Spinal Muscular Atrophy

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 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. In July 2018, the U.S .Secretary of Health and Human Services, Dr. Alex Azar, accepted a recommendation to add SMA to the Recommended Uniform Screening Panel for newborns — a landmark decision for the SMA community. Including SMA on the recommended panel helps to ensure that every baby born can be screened for SMA and have early access to life-changing and life-saving treatments.

3. There is wide variability in age of onset, symptoms, and rate of progression in the different forms of SMA. In chromosome 5 SMA, these differences are indicated by classifications into types 1 through 4.
   - **Type 1 SMA** is the most severe. Onset typically occurs between birth and 6 months, and babies with this type of SMA never learn to sit independently.
   - In **type 2 SMA**, onset occurs between 6 and 18 months; these infants typically gain the ability to sit but not to stand.
   - In **type 3 SMA**, onset occurs in children 18 months or older; these children typically achieve the ability to stand and to walk.
   - In **type 4 SMA**, 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. 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.

8. Thanks to medical and scientific advances, quality of life is improving for individuals with SMA, and life expectancy is increasing. Many young adults with SMA attend college, have careers, and eventually get married and have children.

HOW IS SMA TREATED?*

In December 2016, the U.S. Food and Drug Administration (FDA), approved nusinersen (brand name Spinraza*) for the treatment of all types (1-4) of chromosome 5 SMA in children and adults. Spinraza is administered by intrathecal injection into the fluid surrounding the spinal cord and is designed to increase production of full-length SMN protein.

In clinical trials, Spinraza was able to improve motor function and survival in patients with infantile-onset SMA compared to untreated patients. It was also shown to improve motor ability in children with later-onset SMA. It may be effective at slowing, stopping, or perhaps reversing SMA symptoms.

In May 2019, the FDA approved onasemnogene abeparvovec-xioi (brand name Zolgensma*) for treatment of children under 2 years of age with a diagnosis confirmed by genetic testing. Zolgensma is a gene therapy administered by a one-time intravenous injection. This therapy results in long-term production of full-length SMN protein within motor neurons, improving muscle function and survival.

In August 2020, the FDA approved risdiplam (brand name Evrysdi*) for the treatment of SMA in adults and children two months of age or older. Evysdi is an oral medication designed to increase levels of the SMN protein by enhancing production from the SMN2 “backup” gene.

In May 2022, Evrysdi was also approved for children under 2 months making the treatment available for all children and adults.

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.

Speech-language pathologists can help with swallowing and speech problems.

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.

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.

Braces for the back can slow development of abnormal spinal curvature.

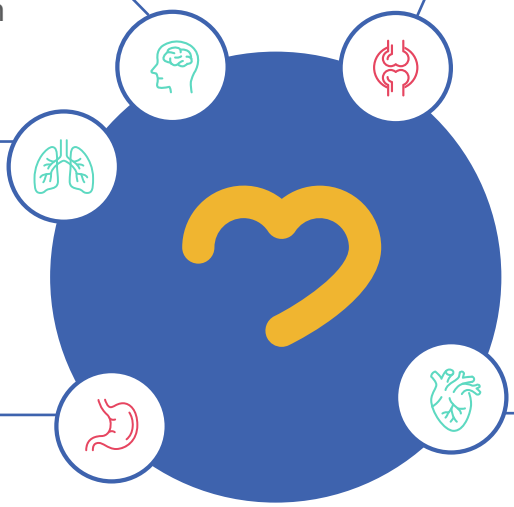
A gastrostomy tube (sometimes called a g-tube or feeding tube) allows liquid nutrition to enter the stomach directly, bypassing the mouth, throat, and esophagus, when weakness in the muscles of the throat makes chewing or swallowing difficult.

Other useful technology can help with writing, art projects, using a computer or cell phone, and electronically controlling the environment (for example, the temperature, lighting, television, etc.).

Spine-straightening surgery may be done to improve comfort and respiratory function.

*MDA does not endorse any brands, services or products, and this does not constitute an endorsement by MDA. MDA makes this information available for informational purposes only. Please talk to your medical advisor to obtain more information on these treatments.

WHAT ARE THE SIGNS AND SYMPTOMS OF SMA?



Nervous system
- Impaired motor function

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

Gastrointestinal
- Dysphagia

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

Heart
- Cardiomyopathy

To learn more about SMA, visit MDA.org or contact the MDA Resource Center at 1-833-ASK-MDA1 (275-6321) or resourcecenter@mdausa.org.

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

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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