage the brain, spinal cord, skin, bones, eyes, airways, and internal organs. The condition is a type of lysosomal storage disorder. Lysosomes are small recycling compartments inside cells.

Symptoms usually begin in infancy or childhood, although the age of onset and rate of progression differ. Early-onset forms tend to be more severe. Later-onset forms may progress more slowly.

Multiple sulfatase deficiency combines features seen in several other inherited conditions. These include metachromatic leukodystrophy, which mainly damages the nervous system, and mucopolysaccharidoses, which can affect bones, joints, facial features, and organs.

There is currently no cure or established treatment that corrects the underlying enzyme problem. Care focuses on comfort, function, nutrition, communication, and the treatment of specific symptoms.

Symptoms

A baby with a severe early form may have symptoms at birth or during the first months of life. Other children may initially develop as expected before their progress slows or they begin to lose skills.

Nervous system symptoms may include:

Spasticity means that muscles become unusually tight because of changes in the brain or spinal cord. It can limit movement and contribute to pain or joint stiffness.

Many affected children develop ichthyosis, meaning dry, thick, scaly skin. This may be present early or become more noticeable with age.

Changes involving bones and connective tissues may include joint stiffness, an abnormal curve of the spine, short stature, or changes in the shape of the chest, hands, and facial features. Some people develop an enlarged liver or spleen. Teeth may emerge late or have weak enamel.

Repeated chest infections, noisy breathing, sleep-related breathing problems, and difficulty clearing mucus can occur. Swallowing problems may allow food, drink, or saliva to enter the airway. This is called aspiration.

Not everyone develops every symptom. The pattern can differ even among people in the same family.

- Delayed development or loss of learned skills
- Reduced muscle tone early on, followed by stiffness or spasticity
- Difficulty sitting, standing, walking, speaking, or swallowing
- Seizures
- Hearing or vision loss
- Changes in behaviour, attention, or thinking

Causes and risk factors

Multiple sulfatase deficiency is caused by harmful changes in the SUMF1 gene. This gene provides instructions for making formylglycine-generating enzyme, or FGE. FGE activates all sulfatase enzymes. When it does not work well enough, several sulfatases have low activity at the same time.

The condition is inherited in an autosomal recessive pattern. This means a person has a harmful gene change in both copies of SUMF1 , usually one inherited from each parent.

Parents who carry one altered copy usually do not have symptoms. When both parents are carriers, each pregnancy has:

These chances apply separately to each pregnancy. Nothing a parent did before or during pregnancy causes the condition.

- A 1 in 4 chance of an affected child
- A 1 in 2 chance of a child who is an unaffected carrier
- A 1 in 4 chance of a child who is neither affected nor a carrier

Diagnosis

Diagnosis usually begins when a child has a combination of developmental, neurological, skin, skeletal, or organ symptoms. Because these features overlap with other rare conditions, testing is needed to confirm the cause.

Enzyme tests measure the activity of several sulfatases in white blood cells or cultured skin cells. Finding low activity in more than one sulfatase supports multiple sulfatase deficiency. Careful sample handling is important because poor handling can affect enzyme results.

Genetic testing looks for harmful changes in both copies of the SUMF1 gene. This can confirm the diagnosis and may allow carrier testing for relatives.

Other tests help assess how the condition is affecting the body rather than confirm its cause. These may include:

Urine or imaging results cannot confirm the condition by themselves. Genetic and enzyme findings should be interpreted together by a specialist experienced in inherited metabolic conditions.

- Brain and spinal imaging, usually with MRI
- Hearing and vision assessments

- Swallowing and feeding evaluations
- Sleep or breathing studies
- Heart, liver, and spleen assessments
- X-rays or other imaging of the bones and joints
- Urine tests for substances that accumulate when sulfatases are impaired

Treatment and management

There is no approved treatment that restores all affected sulfatase activity. Enzyme replacement treatments used for some other lysosomal storage disorders do not correct the multiple enzyme deficiencies in this condition.

Care is usually coordinated through a metabolic or genetics service. The wider team may include neurology, respiratory medicine, rehabilitation, nutrition, gastroenterology, orthopaedics, audiology, eye care, dentistry, and palliative care.

Treatment may include physical and occupational therapy to support movement, positioning, daily activities, and joint comfort. Splints, adapted seating, wheelchairs, and communication devices can help maintain participation as abilities change.

Speech and swallowing specialists can assess communication and feeding. Food textures or eating positions may be adjusted when swallowing becomes difficult. Some people eventually need tube feeding to provide nutrition, fluids, or medicines and reduce the effort of eating. Tube feeding does not remove every risk of aspiration.

Medicines may be used to manage seizures, muscle stiffness, reflux, constipation, pain, or sleep problems. The exact choice is based on the person's symptoms and overall health.

Airway clearance techniques, breathing support during sleep, and prompt treatment of respiratory infections may be needed. Hearing aids, vision supports, skin care, dental care, and treatment for orthopaedic problems can also improve comfort and function.

