ENLARGED ABDOMEN

ENLARGED SPLEEN

ENLARGED LIVER

SHORTNESS OF BREATH

COUGHING

NOSEBLEEDS

EASY BRUISING

ABDOMINAL PAIN

DIARRHEA

FATIGUE

APRIL & GARRETT

Real patients diagnosed with ASMD

We were diagnosed with ASMD, could our diagnosis be yours?

Understanding ASMD

ASMD is a genetic condition that is also known as Niemann-Pick disease types A, A/B, and B.

ASMD

ACID SPHINGOMYELINASE DEFICIENCY

INFORMATION FOR YOU AND YOUR FAMILY

Your questions about ASMD, answered

In this guide, you will find information on:

JJ
Living with ASMD

What is ASMD?

A rare, inherited disease with symptoms that can affect multiple organs

ASMD is a lysosomal storage disorder caused by the **deficiency of an important enzyme**

This genetic disease can be **passed down in families,** and symptoms may appear at any point from infancy to adulthood

The symptoms of ASMD can affect individuals differently and often worsen over time, **which can lead to serious health issues**

There are three types of ASMD, which vary in symptom severity and appearance

Knowing the ASMD types can help you and your doctor talk about the disease and better understand the symptoms.

Type A | Starts from infancy and rapidly worsens—affecting the brain and nervous system, as well as other organs.

Type A/B | Can start from infancy to childhood, often worsening over time and impacting multiple organs—including the brain and nervous system.

Type B | The most common type of ASMD, it can start at any age and symptoms often worsen. Type B may affect multiple organs, with little to no impact on the brain.

What causes ASMD?

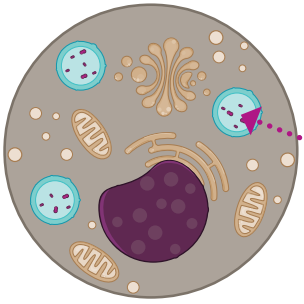
An altered gene leads to deficiency of ASM enzyme

ASMD is caused by alterations to one of your genes (a section of your DNA) called *SMPD1*. The *SMPD1* gene provides the instructions to make the enzyme acid sphingomyelinase (ASM)—but when *SMPD1* is altered, it cannot make enough of the ASM enzyme.

What does the ASM enzyme do?

- Inside cells, enzymes break down fats and other substances. The ASM enzyme breaks down a fatty substance called sphingomyelin within the lysosomes (sac-like structures) of certain cells
- If there is not enough ASM, sphingomyelin cannot be broken down efficiently, and builds up in organs such as the liver, spleen, and lungs
- Over time, this leads to health complications, as these key organs cannot function properly

Buildup of sphingomyelin in cells can impact major organs

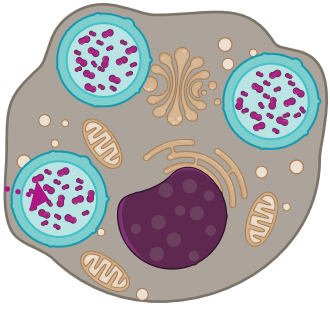


Cell with normal ASM enzyme activity

There is enough ASM enzyme to break down sphingomyelin, so cells function as normal

Cell with decreased ASM enzyme activity

Low ASM enzyme activity from ASMD leads to buildup of sphingomyelin in cells of the body, causing symptoms and potential damage to organs



 **Cell**

 **Lysosome**

 **Sphingomyelin** (a fatty substance)

Sphingomyelin buildup in your cells can lead to worsening symptoms and serious health complications over time.

Early diagnosis is essential for managing some of these symptoms.

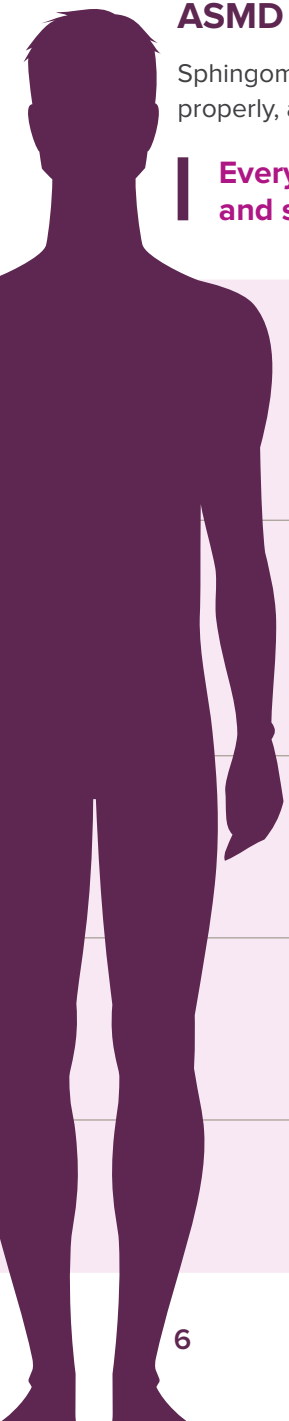
ANNE
Living with ASMD

What are the signs & symptoms of ASMD?

