CONDITION

Sphingolipidosis 1

Sphingolipidosis 1 is a rare inherited condition that disrupts fatty molecules needed for normal brain and nerve function.

WHAT IT IS
Inherited sphingolipid disorder affecting brain myelin

BODY SYSTEM
Nervous system

MAIN SYMPTOMS
Developmental delay, movement stiffness, seizures, swallowing problems

WHAT CAUSES IT
Inherited changes in both DEGS1 gene copies

HOW IT IS DIAGNOSED
Genetic testing showing two disease-causing DEGS1 variants

MAIN TREATMENT
Supportive neurological, therapy, nutrition, and breathing care

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

IS IT AN EMERGENCY?
Sometimes, with prolonged seizures or serious breathing difficulty

LONG-TERM OUTLOOK
Often progressive disability; severe forms may shorten life

Overview

Sphingolipidosis 1 is a very rare inherited condition affecting how the body processes sphingolipids. These are fatty molecules that help build cell membranes and protect nerve cells.

The condition is caused by harmful changes in the DEGS1 gene. This gene provides instructions for making an enzyme involved in converting one type of sphingolipid into another. When the enzyme does not work properly, the balance of these fats is disrupted.

The nervous system is especially sensitive to this imbalance. In particular, it can affect myelin , the fatty covering that insulates nerve fibres and helps signals travel quickly through the brain and spinal cord. Brain scans may show too little normally formed myelin, called hypomyelination .

Most reported cases have begun during infancy or childhood. The condition can affect development, movement, muscle control, feeding, and breathing. Severity is not the same for everyone, and knowledge about the full range of the condition is still developing because so few people have been identified.

Symptoms

Symptoms may begin in early infancy, later childhood, or after a period of apparently typical development. Some children gain skills more slowly than expected. Others lose skills they had already learned, known as developmental regression.

Possible symptoms include:

A person may have only some of these features. Symptoms can also change over time. For example, low muscle tone may be more noticeable early in life, while stiffness and involuntary movements may become more prominent later.

Communication and learning can be affected. However, movement or speech difficulties do not always show what a person understands. Some people may benefit from eye-gaze systems, picture boards, switches, or other communication technology.

- Delayed sitting, standing, walking, talking, or learning
- Low muscle tone, which can make the body feel unusually floppy
- Muscle stiffness or tightness, also called spasticity
- Twisting or repetitive movements caused by dystonia
- Poor balance, coordination, or head control
- Seizures
- Uncontrolled eye movements or difficulty coordinating eye movements
- Weakness, reduced movement, or loss of independent walking
- Problems chewing or swallowing
- Slow weight gain or difficulty getting enough nutrition
- Abnormal breathing, weak coughing, or repeated chest infections

Causes and risk factors

Sphingolipidosis 1 is caused by disease-causing variants in both copies of the DEGS1 gene. A

variant is a change in genetic instructions. The resulting enzyme deficiency disrupts the normal conversion of dihydroceramides into ceramides, two related types of sphingolipid.

The condition follows an autosomal recessive inheritance pattern. This usually means each parent carries one altered DEGS1 copy but does not have the condition.

When both parents are carriers, each pregnancy has:

These chances start again with every pregnancy. They do not change based on the outcome of an earlier pregnancy.

The main risk factor is having two carrier parents. Parents may be related by blood or come from a community where a particular variant is more common, but many families have no known history of the condition. It is not caused by anything a parent did during pregnancy.

- A 1 in 4 chance that the child will inherit both altered copies
- A 1 in 2 chance that the child will be an unaffected carrier
- A 1 in 4 chance that the child will inherit neither altered copy

Diagnosis

Diagnosis usually starts with an assessment of development, movement, muscle tone, feeding, vision, and seizures. A neurological examination checks how the brain, spinal cord, nerves, and muscles are working.

Magnetic resonance imaging, or MRI , uses a strong magnet to produce detailed pictures of the brain. In sphingolipidosis 1, MRI may show hypomyelination or other changes in the brain's white matter. White matter contains the nerve fibres that connect different brain regions.

MRI findings are important, but they are not unique to this condition. Other inherited neurological conditions can produce similar images.

Genetic testing is used to confirm the diagnosis. It must identify disease-causing variants in both DEGS1 copies. Testing may involve a panel of genes linked to white-matter conditions, analysis of all protein-coding genes, or broader genome testing.

Specialist laboratories may measure sphingolipids in blood cells or cultured skin cells. An abnormal ratio of dihydroceramides to ceramides can support the diagnosis and help specialists interpret uncertain genetic findings. This testing is not routinely available everywhere.

Parents and siblings may be offered targeted genetic testing after the variants in the family are known. A genetics professional can explain what the results mean for each relative.

Treatment and management

There is currently no established treatment that corrects the DEGS1 gene change or restores normal sphingolipid processing. Care therefore focuses on symptoms, comfort, development, communication, and preventing avoidable complications.

Physical therapy can help maintain movement, positioning, joint flexibility, and comfort. Supportive equipment may include braces, standing frames, specialist seating, wheelchairs, or sleep-positioning systems.

Occupational therapy can help with daily activities, hand use, sensory needs, and access to toys, schoolwork, or communication devices. Speech and language support may address both communication and swallowing.

Seizures may be treated with antiseizure medicines. The choice of medicine is based on seizure type, other health needs, and possible side effects. A written seizure plan can explain what caregivers should do and when rescue treatment or emergency help is needed.

Stiffness and involuntary movements may be managed with therapy, positioning, medicines, or selected procedures. The aim is not only to change muscle tone but also to improve comfort, sleep, care, and useful movement.

