Other Disorders

Screening, Technology, and Research in Genetics is a multi-state project to improve information about the financial, ethical, legal, and social issues surrounding expanded newborn screening and genetic testing – http:// www.newbornscreening.info

Disorder name: Spinal Muscular Atrophy
Acronym: SMA

This fact sheet contains general information about SMA. Every child is different and some of these facts may not apply to your child specifically. Certain treatments may be recommended for some children but not others. All children with SMA should be followed by a team of specialist doctors in addition to their primary doctor.

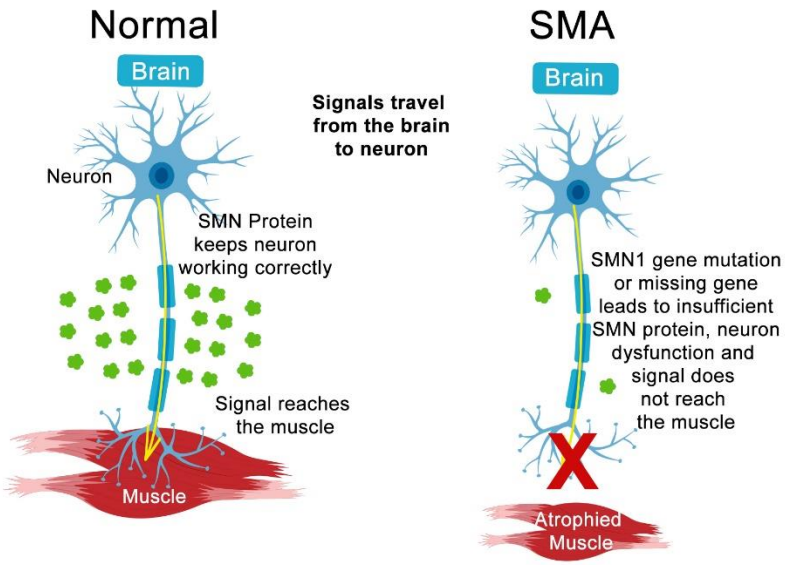
What is SMA?

Spinal Muscular Atrophy, also known as SMA, is an inherited neurologic condition. SMA affects the **motor neurons** in the spinal cord. Motor neurons are a type of specialized nerve cell that send signals from the brain to the muscles in the body. When motor neurons are not working correctly or are absent, they are unable to send these signals to the muscles correctly. Without the correct signals, the muscles have trouble working. Over time, the motor neurons get worse, causing muscles to start to weaken and atrophy (waste away). People with SMA can have a range of different symptoms starting at different ages. All

individuals with SMA have problems with movement. In addition, they may have trouble eating and speaking and can have breathing problems, which can be severe. People with SMA have average intelligence and emotional development. SMA affects the muscles on both sides of the body and affects the proximal muscles, which are the muscles closest to the center of the body, such as the muscles of the shoulder, pelvis, upper arms, and legs.

What causes SMA?

SMA is an inherited condition caused by problems with a specific protein called survival motor neuron (SMN) protein. The SMN protein plays a role in maintaining the motor neurons. When the SMN protein is damaged or missing, it does not work correctly, leading to the deterioration of the motor neurons over time. As this deterioration progresses, the motor neurons cannot talk to the muscles, which grow weaker and smaller.



What are the symptoms and types of SMA?

Symptoms of SMA include muscle weakness, difficulty moving, and breathing problems. Speech and feeding problems, scoliosis, and joint problems can develop. SMA is progressive, meaning nerve damage and symptoms worsen over time.

There are 5 subtypes of SMA, which can be classified based on the age of onset and the severity of symptoms. These separate types of SMA were more commonly used in the past, and it is now known that there is overlap between these types of SMA.

Type 0
SMA type 0 is the most severe form of SMA. Symptoms may begin before birth. Babies with SMA type 0 usually have severe weakness, poor muscle tone, absent reflexes, and breathing problems at birth. They may also have heart issues and contractures. Infants with Type 0 SMA often have very limited life expectancy, and many do not survive past infancy.

Type I
Babies with SMA type I develop symptoms between 0 and 6 months of age. They have significant muscle weakness, leading to difficulties in feeding, breathing, and problems with movement. Their muscle weakness affects their ability to move and they may not have head control or be able to sit without support. Historically, the life expectancy for children with Type 1 SMA was very limited, often only a couple of years.

