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 any adult 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 children diagnosed with SMA

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 and get them to the treatments that vastly improve their outcomes

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

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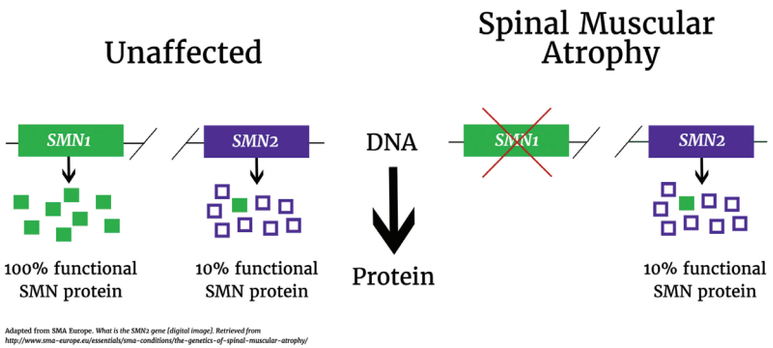
Spinal Muscular Atrophy

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 a common genetic cause of infant death worldwide and is found throughout the Plain communities.



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.

Babies who have two copies of *SMN2* show symptoms in the first few weeks of life and die early in life without treatment. Those with three copies of *SMN2* generally don't walk and can have a breathing difficulties and scoliosis if they don't receive treatment. Children with four copies of *SMN2* have a longer period before they show symptoms of SMA. Mennonites are known to have two, three, or four copies of *SMN2*, while Amish children with SMA have two copies of *SMN2*, associated with the severe, early onset type.

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. Some children with SMA who have two copies of *SMN2* receive gene therapy and Spinraza® or Evrysdi™ as soon as possible after they are diagnosed.

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*

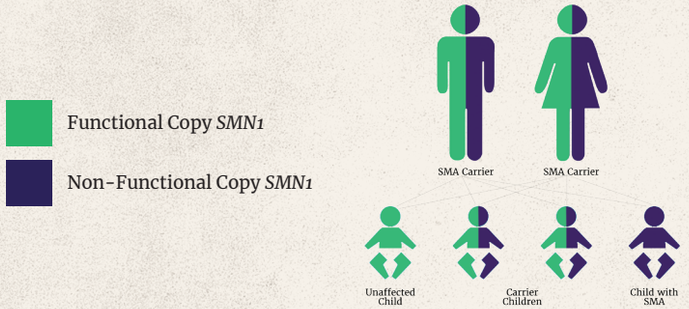
- In December 2016, the FDA approved Spinraza (nusinersen) as the first targeted therapy for all types of SMA.
- Spinraza works by increasing the amount of SMN protein produced by *SMN2* to achieve protein levels closer to what *SMN1* would produce if functioning properly.
- Spinraza must be given every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

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. All children with SMA within one family will have the same number of copies of *SMN2*. Carrier testing can determine which couples could have children with SMA.



Why do carrier testing?

Carrier testing for SMA determines the number of *SMN1* genes a person has. Generally, carriers for SMA have only one copy of the *SMN1* gene: they have a deletion of the *SMN1* gene as well. Likewise, non carriers of SMA have two copies of the *SMN1* gene, each copy inherited from a different parent. In rare instances *(less than 5% of the time)* someone can have two copies of the *SMN1* gene next to each other and inherited from one parent, while they inherit the gene deletion from the other parent. These individuals are "silent" carriers because they have two copies of the *SMN1* gene so they appear to be non carriers but have the deletion of *SMN1* they can pass to their children.

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.

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

SMA is part of newborn screening in the United States. We highly recommend **all** babies undergo newborn screening.