Spinal Muscular Atrophy

genetics.edu.au

This fact sheet talks about the genetic condition **spinal muscular atrophy**, and describes the causes, symptoms, screening and diagnostic tests, and management options.

In summary

- Spinal muscular atrophy (SMA) is a genetic condition that causes weakness and wasting of the muscles.
- Around 1 in 10,000 people are born with SMA, and about 1 in 40 people are healthy genetic carriers.
- If both members of a reproductive couple are genetic carriers, there is a 1 in 4 (25%) chance each of their children will have SMA.
- Treatment is available that can improve muscle function and extend the lifespan of people with SMA.

What is spinal muscular atrophy?

Spinal muscular atrophy (SMA) is a health condition that causes progressive weakness and wasting (atrophy) of the muscles used for movement. This is due to the loss of the special nerve cells (motor neurons) in the spinal cord that send messages to the muscles. It is estimated that 1 in every 10,000 babies are born with SMA.

SMA is a physical condition that affects movement and mobility. The symptoms differ between people with SMA and can affect:

- Control of the movement of the body, arms and legs
- Actions such as breathing, coughing and swallowing.

There are different types of SMA, and the condition can affect each individual differently. The original classification of SMA into five types was based on the age symptoms were first seen and the severity of the symptoms if no treatment was given. This historical classification is no longer very applicable for newly diagnosed individuals starting treatment.

Our bodies are made up of billions of cells. In each cell is a copy of our genetic information, which is carried on DNA. This is generally packaged into 46 chromosomes, arranged into 23 pairs. One pair is the sex chromosomes, X and Y. Most of the time, people of male sex have one X and one Y chromosome. Most people of female sex have two X chromosomes. The other 22 pairs of chromosomes are called autosomes.

Chromosomes contain genes, which provide instructions for our body to grow and function. We all have variation in our genes which makes us unique. Some gene variations, however, may mean that the gene does not work properly or works in a different way that is harmful. A variation that causes a health or developmental condition is called a **pathogenic variant**.

Gene variants may be inherited from a biological parent or happen for the first time in a person. Once a person has a gene variant it may be passed on to future generations. This is referred to as genetic inheritance.

Current classifications of SMA include the way the condition was diagnosed, symptoms when treatment was started, age, and current motor function (non-sitter, sitter and walker). These classifications are used to guide prognosis and approaches to care and support.

What causes spinal muscular atrophy?

SMA is a genetic condition caused by changes in a gene called *SMN1*. The *SMN1* gene instructs the body to make a protein called survival motor neuron (SMN). The motor neurons in the spinal cord that send messages to muscles need this protein to survive. If SMN is not present, there will be fewer motor neurons sending messages. As a result, the skeletal muscles become weaker and waste away.

We all have two copies of the *SMN1* gene – one copy from our biological mother and one copy from our biological father. Sometimes there are changes (pathogenic variants) in the genetic code of the *SMN1* gene that mean the SMN protein is either not made or does not work properly.

If only one copy of the *SMN1* gene is not working, the other copy directs the body to produce working SMN protein. When there are changes in both copies of the *SMN1* gene, no working SMN protein is made and SMA develops. The *SMN2* gene can also instruct the body to make the SMN protein. The more copies of the *SMN2* gene a person has, the more SMN protein they can make. However, most people with SMA do not have enough copies of the *SMN2* gene to prevent SMA from developing.

How is spinal muscular atrophy inherited?

In almost all people with SMA, a non-working copy of the *SMN1* gene was passed down (inherited) from both biological parents. The parents did not show any signs of SMA because they each had a working copy of the gene, which compensated for the non-working gene. This is known as autosomal recessive inheritance.

People with only one non-working copy of the *SMN1* gene are called genetic carriers. In Australia, 1 in 40 people are carriers of a non-working *SMN1* gene. The children of two healthy carriers will only develop SMA if they inherit non-working copies of *SMN1* from both biological parents.

Very rarely, one copy of a non-working *SMN1* gene is inherited from a biological parent, and a change in the other, previously working, *SMN1* gene occurs when the person is conceived. The child will have no working copies of the *SMN1* gene, and will develop SMA. New gene changes such as these happen by chance and are very uncommon.

How is spinal muscular atrophy diagnosed?

Newborn screening

Newborn bloodspot screening is offered soon after birth to all children born in Australia and New Zealand. These tests screen for a range of health conditions including SMA. Newborn screening is done so children with serious health conditions can be identified and started on treatment early.

Families are made up in many ways. A child's parents may include one, both, or neither of the two people that gave egg and sperm to make them. In this fact sheet, the person giving the egg is called the biological mother and the person giving the sperm is called the biological father. Together, these two people are known as a reproductive couple.

The newborn screen for SMA identifies the most common genetic change, which occurs in 95% of individuals with SMA. Children who test positive for SMA on newborn screening are referred to a specialist centre. They will then have another genetic test to confirm the result.

Diagnostic testing

If SMA was not picked up on a newborn screening test and a doctor suspects a child may have SMA, they will be urgently referred to a child neurologist.

Symptoms that suggest SMA in a child under the age of 1 year include muscle weakness, low muscle tone or floppiness (hypotonia), poor head control, reduced or absent tendon reflexes, while being bright eyed and smiling.

How are genetic carriers identified?

Where there is a family history of spinal muscular atrophy

Genetic testing to identify carriers of SMA is available for people who have a family member who is a carrier of SMA or who has SMA. For example, the first-degree relatives (parents, children, brothers and sisters) of a person identified as a genetic carrier of SMA have a 1 in 2 (50%) chance of also being a genetic carrier.

