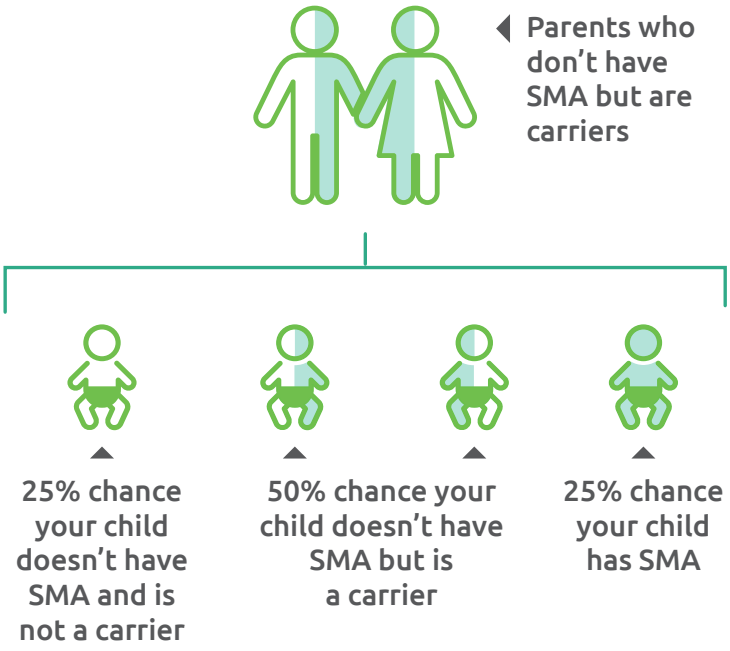
Facts About SMA

Spinal muscular atrophy (SMA) is a rare genetic disease and, if diagnosed early, can be treated quickly to stop the progression of the disease.

How SMA is inherited

SMA is an autosomal recessive disorder. This means that in order to have SMA, a person must have 2 copies of a nonworking *survival motor neuron 1* (*SMN1*) gene or be missing both copies of the *SMN1* gene.



About 1 in 50

people in the United States (or 6.6 million* Americans) is a genetic carrier of SMA, and most don't know it.

A carrier is a person who has a mutation in 1 copy of a gene but doesn't have the disease.

*Calculations are based on an estimated US population of 330 million.

SMA affects about 1 in every 11,000 babies born in the US.

As more children are diagnosed early through newborn screening, treatment can be started immediately to stop the progression of SMA and improve outcomes.

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What causes SMA?

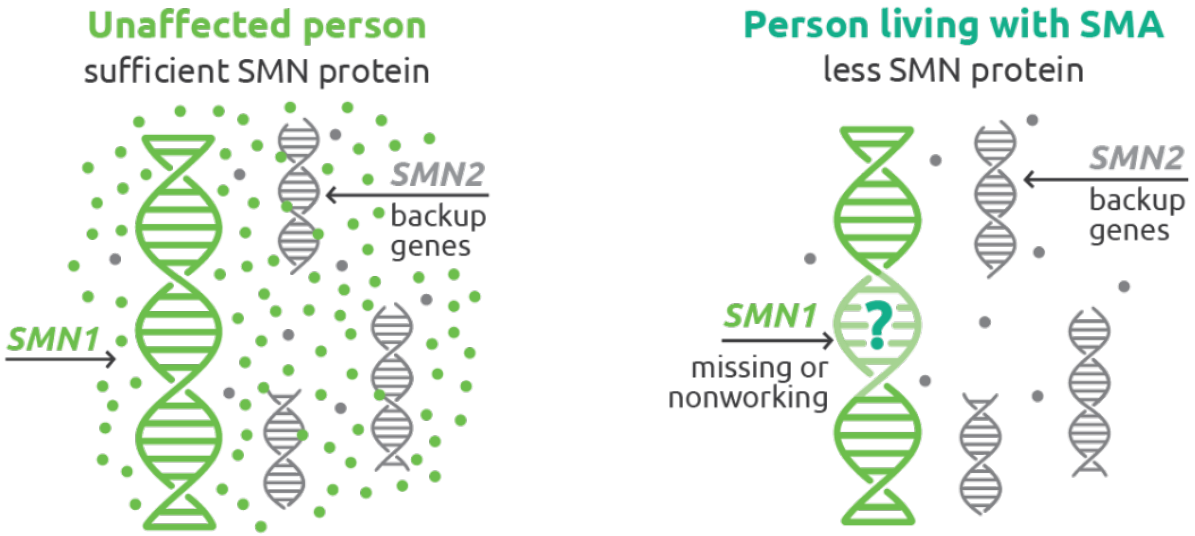
The genetic root cause of SMA is the *SMN1* gene that is missing or not working properly. When this main gene is missing or not working properly, the body cannot make enough survival motor neuron (SMN) protein, which is needed for motor neuron cell survival. Everyone is born with a certain amount of motor neuron cells, which are responsible for communicating with the arms, legs, throat, and many other areas in the body to tell them to work properly. Without enough SMN protein, select motor neuron cells throughout the body may lose function and die. As a result, patients with SMA experience muscle weakness and may develop difficulty breathing, swallowing, or speaking.