ASMD can impact multiple organs and body systems

Sphingomyelin buildup in cells may eventually cause organs to not function properly, and can result in a variety of signs and symptoms.

Everyone experiences the disease differently, as certain signs and symptoms may develop over time or not at all.



Lungs

Coughing, difficulty breathing, and chronic fatigue *due to scarring of the lungs (interstitial lung disease) and infections (i.e., pneumonia)*

High blood pressure affecting your heart and lungs *(pulmonary hypertension)*

Liver

Enlarged liver *(hepatomegaly)*

Scarring of the liver *(liver fibrosis)*

Abnormal cholesterol levels *(dyslipidemia)*

Increased liver enzymes *can be seen on lab tests*

Spleen

Enlarged spleen *(splenomegaly)*

Abdominal pain, pressure, and loss of appetite *due to splenomegaly*

Blood

Fatigue *due to decreased red blood cells (anemia)*

Easy bruising and bleeding *due to decreased blood platelets (thrombocytopenia)*

Gastrointestinal

Abdominal pain and loss of appetite

Diarrhea

6

Brain/Nervous system mainly types A and A/B

Decreased muscle tone *(hypotonia)*

Impaired balance and coordination *(ataxia)*

Developmental delays in children

Tingling in hands and feet *due to nerve damage (peripheral neuropathy)*

Eyes mainly types A and A/B

Red spot on retinas *(cherry red maculae)*

Heart mainly types A/B and B

Damage to heart blood vessels *(coronary artery disease)*

Abnormal heartbeat *can be seen on electrocardiogram (EKG)*

Skeletal

Back, limb, and/or joint pain

Frequent bone fractures *due to weakening of bones (osteopenia and osteoporosis)*

Growth delay in children

The most common symptoms you may see or feel:

Protruding abdomen

Coughing and difficulty breathing

Easy bruising and bleeding

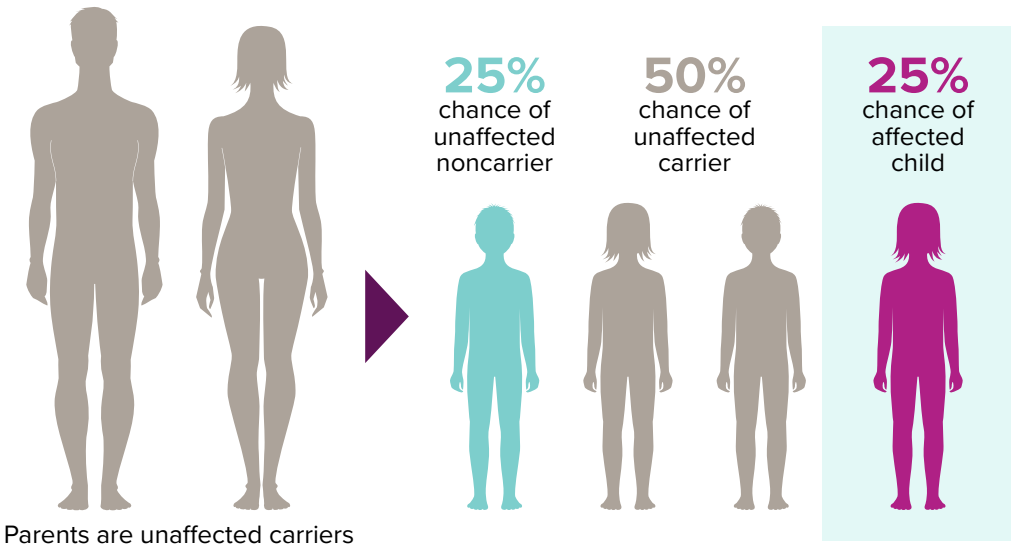
Abdominal pain and diarrhea

How is ASMD inherited?

ASMD is a genetic condition passed down in families

- Genes are passed down from parents to their children, with children receiving one copy of a gene from each parent
- ASMD is caused by changes to the *SMPD1* gene
- For ASMD to be passed from parents to their child, two copies of the altered *SMPD1* gene are needed—one copy from each parent
- If a child inherits just one copy of the altered gene, they will not have ASMD, but they will be a "carrier"
- A carrier for ASMD does not experience any symptoms, but can pass the altered gene and disease on to their children

Even if neither parent has ASMD, they may still pass the condition to their children



Parents are unaffected carriers

Because ASMD runs in families, knowing how ASMD is inherited is critical. Family screening for ASMD can help get to a diagnosis quicker so that symptoms can be managed earlier.