Reproductive carrier screening

This is an optional genetic test available to any individual or couple planning a pregnancy or early in pregnancy. Screening for SMA is included as part of "reproductive carrier screening" (RCS) tests because it is one of the most common genetic conditions in Australia. RCS can be arranged by a general practitioner (family doctor) or obstetrician and is ideally done prior to pregnancy.

Combined RCS for fragile X syndrome, cystic fibrosis, and SMA is covered through Medicare. This means there is no cost for most people. More information is available in the reproductive carrier screening fact sheet.

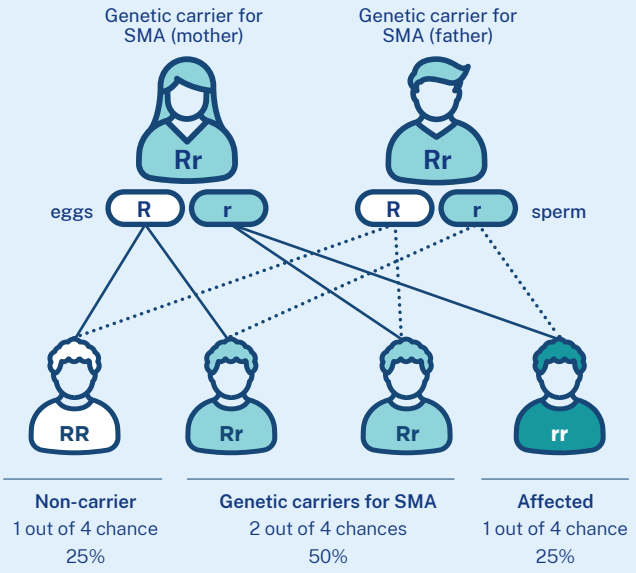
If both members of a couple are found to be genetic carriers, they have an increased chance of having a child with SMA (see Figure 1). They can discuss family planning and options for current or future pregnancies with their doctor or genetic counsellor.

What does it mean if a person is found to be a genetic carrier?

When **both members of a reproductive couple are healthy carriers** and each carry one non-working copy of the *SMN1* gene (*Figure 1*), in every pregnancy there is a:

- 1 in 4 (25%) chance their child will inherit both working copies of the *SMN1* gene. The child will not be a carrier and will not develop SMA.
- 1 in 2 (50%) chance their child will inherit a working and a non-working copy of the *SMN1* gene. They will be an unaffected genetic carrier.
- 1 in 4 (25%) chance their child will inherit both non-working copies of the gene. These children will develop SMA.

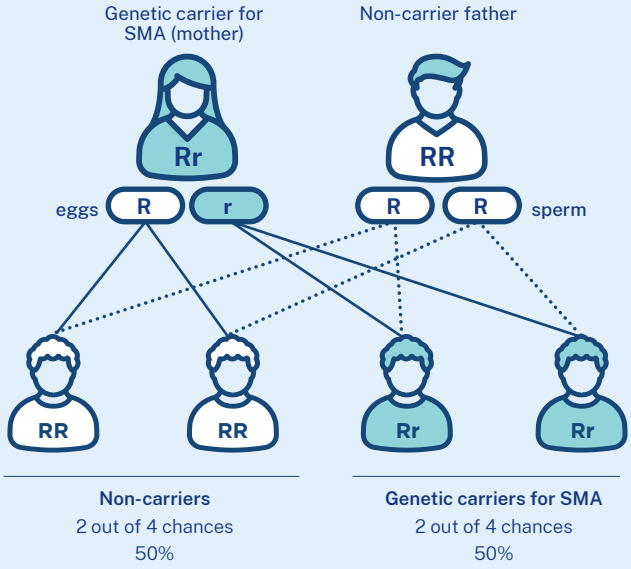
Figure 1:
Autosomal recessive inheritance where both parents are genetic carriers of the non-working *SMN1* gene copy. The non-working *SMN1* gene copy is shown as 'r'; the working copy by 'R'.



If **one person is a carrier for SMA**, and their reproductive partner is **not** found to be a carrier (Figure 2), in every pregnancy there is a:

- 1 in 2 (50%) chance their child will inherit both copies of the working gene. The child will not develop SMA and will not be an unaffected genetic carrier.
- 1 in 2 (50%) chance their child will inherit one non-working and one working copy of the *SMN1* gene. The child will be an unaffected genetic carrier of SMA.
- A very low chance the couple will have a baby with SMA. This is because, very rarely, genetic screening does not detect that the other biological parent is a genetic carrier for SMA. Or, a pathogenic variant may develop in the working copy of the gene when the child is conceived.

Figure 2:
Autosomal recessive inheritance when only one parent is a genetic carrier of the *SMN1* gene. The non-working *SMN1* gene copy is shown as 'r'; the working copy by 'R'.



What treatment options are available?

There is currently no cure for SMA, but many treatments are available that preserve motor neurons, improve muscle function and extend lives. Treatment is generally more effective when given earlier in life.

The available treatments work by increasing the amount of SMN protein in the body, for example, nusinersen (Spinraza™), risdiplam (Evrysdi™) and onasemnogene abeparovec-xioi (Zolgensma™). In Australia, the Therapeutic Goods Administration (TGA) regulates the availability of treatments based on evidence showing how safe and effective they are in people with SMA.

Individuals with SMA also receive treatment that helps manage symptoms and improve quality of life (known as supportive care). This can include breathing and feeding support, splints/braces, occupational therapy or physiotherapy.

What supports are available?

Several organisations provide information and support to individuals and families affected by SMA, including Spinal Muscular Atrophy Australia. Other organisations (e.g. Carer Gateway or Carers NSW) can also offer general advice and support in caring for a family member with long-term needs.

Content updated November 2024
SHPN: (HETI) 241003