The role of a backup gene

There is a backup gene for the *SMN1* gene, called the *SMN2* gene. People can have 1 or more copies of this backup gene. This gene, like the *SMN1* gene, tells the body to make SMN protein. For people with SMA, the *SMN2* gene is the only source of SMN protein production; however, it is unable to produce as much working protein as the *SMN1* gene. **In fact, the *SMN2* gene makes only about 10% of working protein compared to the protein produced by the *SMN1* gene. That is why it is essential to replace the function of the missing or nonworking *SMN1* gene.**

Even people with several copies of the *SMN2* gene may not produce as much SMN protein as those with the working *SMN1* gene, and their motor neuron cells may not work as they should. Usually, the more copies of the *SMN2* gene a person has, the less severe his or her SMA is.

The *SMN1* and *SMN2* genes



Facts About SMA

Types of SMA classified by severity

Doctors and families commonly use the types of SMA to classify the severity of the disease. Historically, doctors classify a person's type of SMA based on when symptoms first appear and which motor milestones have been reached.

There are 4 *main* types of SMA (Types 1-4). SMA Type 1 is the most common and is very serious. The fifth type is SMA Type 0. This is the most severe type and can be fatal before the child is born.

The number of *SMN2* backup genes plays a role in severity

The severity of SMA is usually related to the number of *SMN2* backup genes a person has, so the fewer *SMN2* copies, the more severe the SMA is likely to be. The number of *SMN2* backup genes can be an important reference point for people because it can help anticipate the possible progression of the disease.

Treatments are changing the typical progression of SMA

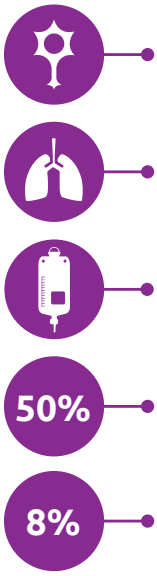
The availability of disease-modifying treatments is further changing how SMA affects people. For example, a child diagnosed with SMA Type 1 who receives early treatment may reach milestones typically achieved by children with SMA Type 2 or Type 3, such as sitting or standing independently. Additionally, children with SMA Type 2 or Type 3 who do not receive treatment may lose the ability to maintain those milestones achieved. Today's approved treatments can affect outcomes, especially when given earlier. Every child responds differently to treatment, and milestones a child may achieve depend on how SMA affects a child before treatment.

SMA Type 1 signs and symptoms

SMA Type 1 is the most common type of SMA and affects about 6 of every 10 children with SMA. It is severe, and signs and symptoms usually begin to appear at less than 6 months of age. SMA Type 1 is a life-threatening condition that needs immediate attention. Signs and symptoms may vary at first, which means caregivers may not see them right away.

Facts About SMA

In the natural history of SMA, children with SMA Type 1 rapidly decline without treatment



At or before birth
SMN protein deficiency and **loss of motor neurons begins**

About 5 months of age
Respiratory support is often needed

About 6 months of age
Nutritional support is added

50%

About 10.5 months of age
Only 50% of **children survive**

8%

About 2 years old
Only 8% of **children are alive** and **free of continuous breathing support**

Based on a natural history study, continuous breathing support means that children need a machine to help them breathe for at least 16 hours every day for 2 weeks or more. **Natural history of SMA refers to the progression of a disease in a person over time without treatment.**

Signs and symptoms of SMA Type 1 may include:

- A "floppy" baby, or hypotonia
- Small or weak muscles
- Difficulty breathing/belly breathing
- Feeding issues, like choking or trouble swallowing
- Weak sucking and labored breathing during feeding
- Tongue fluttering
- Bell-shaped chest (a result of muscle weakness)
- Weak cough
- Lack of reflexes
- "Frog legs", or the inability to kick while lying on back
- Lack of motor development, like being unable to lift head or roll over
- Inability to sit
- Weak cry

Take action fast

Making a quick and informed decision is critical because SMA affects motor neuron cells that control muscles throughout the body, and those muscles weaken and waste away every day.

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10/2021 US-UNB-20-0127 V3