MDA Muscular Dystrophy Association

Spinal Muscular Atrophy (SMA)

Spinal muscular atrophy (SMA) is a genetic neuromuscular disorder affecting approximately 1 in 10,000 live births. It is estimated to affect roughly 10,000 children and adults in the United States, and about 1 in every 50 Americans is a genetic carrier. The disease can affect infants and adults of any race or gender.

SMA is classified as a motor neuron disease, a progressive neuromuscular disorder that destroys muscle-controlling nerve cells called motor neurons. In SMA, motor neurons in the spinal cord are affected.

In the most common form of SMA (chromosome 5 SMA, or SMN-related SMA), loss of or mutation in the survival motor neuron 1 (SMN1) gene interferes with the production of SMN protein, which is needed to maintain healthy, functional motor neurons. Without SMN protein, motor neurons degenerate and become nonfunctional. When this happens, they are no longer able to send signals to muscles, which then weaken and become smaller because of inactivity.

The SMN1 gene is located on chromosome 5. The neighboring SMN2 genes can partially compensate for nonfunctional SMN1 gene by making some SMN protein, and some of the therapeutic strategies for chromosome 5 SMA focus on encouraging the production of fully functional SMN protein from this “backup” gene.

Other forms of SMA are not related to a loss of the SMN1 gene, arising instead from defects in different genes on different chromosomes. These forms vary greatly in severity and in the muscles most affected.

People can have multiple copies of the SMN2 gene. The more SMN2 genes a person has, the more functional SMN protein is available and the milder the SMA disease course is likely to be. Genetic testing can determine how many SMN2 genes a person has and roughly predict the course of SMA that is likely to result.

All known forms of SMA are genetic and have different inheritance patterns and implications for family planning. If you or your child has received an SMA diagnosis, talk with your doctor, and perhaps a genetic counselor to find out more about the genetics and prognosis for the particular form of SMA involved.

There is no cure for SMA. The first disease modifying therapy was approved in 2016 and more therapies have been approved since then.

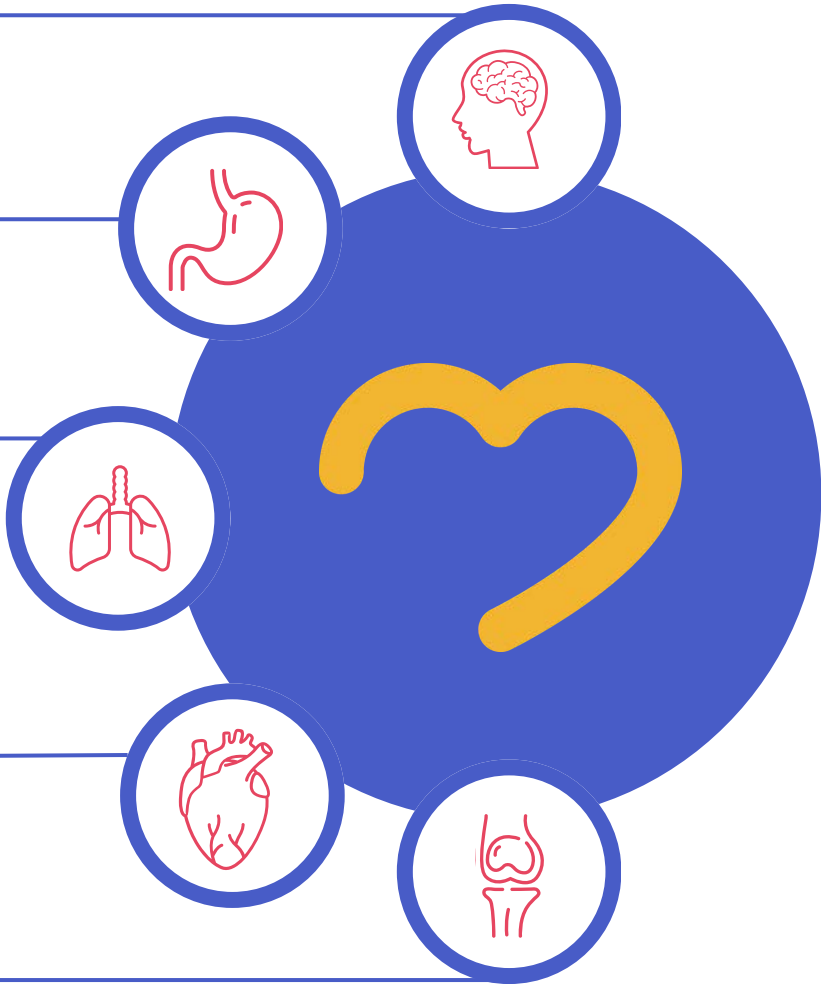
What are the Signs and Symptoms of Spinal Muscular Atrophy?

Nervous System
- Impaired Motor Function

Gastrointestinal
- Dysphagia

Lungs
- Breathing difficulties
- Respiratory infections
- Chest infections
- Respiratory failure

Heart
- Cardiomyopathy



Skeleton and Muscle
- Muscle weakness
- Fatigue
- Spasticity
- Bone fractures
- Contractures
- Hip dislocation
- Scoliosis
- Kyphosis

What Should I Know About SMA?

1. With advances in medical care, the outlook for SMA has improved and the known natural history of the disease is being rewritten.

2. There are several FDA-approved treatments available for SMA with many others in the drug development pipeline. While none of the available treatments are a cure, they may slow the progression of the disease.

