CONDITION

# Sphingomyelinase deficiency

Sphingomyelinase deficiency is an inherited condition that causes fatty material to build up in organs and sometimes the nervous system.

**WHAT IT IS**
Inherited enzyme deficiency causing fatty material buildup

**BODY SYSTEM**
Liver, spleen, lungs, blood, brain, and nerves

**MAIN SYMPTOMS**
Enlarged abdomen, breathing problems, bruising, developmental loss

**WHAT CAUSES IT**
Inherited SMPD1 gene changes

**HOW IT IS DIAGNOSED**
Enzyme testing and SMPD1 genetic testing

**MAIN TREATMENT**
Enzyme replacement and symptom-focused supportive care

**CAN IT BE CURED?**
No, treatment controls some body effects

**IS IT AN EMERGENCY?**
Sometimes, with severe breathing difficulty or uncontrolled bleeding

**LONG-TERM OUTLOOK**
From severe early decline to long-term adult survival

## Overview

Sphingomyelinase deficiency is usually called acid sphingomyelinase deficiency, or ASMD. It is a rare inherited condition in which the body does not make enough working acid sphingomyelinase enzyme.

This enzyme normally breaks down sphingomyelin, a fatty substance found in cells. Without enough enzyme activity, sphingomyelin collects inside cells. The buildup mainly affects the liver, spleen, lungs, and blood. In some forms, it also damages the brain and nerves.

ASMD was previously divided into Niemann-Pick disease types A, A/B, and B. Doctors now view these as a range:

These categories can overlap. Even relatives with the same gene changes may not have

exactly the same symptoms.

ASMD is different from Niemann-Pick disease type C. The conditions can cause some similar symptoms, but they involve different genes and require different testing.

- Infantile neurovisceral ASMD causes early organ and nervous system problems
- Chronic neurovisceral ASMD causes organ problems with some nervous system involvement
- Chronic visceral ASMD mainly affects organs outside the brain

## Symptoms

Symptoms may begin in infancy, childhood, or adulthood. Some people have serious early illness, while others have milder problems that progress slowly.

An enlarged spleen is a common early finding. It may make the abdomen look swollen or cause fullness and discomfort under the left ribs. An enlarged liver can also increase abdominal size.

Other possible symptoms include:

Lung involvement happens when affected cells collect in the tissue between the air sacs. This is called interstitial lung disease. It can reduce how well oxygen passes into the blood, although lung scans may show changes before breathing symptoms become obvious.

Low platelets can contribute to bruising and bleeding. Platelets are blood cells that help form clots. An enlarged spleen may trap platelets and other blood cells.

When the nervous system is involved, a baby or child may have weak muscle tone, feeding problems, delayed development, loss of previously learned skills, or difficulty moving the eyes. Severe infantile ASMD usually progresses quickly. Chronic neurovisceral ASMD generally progresses more slowly.

Some people have a cherry-red spot at the back of the eye. This is a finding seen during an eye examination and does not necessarily mean that vision is affected.

- Shortness of breath, reduced stamina, or repeated chest infections
- Easy bruising, nosebleeds, or prolonged bleeding
- Slow growth or delayed puberty
- Tiredness and weakness
- Bone or joint pain
- Abnormal blood cholesterol and triglyceride levels

## Causes and risk factors

ASMD is caused by harmful changes in both copies of the `SMPD1` gene. This gene provides instructions for making acid sphingomyelinase.

The condition follows an autosomal recessive inheritance pattern. This means a child usually inherits one altered gene copy from each parent. Parents who carry one altered copy generally do not develop ASMD.

When both parents are carriers, each pregnancy has:

These chances start again with every pregnancy. They do not change based on the sex of the child or what happened in an earlier pregnancy.

ASMD is not caused by diet, infection, parenting, or anything someone did during pregnancy. Having a relative with ASMD or carrying an `SMPD1` gene change is the main risk factor.

- A 1 in 4 chance of a child having ASMD
- 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

Symptoms and an enlarged liver or spleen may raise suspicion of ASMD, but they cannot confirm it. Other inherited, blood, liver, and storage conditions can look similar.

Diagnosis requires a test showing low acid sphingomyelinase activity. The enzyme can be measured using blood cells or another suitable sample. A dried blood spot may be used for initial testing, but an abnormal screening result may need confirmation with another sample.

Genetic testing looks for harmful changes in both copies of the `SMPD1` gene. It can confirm the diagnosis, help identify relatives who are carriers, and sometimes provide information about the likely range of symptoms. A genetic result cannot always predict the exact course.

After diagnosis, tests may assess which parts of the body are affected. These can include blood counts, liver tests, cholesterol tests, lung function tests, chest imaging, abdominal imaging, and checks of growth, development, movement, hearing, and eye health.

A liver or bone marrow biopsy is not usually needed to confirm ASMD. Because an enlarged spleen and low platelets may increase bleeding risk, any invasive procedure needs careful planning.

## Treatment and management

There is no treatment that removes ASMD from every cell or reverses established nervous system damage. Management focuses on slowing treatable organ problems, monitoring changes, and supporting daily health.

Olipudase alfa is an enzyme replacement therapy available in some countries for children and adults with ASMD manifestations outside the brain. It replaces some missing acid sphingomyelinase activity and can improve problems such as enlarged liver and spleen, abnormal blood fats, and reduced lung function.

This treatment does not cross the protective barrier around the brain. It is therefore not expected to treat nervous system damage. It is given by intravenous infusion under specialist supervision. Doses are increased gradually, and monitoring is needed because infusion reactions and temporary liver test changes can occur.