Palliative care can be introduced alongside other treatment. It supports comfort, symptom control, decision-making, and family wellbeing; it is not limited to care at the end of life.

Experimental treatments are being studied, but their safety and effectiveness have not been established. A specialist can explain whether any appropriate research studies are available.

Complications

The buildup of material inside cells causes continuing nervous system damage. Over time, a person may lose movement, speech, swallowing, vision, hearing, or other previously learned abilities.

Possible complications include:

Respiratory complications are a major concern, particularly in severe early-onset forms. Problems may result from aspiration, infection, weak breathing muscles, or narrowing of the airway.

Medical procedures and anaesthesia may require extra planning because airway, breathing, spine, and heart problems can occur. The anaesthesia team should be told about the diagnosis before any planned procedure.

- Aspiration and repeated lung infections
- Weak coughing or difficulty clearing airway secretions
- Seizures
- Painful muscle stiffness and joint contractures
- Scoliosis and reduced mobility
- Poor nutrition, dehydration, or constipation
- Sleep-related breathing problems
- Increasing dependence on others for daily care

Prevention

Multiple sulfatase deficiency cannot be prevented through diet, exercise, vaccination, or choices made during pregnancy. It is caused by inherited SUMF1 gene changes.

Genetic counselling can help families understand inheritance and testing options. Once the specific family gene changes are known, options may include carrier testing for adult relatives, testing during pregnancy, or preimplantation genetic testing with in vitro fertilisation.

These are personal choices. Genetic counselling provides information and support without assuming which option is right for a family.

Living with it and what to expect

Multiple sulfatase deficiency is progressive, meaning symptoms tend to increase over months

and years. Development may slow, stop, or move backwards. Skills such as walking, speaking, eating, and communicating may become harder.

The rate of change is not the same for everyone. Babies with symptoms at or soon after birth usually have a severe course. Children whose symptoms begin later may retain abilities for longer, but the condition still usually progresses. A small number of people have survived into adulthood with later-onset forms.

Life expectancy is often shortened, especially when symptoms begin early. It is not possible to predict an individual lifespan from the diagnosis alone. Breathing problems, aspiration, infections, and the severity of nervous system involvement have an important effect on outlook.

Regular follow-up focuses on identifying treatable problems early. Appointments may monitor nutrition, swallowing, breathing, sleep, seizures, movement, pain, hearing, vision, bones, and communication.

Children can continue to benefit from education, play, relationships, and familiar routines even as their physical or learning needs change. Adapted communication methods may help them express preferences and remain involved.

Families often need practical support with equipment, transport, home adaptations, respite care, and school planning. Social workers, therapists, rare-condition organisations, and palliative care teams can help coordinate these services.

When to get medical help

Arrange a routine or prompt review if you notice a new loss of skills, increased muscle stiffness, feeding difficulty, weight loss, repeated chest infections, worsening sleep, new pain, or changes in hearing or vision. These changes are not always emergencies, but they may need assessment and a care-plan update.

Seek urgent medical advice for persistent vomiting, signs of dehydration, a suspected chest infection, a new seizure, or a clear increase in choking or coughing during meals.

Call emergency services if the person:

Follow an existing seizure or emergency care plan if one has been provided. Its instructions may recommend acting sooner.

- Is struggling to breathe or has blue or grey lips
- Is choking and cannot breathe or cough effectively

- Has a seizure lasting five minutes or longer
- Has repeated seizures without recovering between them
- Is unusually difficult to wake
- Suddenly becomes limp, unresponsive, or severely weak

Common questions

Is multiple sulfatase deficiency the same as metachromatic leukodystrophy?

No. Both can damage the brain's white matter, which carries signals between different parts of the nervous system. Metachromatic leukodystrophy involves deficiency of one main sulfatase. Multiple sulfatase deficiency affects many sulfatases and can therefore cause a broader combination of nervous system, skin, bone, and organ symptoms.

Can multiple sulfatase deficiency be cured?

There is currently no cure or established treatment that corrects the underlying problem. Treatment aims to manage symptoms, reduce complications, preserve comfort, and support communication and daily life.

Can someone develop it as an adult?

The genetic changes are present from birth. Symptoms usually appear during infancy or childhood, but milder forms may not become clear until later. Survival into adulthood is possible, particularly with later-onset forms.

Does it always cause loss of skills?

Loss of developmental or physical skills is common because the condition is progressive. The age when this begins and how quickly it happens differ. Some people have a slower course and retain certain abilities for years.

Can brothers or sisters have different symptoms?

Yes. Siblings with the same SUMF1 gene changes may still differ in age of onset, symptoms, and rate of progression. Genetic results can provide useful information, but they cannot predict the course with certainty.

How rare is multiple sulfatase deficiency?

It is considered an ultra-rare condition. The exact frequency is not known, partly because symptoms overlap with other inherited metabolic conditions and some people may remain undiagnosed.

Sources

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