CONDITION

Niemann-pick disease

Niemann-pick disease is a group of inherited conditions that cause harmful fat buildup in cells, affecting organs and sometimes the brain.

WHAT IT IS
Inherited conditions causing fats to build up inside cells

BODY SYSTEM
Liver, spleen, lungs, blood, and nervous system

MAIN SYMPTOMS
Enlarged abdomen, poor growth, breathing problems, movement changes

WHAT CAUSES IT
Inherited gene changes affecting fat processing

HOW IT IS DIAGNOSED
Enzyme, biomarker, and genetic tests

MAIN TREATMENT
Subtype-specific therapy and supportive care

CAN IT BE CURED?
No - treatments manage or slow effects

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

LONG-TERM OUTLOOK
Ranges from early severe illness to long-term adulthood

Overview

Niemann-pick disease is the traditional name for a group of rare, inherited conditions in which certain fats build up inside cells. These fats can collect in the liver, spleen, lungs, bone marrow, and brain.

There are two main forms:

These forms have different causes, symptoms, treatments, and expected courses. Knowing the exact subtype is therefore important.

ASMD often affects the liver, spleen, lungs, blood counts, and growth. Severe infantile ASMD also affects the brain and nervous system. NPC commonly causes liver or spleen enlargement early in life, followed by problems with movement, balance, speech, swallowing, thinking, or

behaviour.

Symptoms may begin before birth, during infancy or childhood, or in adulthood. Some forms progress quickly, while others change slowly over many years.

- Acid sphingomyelinase deficiency , or ASMD , includes conditions once called Niemann-Pick types A, A/B, and B
- Niemann-Pick type C , or NPC , is a separate condition caused by difficulty moving cholesterol and other fats through cells

Symptoms

Symptoms differ according to the subtype, age of onset, and organs affected. Members of the same family may not have exactly the same course.

A baby or child with ASMD may have:

Older children and adults with chronic ASMD may have reduced exercise tolerance, shortness of breath, abdominal discomfort, low blood counts, and abnormal cholesterol levels. Bone and joint pain can occur. Some people are shorter than expected for their family.

NPC symptoms also differ with age. Babies may develop jaundice, meaning yellow skin or eyes, or prolonged liver disease. An enlarged liver or spleen may be found before nervous system symptoms appear.

Later signs can include:

In teenagers and adults, psychiatric symptoms or changes in thinking may appear before obvious movement problems. These symptoms have many possible causes and do not by themselves mean someone has NPC.

- A swollen-looking abdomen caused by an enlarged liver or spleen
- Feeding difficulties, poor weight gain, or slow growth
- Frequent chest infections or breathing problems
- Easy bruising or bleeding because of low platelet levels
- Delayed development or loss of skills in severe infantile ASMD
- Clumsiness, unsteady walking, or frequent falls
- Difficulty moving the eyes up and down
- Slurred speech or trouble swallowing
- Muscle stiffness, twisting movements, or tremor

- Seizures
- Sudden loss of muscle tone triggered by laughter or emotion, called cataplexy
- Changes in memory, learning, mood, behaviour, or school performance

Causes and risk factors

Niemann-pick conditions are caused by inherited gene changes.

ASMD is caused by changes in the SMPD1 gene. These changes reduce the activity of acid sphingomyelinase, an enzyme that helps break down a fatty substance called sphingomyelin. Without enough working enzyme, sphingomyelin collects inside cells.

NPC is usually caused by changes in the NPC1 gene and less often by changes in NPC2 . These genes help move cholesterol and other fats within cells. When they do not work properly, fats become trapped.

Both ASMD and NPC usually follow an autosomal recessive inheritance pattern. This means a child must inherit one altered copy of the relevant gene from each biological parent. Parents who carry one altered copy generally do not have the condition.

When both parents carry a change in the same gene, each pregnancy has:

These chances apply separately to every pregnancy. The conditions are not caused by anything a parent did during pregnancy.

- A 1 in 4 chance that the child will have the condition
- 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 may begin after symptoms, an enlarged liver or spleen, abnormal blood results, or a known diagnosis in a relative. Because the features overlap with many other conditions, specialist testing is needed.

For suspected ASMD, a blood test can measure acid sphingomyelinase activity. Low enzyme activity supports the diagnosis. Genetic testing for changes in SMPD1 can confirm it and may help clarify the likely subtype.

For suspected NPC, blood tests can measure substances that rise when cells cannot process fats normally. These are called biomarkers. Genetic testing looks for changes in NPC1 and

NPC2 .

If genetic or biomarker results are unclear, a specialist laboratory may examine skin cells grown from a small biopsy. A test called filipin staining shows how cholesterol is stored inside those cells. This test is used less often now that genetic and biomarker testing have improved.

Other tests assess which organs are affected. They may include blood counts, liver tests, lung function tests, hearing checks, eye movement assessment, scans, swallowing tests, and developmental or neurological assessments. These tests support care planning but do not usually confirm the condition by themselves.

Genetic counselling can help you understand test results, inheritance, and whether testing may be useful for relatives.

Treatment and management

There is no single treatment for every Niemann-pick subtype. Care is usually coordinated by a specialist team and adjusted as symptoms change.

For ASMD, olipudase alfa is an enzyme replacement therapy for the effects outside the brain. It is given through a vein and can improve or stabilize features such as spleen enlargement, lung involvement, and some blood or liver measures. It does not cross effectively into the brain, so it is not expected to treat nervous system damage in severe infantile ASMD. Infusions require monitoring because reactions can occur.