Type II
Children with SMA type II develop symptoms between 6 to 18 months of age. They have muscle weakness, difficulty sitting up and rolling over, and absence of some **reflexes**. While they can stand, they are unable to walk independently. Children with Type 2 SMA can often live into adulthood, although they may require mobility aids such as walkers and may need treatments and therapies to help them breathe.

Type III
Individuals with SMA type III usually show symptoms after the age of 18 months. Symptoms begin with progressive muscle weakness and can cause fatigue and difficulty walking stairs. Most individuals can walk independently when symptoms first start but may lose the ability to walk over time. Individuals with SMA type 3 have a near-normal lifespan and live into adulthood with appropriate medical care and support.

Type IV
Individuals with SMA type IV have a later onset of symptoms – usually in adulthood. Individuals often have hand tremors, fatigue, and progressive muscle weakness in the limbs. Individuals usually have an expected lifespan but may experience muscle weakness, causing unsteadiness while walking, falls, and other movement problems.

What treatments are available for SMA?

While there is currently no cure for SMA, there are medications and treatments that can help manage and lessen symptoms and extend life expectancy.

For treatment to be most effective, it is important that it start at the right time. You may want to speak with your insurance, doctor, and family about the cost of

treatments. Following up with doctors is critical as they help plan and adjust treatment for your child.

Medications

Nusinersen (Spinraza™) is a prescription medication that can be given to patients of all ages and is injected into the spine in a specialized treatment center. It requires multiple doses in the first year and maintenance doses 3 times a year. Nusinersen works by increasing the ability of the *SMN2* gene to produce functional SMN protein. Having SMN protein that works correctly improves motor neuron function and the muscles' functions.

Risdiplam (Evrysdi®) is a prescription medication taken by mouth once a day. The medication increases the ability of the *SMN2* gene to produce functional SMN protein, which improves motor neuron function and the muscles' function. Risdiplam can also be given through a feeding tube if needed.

Gene Therapy

Onasemnogene abeparvovec (Zolgensma™) is a prescription gene replacement therapy that can be given to SMA patients under 2 years old. Zolgensma is administered as a one-time infusion into the bloodstream via an intravenous line (IV). From the bloodstream, Zolgensma goes to the motor neurons and delivers a working copy of the *SMN1* gene to the motor neurons. This new *SMN1* gene then produces a working SMN protein. As motor neurons receive the working SMN protein, they become healthier and more functional. This leads to improved muscle function and motor control, reducing the severity of SMA symptoms and slowing down the progression of the disease.

Supportive Therapies

For people with SMA, supportive care is important to manage symptoms. Some patients receiving medication or gene therapy may still require ongoing supportive care and therapies to manage the breathing, feeding, and orthopedic problems caused by muscle weakness. You may be advised to see a doctor who specializes in caring for children with SMA or be seen at a specialized treatment center. Specialists can work with your regular pediatrician to ensure up-to-date treatment for your child.

Neurology

A neurologist cares for people with disorders of the nerves. They are often the primary doctor for people with SMA. They can help diagnose and monitor the progression of SMA. They can check nerve health and muscle strength and recommend treatments and therapies to help with complications.

Pulmonary Care

Pulmonologists specialize in lung care and breathing issues. Management with pulmonary care may include visits to the pulmonologist every 3-6 months,

removal of mucus and airway clearance, assessment of quality of sleep, and measurement of oxygen levels in the blood.

Nutrition and Gastrointestinal Care

Gastroenterologists and nutritionists help to identify problems and make plans to ensure that nutritional needs are met. SMA can cause some people to struggle with eating and digestion. Constipation, undernutrition, and acid reflux are common symptoms.

Orthopedic and Musculoskeletal Care

Orthopedists help treat issues with the bone such as scoliosis and joint problems. Physical therapy can help people with SMA build muscle strength, increase mobility, and address challenges in daily life. Orthotic specialists help patients use frames, wheelchairs and other devices to improve movement and quality of life.

What happens when SMA is treated?

Currently, no treatment reverses or completely stops the symptoms of SMA. However, children who receive prompt and early treatment can live healthier and more productive lives. In patients with SMA, medication or gene therapy slows the progression of muscle weakness and improves survival. The goal of treatment is to lessen the health problems that occur with SMA and improve the quality of life of the person with SMA.

