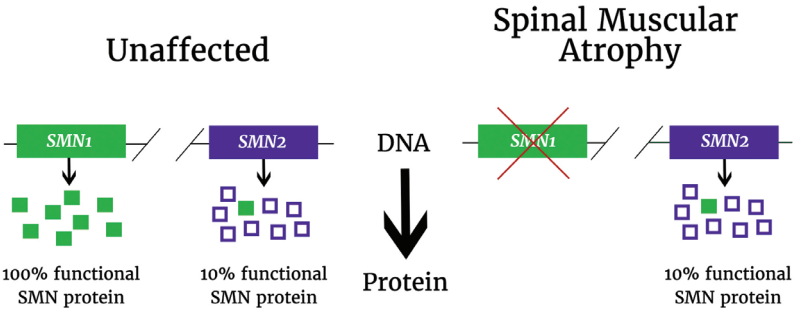
# Spinal Muscular Atrophy

# SMA

Clinic *for* Special Children®

# What is SMA?

Spinal muscular atrophy (SMA) is a genetic condition that causes progressive degeneration of the motor nerve cells in the spinal cord and brainstem resulting in weakness of the muscles involved in breathing and voluntary movement. It is the most common genetic cause of infant death worldwide and is found throughout the Plain communities. SMA is typically grouped into different types based on severity and onset of symptoms: SMA Type 1 is the most severe and often fatal early in life when SMA therapies are not elected. Those with SMA Type 2 generally don't walk and can have breathing difficulties and scoliosis, and SMA Type 3 patients may walk but lose that ability over time. SMA Types 1, 2, and 3 are found within the Mennonite community, whereas the Amish are known to have SMA type 1, and the Hutterites are known to have SMA type 3. Patients with all three types of SMA are candidates for therapies to improve or prevent symptoms of the condition.




Adapted from SMA Europe. *What is the SMN2 gene [digital image].* Retrieved from http://www.sma-europe.eu/essentials/sma-conditions/the-genetics-of-spinal-muscular-atrophy/

# What causes SMA?

SMA is caused by the lack of an essential protein in the motor nerve cells called survival motor neuron protein, or SMN. The *SMN1* gene directs the production of SMN protein. We all have two copies of this gene, one from each parent. A nearby gene called *SMN2* functions as a "back-up" for making the protein, but is not as efficient in making SMN protein. In people with SMA, neither copy of the *SMN1* gene functions properly and they must rely only on *SMN2* to make the important SMN protein. The number of copies of the *SMN2* gene can vary, and the more copies of *SMN2*, the less severe the disease. For example, individuals with type 1 SMA have 2 copies of *SMN2*. *SMN2* copy number typically ranges from 2 to 4 in the Plain communities.

# Current Treatments

There are currently three approved therapies for SMA. All require a doctor's prescription and other tests to monitor their effect after they are given. Patients from the Plain communities may be able to access these medications through patient assistance programs with the companies who make these medicines. We can help you learn more about this.

These targeted therapies work best when given earliest in life, even before symptoms of SMA are obvious. Children who received these medicines have a less serious disease, and many have few or no features of SMA. They are all new medicines, so long term durability and safety are still being studied.

## Zolgensma® (onasemnogene) *Gene replacement therapy*

- In May 2019, the FDA approved Zolgensma as the first gene therapy for the treatment of children less than 2 years old with all types of SMA.
- The Clinic for Special Children participated in the clinical trial of gene therapy for SMA in presymptomatic babies under six weeks of age.
- Gene therapy uses a modified virus to insert a functioning *SMN1* gene into human cells, allowing those cells to make greater amounts of SMN protein.
- The dose is given as a one-time intravenous (IV) infusion in babies who do not have immunity to the type of virus used to deliver the working gene.