For NPC, treatment options depend on age and country. In the United States, arimoclomol is approved with miglustat for neurological symptoms in adults and children aged 2 years and older. Miglustat is also used for neurological manifestations of NPC in several other countries. These treatments are intended to slow or manage neurological progression; they do not remove all symptoms or reverse established damage.

Supportive treatment remains important for every subtype. It may include:

Swallowing difficulties may require changes to food texture or, in some cases, feeding through a tube. The aim is to maintain nutrition and reduce food or drink entering the lungs.

An enlarged spleen is generally protected rather than removed. Spleen removal can worsen lung disease in ASMD and is usually avoided unless there is a compelling specialist reason.

- Nutrition support for poor growth or swallowing difficulty
- Physical and occupational therapy for movement and daily activities
- Speech therapy and communication support

- Treatment for seizures, muscle stiffness, pain, or sleep problems
- Respiratory care, vaccines, and prompt treatment of chest infections
- Educational, psychological, and social support

Complications

Fat buildup can gradually damage affected organs.

Liver complications may include scarring, reduced liver function, or increased pressure in the veins around the liver. An enlarged spleen can trap blood cells, causing low platelets, anaemia, easy bruising, or bleeding.

Lung involvement may reduce oxygen transfer and exercise tolerance. Swallowing problems can allow food, drink, or saliva into the lungs, leading to aspiration pneumonia.

Neurological complications are most prominent in severe infantile ASMD and NPC. They can include increasing difficulty with walking, speaking, swallowing, learning, memory, and independent daily activities. Seizures and cataplexy may cause falls or injuries.

Reduced mobility, poor nutrition, and long-term illness can also affect bone strength, sleep, mood, education, employment, and family life.

Prevention

Niemann-pick conditions cannot be prevented through diet, exercise, or lifestyle because they are inherited.

If a gene change is known in your 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.

Early diagnosis cannot prevent the underlying condition, but it may allow earlier treatment, monitoring, and support. Testing relatives may identify people who have mild or not-yet-recognised symptoms.

Living with it and what to expect

The long-term course is closely linked to the exact subtype and the age when symptoms begin.

Severe infantile ASMD usually progresses quickly and can shorten life substantially. Chronic ASMD may allow survival into adulthood, although lung, liver, blood, and bone complications can require ongoing care.

NPC is progressive, meaning symptoms tend to increase over time. Earlier neurological onset is often linked with faster progression. People whose neurological symptoms begin in adolescence or adulthood may experience a slower course over many years. No test can predict an individual course with certainty.

Regular follow-up is used to monitor breathing, liver and spleen size, blood counts, growth, nutrition, swallowing, movement, hearing, vision, and learning or thinking. Routine appointments are also a time to discuss new symptoms, equipment needs, school or workplace support, and advance care preferences.

Daily life may involve therapy appointments, medicines, mobility equipment, communication aids, or help with eating and personal care. Some people with chronic ASMD remain active and independent for many years. People with NPC may gradually need more support with movement, communication, and decision-making.

Emotional support matters for the person with the condition and for family members. Rare-condition organisations, genetic counsellors, social workers, and palliative care teams can help with practical planning and symptom relief. Palliative care can be provided alongside active treatment; it is not limited to the final stage of illness.

When to get medical help

Arrange a routine medical review if you or your child develops a new or gradual change such as increasing falls, worsening speech, reduced appetite, weight loss, more bruising, declining school performance, or greater difficulty with usual activities.

Contact the usual specialist team promptly about:

Seek emergency help for severe breathing difficulty, blue or grey lips, choking that does not clear, a prolonged seizure, repeated seizures without recovery, or sudden unresponsiveness.

Severe pain in the upper left abdomen after a fall or blow also needs urgent assessment because an enlarged spleen can be vulnerable to injury.

- New coughing or choking during meals
- Increasing shortness of breath
- A noticeable change in swallowing

- New seizures, cataplexy, or repeated falls
- Yellow skin or eyes
- Rapidly increasing abdominal swelling

Common questions

Is Niemann-pick disease the same as high cholesterol?

No. NPC affects how cholesterol and other fats move inside cells, but it is not the same as common high blood cholesterol caused by genetics, diet, or other health conditions. ASMD mainly involves buildup of sphingomyelin.

Can adults develop Niemann-pick disease?

The gene changes are present from birth, but symptoms may not become clear until adulthood. Adult-onset NPC can first appear as changes in balance, eye movement, thinking, mood, speech, or coordination. Chronic ASMD may also be diagnosed in adults.

Is Niemann-pick disease contagious?

No. It cannot spread through contact, coughing, food, blood, or sexual activity. It is inherited through gene changes passed down in families.

Can a person have it if both parents are healthy?

Yes. Parents who each carry one altered gene copy usually have no symptoms. A child can inherit the altered copy from both parents and have the condition.

Is there a cure for Niemann-pick disease?

There is currently no cure. Subtype-specific treatments may improve some organ problems or slow neurological progression. Supportive care can also reduce symptoms and help maintain function and quality of life.

What is the difference between types A, B, and C?

Types A and B are older names within ASMD. Type A describes severe infantile disease with neurological involvement, while type B usually describes a more chronic form mainly affecting organs outside the brain. Type C is a separate condition caused by changes in NPC1 or NPC2 .

Sources



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