Other care is based on the organs affected. It may include:

Removing an enlarged spleen is not routine treatment. The spleen has important immune functions, and its removal may worsen lipid buildup in other organs. It is generally considered only in unusual circumstances.

Regular follow-up often involves a metabolic or genetics team working with liver, lung, blood, heart, rehabilitation, and child-development specialists as needed.

- Breathing support, respiratory therapy, or treatment of chest infections
- Physical, occupational, speech, and feeding therapies
- Nutritional and growth support
- Management of bleeding or low blood cell counts
- Treatment of cholesterol and cardiovascular risk where appropriate
- Pain relief and bone health support
- Palliative care for comfort and family support in severe forms

## Complications

Sphingomyelin buildup can cause progressive scarring and loss of organ function. Possible complications include chronic lung disease, low blood oxygen, liver fibrosis or cirrhosis, and high pressure in the blood vessels leading through the liver.

A very enlarged spleen is more vulnerable to injury. It can also trap enough blood cells to

worsen bruising, bleeding, tiredness, or infection risk.

Abnormal cholesterol and triglyceride levels may contribute to early artery disease. Cardiovascular risk needs individual assessment rather than being judged from age alone.

Bone thinning, fractures, growth problems, and delayed puberty can occur. Severe neurological forms can lead to increasing difficulty with swallowing, movement, communication, and breathing.

Not everyone develops all these complications. Their likelihood and timing are influenced by the amount of remaining enzyme activity, the form of ASMD, age, and access to treatment and monitoring.

## Prevention

ASMD cannot be prevented through lifestyle changes because it is inherited.

Genetic counselling can help people understand family testing and reproductive options. When the `SMPD1` changes in a family are known, options may include carrier testing for adult relatives, testing during pregnancy, or testing embryos created through in vitro fertilisation.

These are personal choices. A genetics professional can explain what each test can and cannot show without assuming which option is right for a family.

Early diagnosis does not prevent the gene changes, but it can allow monitoring and treatment to begin before some complications become advanced.

## Living with it and what to expect

The course of ASMD ranges widely. Severe infantile neurovisceral ASMD causes developmental loss and worsening organ disease during early childhood. Current enzyme replacement therapy may help disease outside the brain, but it does not treat the progressive neurological injury that drives this form.

People with chronic neurovisceral ASMD may have a mixture of learning, movement, and organ problems that change over years. Support at school, rehabilitation, and help with communication or mobility may become important.

Many people with chronic visceral ASMD reach adulthood. Some continue education, work, and family life while attending regular appointments and managing fatigue, breathing limits, or an enlarged abdomen. Others develop significant lung, liver, bleeding, or cardiovascular complications.

Follow-up commonly tracks spleen and liver size, breathing, oxygen levels, blood counts, liver function, blood fats, growth, bone health, and everyday function. The schedule is based on age, symptoms, organ involvement, and treatment.

Contact sports or activities with a high chance of abdominal impact may be unsafe when the spleen is very enlarged. A specialist can explain how spleen size affects participation without unnecessarily restricting ordinary activity.

Plans may change over time. New breathlessness, reduced exercise ability, bruising, abdominal growth, feeding difficulty, or loss of skills should be reported rather than left until the next scheduled review.

## When to get medical help

Arrange routine or prompt medical review for new or worsening symptoms such as increased tiredness, frequent bruising, recurrent chest infections, reduced stamina, abdominal discomfort, feeding problems, or changes in development and movement.

If you receive enzyme replacement therapy, report symptoms during or after an infusion promptly. These may include rash, fever, headache, nausea, breathing symptoms, or feeling faint. The infusion team can assess whether treatment needs to be paused or adjusted.

Seek urgent medical care after a significant blow to the abdomen, especially if there is new pain beneath the left ribs, left shoulder pain, dizziness, weakness, or fainting. These can be signs of bleeding from an injured spleen.

Call emergency services for:

These symptoms are not a routine part of follow-up and need immediate assessment.

- Severe or rapidly worsening difficulty breathing
- Blue or grey lips or skin
- Uncontrolled or heavy bleeding
- Fainting with abdominal pain
- Sudden severe weakness or unresponsiveness

## Common questions

Is sphingomyelinase deficiency the same as Niemann-Pick disease?

ASMD was historically called Niemann-Pick disease type A, A/B, or B. It is not the same as

Niemann-Pick disease type C, which has different genetic causes and treatments.

Can adults have mild sphingomyelinase deficiency?

Yes. Chronic visceral ASMD may not be diagnosed until adolescence or adulthood. Even so, apparently mild disease can affect the lungs, liver, spleen, bones, blood fats, or blood cell counts and needs ongoing monitoring.

Can enzyme replacement cure ASMD?

No. Olipudase alfa can treat several effects outside the brain, but it does not correct the inherited gene changes or reach the brain. Continued treatment and monitoring are needed.

Will my child lose developmental skills?

Not every child with ASMD has neurological decline. Loss of skills is mainly associated with neurovisceral forms. Enzyme and genetic results, development over time, and neurological assessment help clarify the likely form, but they cannot predict every change.

Can someone with ASMD have children?

Often, yes. A person with ASMD passes an altered `SMPD1` gene copy to each child. Whether a child could have ASMD also depends on the other biological parent's carrier status. Genetic counselling can explain testing and reproductive options.

Is there a special diet for sphingomyelinase deficiency?

No diet removes stored sphingomyelin or replaces the missing enzyme. Nutrition support may still help with poor growth, swallowing problems, liver disease, or other individual needs. Major dietary restrictions should not be started without specialist advice.

## Sources

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