Spinal muscular atrophy (SMA)

Summary

- Spinal muscular atrophy is a genetic condition that affects the nerves that control muscle movement – the motor neurons.
- It is named ‘spinal’ because most of the motor neurons are located in the spinal cord. ‘Muscular’ is in the name because it mainly affects the muscles that don’t receive signals from the motor neurons. ‘Atrophy’ is the medical term for wasting away or getting smaller, which is what generally happens to muscles when they’re not active.

SMA affects muscles throughout the body, although the muscles closest to the trunk of the body – the shoulders, hips, and back – are often most severely affected. Sometimes, feeding and swallowing can be affected. Involvement of respiratory muscles (muscles involved in breathing and coughing) can lead to an increased tendency for pneumonia and other lung problems.

Sensation and the ability to feel are not affected. Intellect is normal and it is often observed that people with SMA are bright and sociable.

SMA is a relatively common ‘rare disorder’. Approximately one in 6,000 babies born is affected, and about one in 40 people are genetic carriers. There is no cure, but there are some promising treatments being tested in clinical trials.

Types of SMA

There is a wide range in the age of onset, symptoms and rate of progression of SMA, and it 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 disease may be different for each child and adult.

SMA type 1 (also called infantile onset or Werdnig-Hoffmann disease)

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, and trouble breathing, swallowing and sucking.

Babies do not reach the developmental milestone of being able to sit up without help. Life span rarely exceeds two years of age.

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

Children learn to sit without help, but generally do not stand or walk independently. Although respiratory complications are a constant threat, 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 and respiratory muscles.

Children learn to stand and walk, but 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 and 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**

The types of SMA described above are the most common types of SMA which are caused by changes to a gene on chromosome 5 called SMN1. There are also some other very rare types of SMA caused by other genetic changes. For example, an X chromosome gene called UBE1 has been identified that, when mutated, causes X-linked SMA. Flaws in the cytoplasmic dynein 1 heavy chain 1 (DYNC1H1) gene on chromosome 14 also have been found to lead to a rare form of SMA, called SMA-LED, which predominantly affects the leg muscles.

There is also an extremely rare form of SMA that particularly affects the breathing muscles. It is called spinal muscular atrophy with respiratory distress (SMARD). SMARD is caused by mutations in a gene on chromosome 11. It is sometimes called autosomal recessive distal spinal muscular atrophy 1 (DSMA1) or distal hereditary motor neuropathy type VI3.

**Cause of SMA**

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 both copies of the SMN1 gene containing a change (which is often referred to as a ‘mutation’). This is what is called an ‘autosomal recessive’ inheritance.

The parents of a person with SMA each carry one copy of the mutated SMN1 gene and are known as ‘carriers’, but they typically 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 the mutated SMN1 gene on to their child. If both parents are carriers, the likelihood of a child inheriting the disorder is 25 per cent, or one in four. About one in every 40 people is a carrier of the gene mutation that causes SMA.

The SMN1 gene mutation 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 mutation 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 size and 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 and reduced severity of the disease. As a general rule, those with SMA type 1 have one or two SMN2 copies, while most people with SMA type 2 carry three SMN2 copies, and people with SMA types 3 and 4 have four or more SMN2 copies.

There are exceptions to this rule 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 other proteins that people naturally produce in their 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

Unfortunately, there is currently no specific treatment for SMA. However, research for a treatment is moving forward at a fast pace, and there are things that can be done to support the child and their family so they can achieve the maximum quality of life.

For instance, since a child with SMA type 1 is prone to respiratory infections and pneumonia, treatment focuses on trying to maintain the child’s 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 and dietetics. A care coordinator may be available to help you manage care with all of these professionals.

Where to get help

- Your doctor
- Paediatrician
- Muscular Dystrophy Australia Tel. (03) 9320 9555

Things to remember

- 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.