Spinal muscular atrophy (SMA)

Summary

- Spinal muscular atrophy is an inherited condition.
- The nerve cells that service the muscles don’t work properly, causing muscle weakness and wasting.
- A child with SMA type 1 rarely lives beyond three years of age.
- There is no cure for SMA, but there are some promising treatments being tested in clinical trials.

Spinal muscular atrophy (SMA) is a genetic condition. It affects the nerves that control muscle movement (the motor neurons).

In someone with SMA, the motor neurons in the spinal cord do not work properly. The messages that the brain tries to send along these motor neurons do not get through to the muscles. This causes the muscles to become weak and damaged. Over time they waste away (atrophy).

SMA affects muscles throughout the body, including:

- the muscles in the shoulders, hips, and back – these are often most severely affected
- the muscles for feeding and swallowing
- the muscles involved in breathing and coughing – if these muscles are involved the person may be more prone to pneumonia and other lung problems.

A person with SMA’s intellect and senses are not affected by the condition.

Approximately one in 6,000 babies born have SMA, and about one in 40 people carry a copy of the altered gene that causes the condition (although they do not have the condition themselves). This is known as being a genetic carrier of the condition.

There is currently no cure for SMA, but there are some promising treatments being tested in clinical trials.

Types of spinal muscular atrophy

There is a wide range in the age of onset, symptoms and rate of progression of SMA. SMA is often classified into types 1 to 4 based on the physical milestones achieved.

The age at which symptoms start generally indicates how severe the condition is. For example, babies who have symptoms at birth have the most severe symptoms and most do not live beyond the age of two (type 1 SMA).

People whose symptoms appear as adults may not develop severe disability and can have a normal life expectancy (type 4 SMA). It is important to note that the course of the condition may be different for each child and adult.

SMA types 1 to 4 are the most common types of SMA. They are caused by changes to a gene on chromosome 5 called SMN1.

SMA type 1

The age of onset for SMA type 1 (also called infantile onset or Werdnig-Hoffmann disease) is birth to six months. Symptoms include:

- generalised muscle weakness
- a weak cry
- trouble breathing, swallowing and sucking.

Babies with SMA type 1 do not reach the developmental milestone of being able to sit up without help. Their life span rarely exceeds two years of age.

**SMA type 2**
The age of onset for SMA type 2 (also called intermediate SMA) is 7 to 18 months. Symptoms include:
- muscle weakness in arms, legs and lower torso
- weak respiratory muscles
- spinal curvature (scoliosis) is often a problem, requiring bracing and surgery.

Children with SMA type 2 learn to sit without help, but generally do not stand or walk independently. Although there is always a risk of respiratory complications, children with type 2 SMA usually live to young adulthood and many live longer.

**SMA type 3**
The age of onset for SMA type 3 (also called Kugelberg-Welander disease) is 18 months to 15 years. This is the mildest form of childhood-onset SMA. Symptoms include:
- weakness in the leg, hip, shoulder, arm muscles
- weak respiratory muscles.

Children with SMA type 3 learn to stand and walk. Some lose the ability to walk in adolescence, while others walk well into their adult years. Life span is unaffected.

**SMA type 4**
The age of onset for SMA type 4 (adult-onset SMA) is 18 to 50 years. Symptoms usually include:
- mild muscle weakness
- tremor
- twitching.

Life expectancy is normal and the muscles for swallowing and breathing are rarely affected. Only a small number of people eventually require wheelchair assistance.

**Other rare types of SMA**
There are some very rare types of SMA caused by changes to genes other than the SMN1 gene on chromosome 5. For example:
- a change to the UBE1 gene on the X chromosome causes X-linked SMA
- changes in the DYNCH1 gene on chromosome 14 have been found to cause a rare form of SMA, called SMA-LED, which predominantly affects the leg muscles
- changes in the IGHMBP2 gene on chromosome 11 cause an extremely rare form of SMA called ‘spinal muscular atrophy with respiratory distress’ (SMARD). SMARD affects the breathing muscles. Its inheritance pattern is autosomal recessive.

**What causes spinal muscular atrophy?**
SMA is a genetic condition caused by a change in a gene called 'survival motor neuron 1' (SMN1). Everybody has two copies of the SMN1 gene – one inherited from each parent. People with SMA have a gene change in both copies of the SMN1 gene. This is what is called an ‘autosomal recessive’ inheritance.