What causes the SMA protein to be absent or not working correctly?

Genes tell the body how to make proteins. The *SMN1* gene instructs the body to make the SMN protein. Everyone has two copies of the *SMN1* gene. People with SMA have changes, also called variants, in both copies of their *SMN1* genes that cause them not to work correctly. Because of the variants in the *SMN1* genes, the SMN protein either does not work correctly or is not made at all. This causes the problems seen in SMA. SMA is caused by variants in the *SMN1* gene.

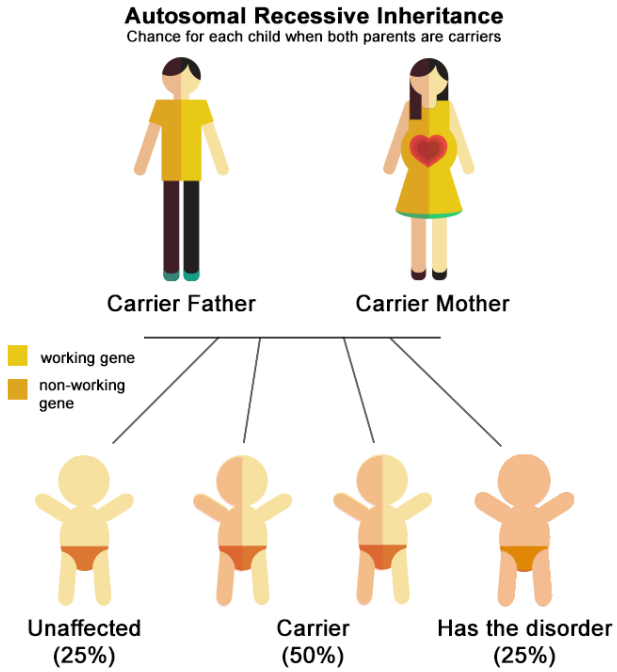
A second gene, called *SMN2*, is also involved in SMA. *SMN2* does not cause SMA. *SMN2* influences the severity of the symptoms of SMA.

How is SMA inherited?

SMA is inherited in an **autosomal recessive** pattern. It affects both males and females equally.

Everyone has two copies of the *SMN1* gene that makes the SMN protein. SMN protein is required for motor neurons to work. In individuals with SMA, both copies of their *SMN1* gene are not working correctly. These individuals most often inherited one non-working *SMN1* gene from each parent. A person with only one working copy of the *SMN1* gene is called a carrier and does not show symptoms of SMA. One working copy of the *SMN1* gene makes enough SMN protein for the body.

Parents of children with SMA typically do not have SMA. Two individuals who are carriers have a chance to have a child together who could inherit two non-working copies of *SMN1* and show symptoms of SMA.



When both parents are carriers of SMA, there is a 25% chance in each pregnancy for the child to have SMA. There is a 50% chance that the child will be a carrier of SMA. Like their parents, children who are carriers will not experience symptoms of SMA but have a chance of passing down their non-working copy of *SMN1* to their children in the future. There is also a 25% chance that the child will not inherit any non-working copies of the *SMN1* gene and will not have SMA.

Genetic counseling is available to families who have children with SMA. Genetic counselors can answer questions about SMA, such as how the condition is inherited, choices during future pregnancies, and how to test other family members. You can ask your doctor about a referral to a **genetic counselor**.

Is genetic testing available?

Genetic testing for SMA can be done on a blood sample. Genetic testing, also called DNA testing, looks for changes in both copies of the *SMN1* genes. In most children with SMA, both gene changes can be found. Rarely, in some children, neither or only one of the two gene changes can be found, even though we know they are present. Variants in *SMN1* cause SMA.

Genetic testing of *SMN2* is also done. *SMN2* produces about 10% of the SMN protein in the body. People can have between 0 to 5 copies of *SMN2*. In general, people with SMA with a higher number of copies of *SMN2* have milder symptoms of SMA. Determining the copy number of *SMN2* can help doctors determine how severe the symptoms of SMA may be. *SMN2* does not cause SMA, but it influences the severity of SMA.

What other testing is available for SMA?

Newborn Screening:

Most states test for SMA through newborn screening. **Newborn screening** is a process where a few drops of blood are taken from a baby's heel to identify different health conditions.