EVREN
Living with ASMD

& his mother, Kara

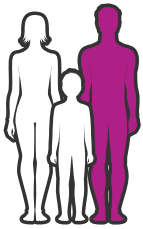
Finding an ASMD diagnosis

Testing is the only way to know if you or your child have ASMD. If a member of your family has ASMD, talk to your doctor about family screening.

Ask your doctor about getting tested:

If you are experiencing any symptoms of ASMD

OR



If a family member has been diagnosed with ASMD

Getting tested for ASMD is simple

- A blood test that measures the amount of ASM enzyme in your blood can confirm an ASMD diagnosis
- Additional confirmation may be done using genetic testing
- Invasive testing procedures, such as bone marrow biopsies, are NOT required to confirm a diagnosis of ASMD

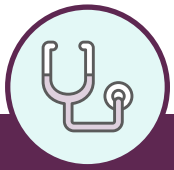
Your ASMD diagnosis can be the first step towards managing your symptoms with your healthcare team.

Living with ASMD

Taking charge of your diagnosis

While an ASMD diagnosis may seem overwhelming, know that you are not alone in your experience. Each person's journey with ASMD is unique, but the feelings of frustration, isolation, and sadness you may have are normal.

Taking charge of symptom management and communication with your healthcare team may help you better control your health.



Get to know your healthcare team

Your team may include multiple specialists coordinated by your primary care physician (PCP)—communication with your doctors is key

Keep track of your symptoms

Sharing your notes with your healthcare team can help them determine how to better manage your symptoms

Reach out to the ASMD community for help and support

There are resources available to support patients with ASMD and their families and caregivers. *See page 12 for more information*

ASMD support resources

You are not alone in your ASMD journey

The ASMD community has a variety of resources available. Below are professional organizations, national advocacy groups, and educational websites that work to support patients with ASMD and their families and caregivers.

All information and resources provided by these organizations are maintained and operated by the entity listed below. Please note this list is meant to serve as a general reference, and additional resources may also be available through other organizations. Sanofi Genzyme does not endorse any particular organization or the content and programs they offer.

National Niemann-Pick Disease Foundation (NNPDF)
nnpdf.org

National Organization for Rare Disorders (NORD)
rarediseases.org

Visit ASMDfacts.com to learn more

To receive updates, you can submit a Stay Up to Date Form on ASMDfacts.com or contact us at **1-800-745-4447**, Option 3 for Patient Services, then press 1 for more information on ASMD

Glossary

Acid sphingomyelinase (ASM)
An enzyme responsible for breaking down the fatty substrate sphingomyelin in some cells of the body.

Acid sphingomyelinase deficiency (ASMD)
A genetic disease with symptoms that can worsen over time and impact multiple organs. The condition occurs due to a lack of the enzyme acid sphingomyelinase.

Anemia
A condition in which the blood doesn't have enough healthy red blood cells to carry the necessary oxygen to the different parts of the body.

Ataxia
The loss of control of muscle movements, resulting in impaired coordination and slurred speech.

Carrier
A person capable of passing on a genetic alteration associated with a disease, but who does not usually display symptoms of the disease.

Enzyme
A substance produced by the body to accelerate chemical reactions.

Gene
A portion of DNA that contains instructions for the development of one or more personal traits or characteristics. Genes are passed on from parents to their children.

Hepatomegaly
Enlargement of the liver.

Hypotonia
Reduced muscle tone and decreased strength.

Lysosome
A membrane-enclosed sac within a cell that contains enzymes.

Osteoporosis
A condition in which bones become more brittle and fragile.

Sphingomyelin
A type of fatty substance found in animal cell membranes, especially in the membrane that surrounds some nerve cells.

Splenomegaly
Enlargement of the spleen.

Thrombocytopenia
A condition in which low blood platelet count often leads to easy bruising and bleeding.

APRIL & GARRETT
Real patients diagnosed with ASMD

ASMD
ACID SPHINGOMYELINASE DEFICIENCY

Is ASMD the answer to your symptoms?

- ASMD is a rare, genetic disease that affects both children and adults
- The multiorgan symptoms of ASMD can worsen over time and lead to serious health complications, as well as impact emotional and social well-being
- Support resources are available for people who have been diagnosed with ASMD and their caregivers

If a family member has been diagnosed with ASMD or you are experiencing symptoms, talk to your doctor about getting tested.

A diagnosis can be achieved with just 1 simple blood test.

Learn more at ASMDfacts.com or contact us at 1-800-745-4447, Option 3 for Patient Services, then press 1 for more information on ASMD

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