## Spinraza® (nusinersen) *Intrathecal medicine*

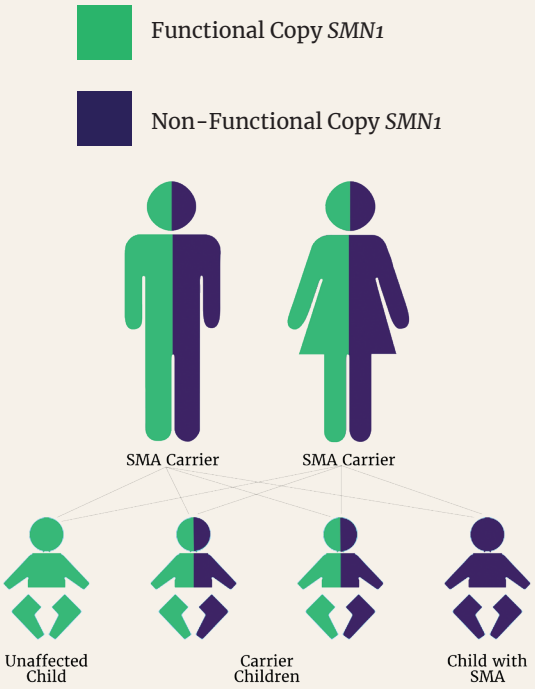
- In December 2016, the FDA approved Spinraza (nusinersen) as the first targeted therapy for all types of SMA.
- Spinraza works by increasing the amount of SMN protein produced by *SMN2* to achieve protein levels closer to what *SMN1* would produce if functioning properly.
- Spinraza must be given every 4 months for life via a lumbar puncture (spinal tap) or an implanted intrathecal catheter.

## Evrysdi™ (risdiplam) *Oral medicine*

- In August 2020, the FDA approved Evrysdi as a medicine for SMA of all types.
- Evrysdi boosts the amount of SMN protein produced by *SMN2* to achieve protein levels closer to *SMN1* if functioning properly.
- Evrysdi is taken by mouth once a day.

## How can I know if I could have children with SMA?

Children with SMA have parents who are carriers. Carriers have one functional copy of the *SMN1* gene and one non-functional copy. If two carrier parents have children, each one of their children has a 25% chance (1 in 4) of being affected with SMA. If parents have a child with SMA type 2, all of their children with SMA will have type 2. Carrier testing can determine which couples could have children with SMA.




## Why do carrier testing?

Time is of the essence. **Research shows that the earlier the targeted treatments for SMA are given, the better they work.**

Couples who know they are carriers for SMA can be informed and prepared. They can have their children tested at birth for the earliest diagnosis and start the treatment of their choice right away. Likewise, if a couple is not at risk to have a child with SMA, they can be reassured throughout the pregnancy that the baby isn't affected.

## When should I do carrier testing?

SMA is found in all Plain communities. All couples of Plain descent should consider carrier testing for this condition.

1 in 50 people worldwide is a carrier for SMA

1 in 25 Mennonites is a carrier for SMA

1 in 8 Hutterites is a carrier for SMA

The carrier frequency in Amish families is unknown but cases have been seen in communities across the country.

Most carriers **do <u>not</u>** have a family history of SMA. For this reason, we recommend carrier testing for anyone of Plain descent.

## How does carrier testing work?

Carrier testing can be done quickly and easily through the Clinic for Special Children as part of the Plain Insight Panel™ (PIP). It requires a blood draw and can be arranged in your local area - we can help you do this. Once the test is complete, our genetic counselor or your healthcare provider will follow-up with you to deliver your results and discuss what they mean to you and your family.

**"Stay hopeful and do your own research to stay informed. The Clinic for Special Children is the most helpful place to go for the treatment of genetic disorders."**

*- JW, Mother of SMA patients*

# Our Goals

1

Identify individuals and couples who are carriers

2

Present therapeutic options to carrier parents so they know which treatments they can use should they have a child with SMA

3

Diagnose pre-symptomatic newborns with SMA in the Plain community within the first few days of life

If you are interested in **carrier testing**, or have any questions about SMA or genetic testing, please contact the Clinic for Special Children.


Clinic *for* Special Children®

535 Bunker Hill Road
PO Box 128
Strasburg, PA 17579

tel (717) 687-9407
fax (717) 687-9237
ClinicforSpecialChildren.org