Newborn screening looks for SMA by checking for variants in a baby's *SMN1* genes. A positive newborn screen for SMA does not mean the baby has SMA. A positive screening test means that further testing must be done to confirm or rule out this condition. It is essential to follow up with your baby's doctor, who will help coordinate care and testing for your baby.

Confirmatory/Diagnostic Testing:

After a positive result on the newborn screen, further **diagnostic testing** is done to confirm an SMA diagnosis. A positive screening result is confirmed using genetic testing. This genetic testing looks for variants in both copies of a baby's *SMN1* gene. *SMN2* genes may be tested to help determine the severity and type of SMA.

Symptomatic testing

Older children or adults with late-onset SMA symptoms can have genetic testing to help diagnose if they have SMA. They can also have a neurologic exam to help clarify their symptoms. Other medical tests may include nerve conductions studies, electromyography and/or muscle biopsy.

Can you test for SMA during a future pregnancy?

Genetic testing can be done during future pregnancies if the genetic changes causing SMA in a family are known. The DNA sample needed for this test is collected by either CVS or amniocentesis.

Parents may choose to have SMA testing during a pregnancy or wait until after the birth. Parents may also choose to use assisted reproductive techniques to decrease the chance that their future children will have SMA. A genetic counselor can discuss your choices and answer questions about testing options before, during, or after pregnancy.

Can other members of the family be tested for SMA?

Having SMA

The younger brothers and sisters of a baby with SMA also have a chance of having SMA even if they have not yet shown symptoms. Finding out whether other children in the family have SMA is important because early treatment may prevent serious health problems. You should talk to your pediatrician and neurologist to arrange for testing of siblings if appropriate.

SMA Carrier testing

If two changes are found in the *SMN1* gene in your child, other family members can have genetic testing to see if they are carriers of SMA.

Brothers and sisters who do not have SMA still have a chance to be carriers like their parents. Except in special cases, carrier testing should only be done on people over 18.

If you are a parent of a child with SMA, your brothers and sisters have a 50% chance to be a SMA carrier. It is important that other family members be told that they could be carriers. There is a small chance they are also at risk of having children with SMA.

All states offer newborn screening for SMA. However, when both parents are carriers, newborn screening results alone are insufficient to rule out SMA in a newborn baby. In this case, diagnostic testing should be done in addition to newborn screening.

How common is SMA?

Overall, SMA is thought to occur in approximately 1 out of every 6,000 -10,000 births in the United States.

SMA type 1 is the most common, followed by SMA type 3 and SMA type 2. SMA Type 4 is the mildest, and the birth prevalence is not well-defined, but it is thought to be less common than the earlier-onset types. SMA type 0 is the rarest form of SMA, and very few babies have been diagnosed with this type of SMA.

Does SMA happen more often in a specific ethnic group?

SMA affects people from all parts of the world. It occurs most commonly in Caucasians and Asians and less frequently in other ethnic groups. About 1 in 45 Caucasians are carriers of SMA, and about 1 in 48 Asians are carriers. SMA carrier frequencies range in other ethnic groups range from 1 in 55 to 1 in 100.

Does SMA go by any other names?

SMA is also sometime called:

- 5q–linked spinal muscular atrophy
- 5q SMA
- Spinal amyotrophy

Before the genetic cause of SMA were understood, the subtypes of SMA were known by other names.

- Type I was known as Werdnig-Hoffman disease and “acute SMA”
- Type II was known as Dubowitz disease and “chronic SMA”
- Type III was known as Kugelberg-Welander disease and “juvenile SMA”
- Type IV was known as “adolescent-onset” or “adult-onset SMA”

Where can I find more information and support?

Medline Plus
https://medlineplus.gov/genetics/condition/spinal-muscular-atrophy/

CureSMA
https://www.curesma.org/

SMA Foundation
https://smafoundation.org/

National Institute of Neurological Disorders and Stroke
https://www.ninds.nih.gov/health-information/disorders/spinal-muscular-atrophy

Document Info	**Created by:**	www.newbornscreening.info
	Reviewed by:	HI and OR Neurologist and Geneticist
	Review date:	December 8, 2023
	Update on:	December 8, 2023

This project is supported by a grant from the Maternal and Child Health Bureau, Health Resources and Service Administration, Genetic Services Branch, MCH Project #: UH7MC30774-01-00 http://mchb.hrsa.gov