3. There is **wide variability** in age of onset, symptoms, and rate of progression in the different forms of SMA. The age at which SMA symptoms begin roughly correlates with the degree to which motor function is affected: The earlier the age of onset, the greater the impact on motor function. In chromosome 5 SMA, these differences are indicated by classifications into types 1 through 4.
   - **Type 1** is the most severe. Onset typically occurs between birth and 6 months, and babies with this type of SMA never learn to sit independently.
   - **Type 2** onset occurs between 6 and 18 months. These infants typically gain the ability to sit but not to stand.
   - **Type 3** onset occurs in children 18 months or older. These children typically achieve the ability to stand and to walk.
   - **Type 4** onset occurs in the 20s or 30s after the individual has learned to walk independently.

4. Other forms of SMA caused by genes other than SMN1 include:
   - **Spinal muscular atrophy with respiratory distress (SMARD):** In this severe form of SMA, infants have respiratory distress in addition to muscle weakness.
   - **Distal SMA:** This form of SMA more severely affects the hand and feet muscles. Disease onset and severity can vary depending on the causative gene.

5. In many forms of SMA, **weakened respiratory muscles** make it difficult to cough and clear secretions, leading to increased risk of serious respiratory infection. A simple cold can quickly progress to pneumonia. Symptoms of breathing difficulties can include headaches, difficulty sleeping at night, and excessive daytime sleepiness.

6. SMA **does not** affect cognition, emotional development, learning or academic ability, or sensory ability.

7. SMA was added to the **Recommended Uniform Screening Panel** for newborns in 2018 and has now been adopted by every state ensuring that every baby born can be screened for SMA and have early access to life-changing treatments.

How is SMA treated?

Treatment for SMA includes supportive interventions, such as physical and occupational therapy, along with disease-modifying therapies that target the underlying cause of the disease. Treatment is individualized and determined by a patient's healthcare team.

- **Muscle relaxants*** may reduce spasticity. Botulinum toxin may be used to treat jaw spasms or drooling, and there are medications that can be used to reduce excessive saliva.
- Antidepressants and anxiolytics may be helpful in treating depression and anxiety.
- **Physical therapy** through exercise can help to restore and maintain muscle strength and function. Stretching helps maintain range of motion.
- **Occupational therapy** can help improve daily living and work skills.
- **Spine-straightening surgery** may be done to improve comfort and respiratory function.
- **Speech-language pathologists** can help with swallowing and speech problems.
- **A gastrostomy tube** (sometimes called a g-tube or feeding tube) allows liquid nutrition to enter the stomach directly, bypassing the mouth, throat, and esophagus, when weakness in the muscles of the throat makes chewing or swallowing difficult.

- **Respiratory devices such as BiPAP** (bilevel positive airway pressure) can help compensate for weakened muscles by assisting the movement of air into and out of the lungs. Vibrating vests can help to loosen and thin mucus secretions, and machines such as the cough assist can help to remove secretions from lungs.
- Bracing for the back can slow the development of abnormal spinal curvature.
- An array of **assistive technology products** can help even very young children explore the world despite having very weak muscles. Standers, walkers, various kinds of powered and manual wheeled vehicles, and braces (orthoses) can help with standing and moving around.
- Other useful tech can help with writing, art projects, using a computer or cell phone, and electronically controlling the environment (for example, the temperature, lighting, TV, etc.)

**Please talk to your medical provider to obtain more information about these treatments for SMA.*

Treatments for SMA

- **Nusinersen (Spinraza®)*** – Approved by the FDA in 2016, Spinraza® modifies the SMN2 gene in order to increase the production of normal and functional SMN2 protein. It is given intrathecally (an injection into the fluid surrounding the spinal cord) and is recommended for most infants with SMA, especially those between 2 and 12 years old.
- **Onasemnogene abeparvovac-xioi (Zolgensma®)*** – Approved by the FDA in 2019, this was the first approved gene replacement therapy for a neuromuscular disease. It is a one-time intravenous infusion that delivers missing genes to patients with SMN1 gene mutation. While not a cure, it aims to halt the disease by producing sufficient levels of SMN protein. It is approved for pediatric patients ages 2 and under.
- **Onasemnogene abeparvovec-brve (Itvisma®)*** – Approved by the FDA in 2025, this gene replacement therapy is for patients with SMA who are two-years of age and older as well as teens and adults with a confirmed mutation in the SMN1 gene. Given as a one-time intrathecal injection, it is designed to deliver a functional copy of the SMN1 gene. In clinical studies, Itvisma® demonstrated statistically significant improvements in motor function and stabilization of motor abilities in people with SMA- outcomes rarely seen in the natural course of the disease.
- **Risdiplam (Evrysdi®)*** – Approved by the FDA in 2020, risdiplam is designed to increase levels of the SMN protein by enhancing production from the SMN2 “backup” gene. It is approved for children and adults.

To learn more about SMA visit **MDA.org** or contact the MDA Resource Center at **833-ASK-MDA1** (275-6321) or **ResourceCenter@mdausa.org**.

**Please talk to your medical provider to obtain more information about these treatments for SMA.*

MDA Glossary

Aspiration
When food or liquid accidentally enters the windpipe instead of the stomach

Atrophy
A decrease in the size and mass of muscle tissue

Chromosome
A structure inside the nucleus of a cell made up of genetic information (DNA) and proteins

Contracture
A shortening of muscles or tendons around joints that can limit mobility

Dysphagia
Difficulty swallowing

Intrathecal
Administered into the fluid surrounding the spinal cord.

Kyphosis
An abnormal forward curvature of the spine that occurs when weakened muscles are unable to hold the spine straight

Mutation
A flaw in the DNA code

Scoliosis
An abnormal sideways curvature in the spine that occurs when weakened muscles are unable to hold the spine straight

Spasticity
An unusual tightness or stiffness of muscles

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