The parents of a person with SMA each carry one copy of the changed SMN1 gene and are known as ‘carriers’. They do not show signs and symptoms of the condition.

In order for carrier parents to have a child affected by SMA, both parents must pass on an SMN1 gene containing a change to their child. If both parents are carriers, the likelihood of a child inheriting the condition is 25 per cent, or one in four. About one in every 40 people is a carrier of the gene variation that causes SMA.
The *SMN1* gene change usually involves the entire gene being missing or, occasionally, some of the code of the gene is changed, making it inactive.

The role of the *SMN1* gene in the body is the production of a protein called Survival of Motor Neuron (SMN). If this protein isn’t produced in sufficient amounts, motor neurons start to die. Motor neurons are nerve cells in the spinal cord that send out nerve fibres to muscles throughout the body and control their movement.

The reason that some people are affected much more severely by the *SMN1* gene change than others is mainly due to the presence of another gene called *SMN2*. This gene produces several different versions of the SMN protein. However, it only produces a small amount of the full-sized, functional version.

Some people have three or four copies of the *SMN2* gene, which can result in larger amounts of full-length SMN protein being produced. This reduces the severity of the disease. As a general rule:

- people with SMA type 1 have one or two copies of *SMN2*
- most people with SMA type 2 have three copies of *SMN2*
- people with SMA types 3 and 4 have four or more copies of *SMN2*.

There are exceptions though, and it has even been observed that siblings with the same number of *SMN2* genes can have very different severities of SMA.

SMA severity also may depend on levels of proteins that occur naturally in your body. These are called ‘disease modifiers’. Two such proteins that have been identified so far are ‘plastin 3’ and ‘ZPR1’. People who naturally produce higher amounts of these proteins tend to have less severe symptoms, but more research is required to fully understand this.

**Complications of infantile spinal muscular atrophy**

Children and adults with SMA are prone to respiratory infections. In the more severe types of SMA, respiratory infections such as pneumonia are often the cause of death. Children with SMA may also have trouble with feeding and require feeding through a tube. Other complications that occur in some types of SMA include contractures (shortening of the muscles, which restrict movement of the joints) and scoliosis (spinal curvature).

**Treatment for spinal muscular atrophy**

There is currently no specific treatment for SMA. However, research for a treatment is moving forward at a fast pace.

Support is available for children with SMA and their families so they can achieve maximum quality of life. For example, as children with SMA type 1 are prone to respiratory infections and pneumonia, treatment focuses on trying to maintain their lung function and health. In contrast, the care of a child or adult with SMA types 3 or 4 will focus on physiotherapy to help maintain muscle strength and mobility.

A multidisciplinary team of healthcare professionals will be needed to manage the symptoms of SMA. This may include specialists in:

- neurology
- genetics
- palliative care
- respiratory medicine
- physiotherapy
- occupational therapy
- speech and language therapy
- gastrointestinal medicine
- dietetics.

Your GP or healthcare professional can provide referrals to the specialists you need and help coordinate your
Genetic counselling and spinal muscular atrophy

If you or your child have been diagnosed with SMA, or if it runs in your family, it may be helpful to speak to a genetic counsellor.

Genetic counsellors are health professionals qualified in both counselling and genetics. As well as providing emotional support, they can help you to understand SMA and what causes it, how it is inherited, and what a diagnosis means for your child's health and development, and for your family. Genetic counsellors are trained to provide information and support that is sensitive to your family circumstances, culture and beliefs.

If SMA runs in your family, a genetic counsellor can explain what genetic testing options are available to you and other family members. You may choose to visit a genetic counsellor if you are planning a family – to find out your risk of passing the condition on to your child, or to arrange for prenatal tests.

The Genetic Support Network of Victoria (GSNV) is connected with a wide range of support groups throughout Victoria and Australia and can connect you with other individuals and families affected by SMA.

The Muscular Dystrophy Australia Community Support Program enables people and families living with SMA to share information, seek advice and receive support in a way that suits them.

Where to get help

- Your GP (doctor)
- Paediatrician
- Muscular Dystrophy Australia Tel. (03) 9320 9555
- Genetic Support Network of Victoria (GSNV) Tel (03) 8341 6315
- Victorian Clinical Genetics Services (VCGS) Tel. 1300 118 247