A swallowing assessment may be needed if eating takes a long time, coughing occurs during meals, or weight gain is poor. Food textures and seating can sometimes be adjusted. If eating by mouth is unsafe or does not provide enough nutrition, tube feeding may be discussed. Tube feeding does not necessarily prevent all aspiration, because saliva or stomach contents can still enter the airway.

Breathing care may include help clearing mucus, treatment of chest infections, and assessment of coughing or sleep-related breathing. Hearing, vision, bone health, dental care, growth, and pain may also need regular review.

Complications

Swallowing weakness can allow food, drink, or saliva to enter the airway. This is called aspiration. It can cause coughing, breathing problems, or aspiration pneumonia.

Reduced movement and ongoing muscle stiffness can lead to joint tightening, known as contractures. Curvature of the spine, hip problems, discomfort, and pressure injuries may also develop. Positioning, equipment, and regular movement can reduce some of these effects.

Other possible complications include:

Not everyone develops every complication. Regular follow-up is intended to identify changes early and support comfort and participation.

- Poor growth, dehydration, or undernutrition
- Repeated or prolonged seizures
- Sleep disruption and breathing problems
- Constipation and reflux
- Reduced bone strength and fractures
- Loss of mobility or communication skills
- Repeated respiratory infections

Prevention

Sphingolipidosis 1 cannot be prevented through diet, exercise, vaccination, or changes during pregnancy. It results from inherited genetic variants.

Once the family's DEGS1 variants are known, genetic counselling can explain options for future pregnancies. Depending on personal values and local availability, these may include testing during pregnancy, testing embryos created through in vitro fertilisation, using donor eggs or sperm, or choosing not to test.

Carrier testing may also be available to adult relatives. Genetic testing is a personal decision, and its emotional, practical, and family effects can be discussed before testing.

Living with it and what to expect

Published reports suggest that sphingolipidosis 1 is often progressive, meaning neurological abilities may decline over months or years. Some people have periods when changes are slow or difficult to notice. Others lose movement, feeding, or communication skills more quickly.

Hypomyelination is generally a lasting feature. Supportive treatment does not replace the missing myelin, but it may help a person stay comfortable, use available abilities, and take part in family, education, and community life.

Day-to-day needs can become complex. Coordinated follow-up may involve neurology, genetics, rehabilitation, nutrition, respiratory care, orthopaedics, and palliative care. Palliative care is not limited to the end of life. It can help at any stage with pain, sleep, symptoms, family support, and decisions about care.

School-aged children may need an individual education plan, accessible transport, communication support, and assistance with personal care. Families may also benefit from respite services, social work support, and contact with rare-condition or leukodystrophy communities.

The effect on life expectancy is uncertain because the condition is extremely rare and long-term information is limited. Severe swallowing, breathing, or seizure complications can be life-limiting. A person's likely course is best estimated from their current abilities, rate of change, breathing and feeding health, and specific genetic findings.

When to get medical help

Arrange routine medical follow-up if you notice new stiffness, reduced movement, changes in alertness, feeding taking longer, coughing during meals, weight loss, constipation, pain, sleep changes, or a change in seizure pattern. These changes are not always emergencies, but they may require assessment or an adjustment to support.

Seek prompt medical advice for fever with chest symptoms, repeated vomiting, signs of dehydration, increasing sleepiness, or possible aspiration.

Call emergency services for:

Follow any individual seizure, breathing, or feeding emergency plan already provided.

- A seizure lasting longer than the person's emergency plan allows
- Repeated seizures without recovery between them
- Severe breathing difficulty, blue or grey lips, or long pauses in breathing
- Choking with an inability to breathe or cough
- Sudden unresponsiveness or a major change in consciousness

Common questions

Is sphingolipidosis 1 the same as every sphingolipidosis?

No. Sphingolipidosis is a broad term for conditions involving sphingolipid metabolism. Sphingolipidosis 1 specifically refers to the inherited condition caused by harmful variants in both DEGS1 gene copies.

Can a child outgrow sphingolipidosis 1?

No. The genetic change remains throughout life. Abilities and support needs can change, but

the underlying condition does not go away with age.

Does it always cause severe disability?

Reported cases often involve substantial neurological disability, but severity and rate of progression are not identical. The small number of known cases makes precise predictions difficult.

Is there a cure or gene therapy?

There is no established cure or approved treatment that corrects DEGS1 deficiency. Research into sphingolipid biology may inform future treatments, but experimental findings are not the same as proven human therapy.

Can someone with this condition understand more than they can show?

Yes, this is possible. Severe movement and speech difficulties can limit how a person responds. Communication assessments and assistive technology may help show preferences, choices, and understanding.

Could another child in the family have it?

If both parents carry the family's DEGS1 variant, each pregnancy has a 1 in 4 chance of being affected. Genetic testing and counselling can clarify the chance for a particular family.

Sources

- Pant DC, Dorboz I, Schluter A, et al. "Loss of the sphingolipid desaturase DEGS1 causes hypomyelinating leukodystrophy." Journal of Clinical Investigation . 2019;129(3):1240-1256.
- Online Mendelian Inheritance in Man. "Sphingolipidosis 1; SPLD1." OMIM entry 618404. Johns Hopkins University.
- National Center for Biotechnology Information. "DEGS1: Delta 4-desaturase, sphingolipid 1." NCBI Gene database.
- National Library of Medicine. "DEGS1 gene." MedlinePlus Genetics.
- van der Knaap MS, Bugiani M. "Leukodystrophies: a proposed classification system based on pathological changes and pathogenetic mechanisms." Acta Neuropathologica . 2017;134(3):351-382.