What is Spinal Muscular Atrophy Type 1?

This information sheet briefly explains the cause, effects and management of Spinal Muscular Atrophy (SMA) Type 1. It is for the families of children diagnosed with SMA Type 1 and may also be useful for healthcare and other professionals.

More information on daily care is available in the leaflet ‘Looking After your Baby with SMA Type 1.’ Links to further information on SMA Type 1 and sources of support are given at the end of this sheet; see further resources.

SMA Type 1 is a complex condition; there is a lot of information to take in and every child with SMA is different.

What is Spinal Muscular Atrophy?

Spinal Muscular Atrophy (SMA) is a rare, genetically inherited neuromuscular condition. It causes progressive muscle weakness and loss of movement due to muscle wasting (atrophy). This may affect crawling and walking ability, arm, hand, head and neck movement, breathing and swallowing. There are different forms of SMA and a wide spectrum of how severely children, young people and adults are affected.

The more common forms of SMA are often described as ‘Types’. Symptoms of SMA Types 1, 2 and 3 begin at different ages in childhood. SMA Type 4 is an adult onset form. The impact of the condition, however, varies greatly within and between each type. Sometimes, to try to describe this, doctors will add ‘a’, ‘b’ or ‘c’ to the type of SMA or, as well as being diagnosed with a type of SMA, a child may also be described as ‘strong’ or ‘weak’ or having ‘early onset’ or ‘later onset’. A child / young person’s ability to sit, stand or walk and how their breathing ability is affected by their SMA are all also very important – especially when it comes to managing the condition.

What causes the main types of SMA?

• The SMN1 gene

The main types of SMA affect the nerve cells called lower motor neurons, which reside in the spinal cord and project out to muscles. These lower motor neurons carry electrical signals from the brain to move the muscles used for crawling and walking. These signals also control movement of arms, hands, head and neck as well as breathing and swallowing. For these lower motor neurons to be healthy, our Survival Motor Neuron 1 genes (SMN1 genes) must produce enough Survival Motor Neuron (SMN) protein.
Most people have two copies of the SMN1 gene. People with the main types of SMA have two faulty copies of the SMN1 gene, which means they are unable to produce enough SMN protein to have healthy lower motor neurons. This causes their lower motor neurons in the spinal cord to deteriorate. This restricts the delivery of signals from the brain to their muscles, making movement difficult. Their muscles then waste due to lack of use; this is known as muscular atrophy. In summary:

- **Brain sends signals along the spinal cord via lower motor neuron nerve cells**
- **SMN1 genes don’t produce enough SMN protein to keep these cells healthy in people who have SMA**
- **Lower motor neurons in the spinal cord deteriorate**
- **Signals can’t efficiently get through to the muscles making movement difficult**
- **Muscles waste (atrophy) due to lack of use**

The SMN1 gene is on the fifth chromosome in the region labelled ‘q’. This is why the main types of SMA are often referred to as ‘5q SMA’.

- **The SMN2 gene**

  A second gene also has a role in producing SMN protein. This is the Survival Motor Neuron 2 gene (SMN2), sometimes referred to as the SMA “back-up gene”.

  However, most of the SMN protein produced by SMN2 lacks a key building block that is usually produced by SMN1. This means that SMN2 cannot fully make up for the faulty SMN1 gene in people with SMA.

  The number of SMN2 genes can vary greatly from person to person, from 0 – 8 copies. The severity of SMA has been linked to how much SMN protein a person makes; individuals with more SMN2 copies typically have a less severe form of SMA than those with fewer copies.
What are the effects of SMA Type 1?

The 2017 international Standards of Care for SMA (SoC)\(^6\)\(^7\) describe very weak infants who are unable to sit unsupported as non-sitters and as having the ‘clinical classification’ of SMA Type 1.

The symptoms of SMA Type 1 usually begin from birth or within the first few weeks or months of life. Sometimes SMA can affect babies even before birth and mothers may remember that their baby had become less active towards the end of their pregnancy. Generally, the earlier the onset of symptoms, the more severe the condition. It is not possible to predict accurately life expectancy but, due to breathing difficulties, without intervention this has usually been less than two years. The SoC note, however, that over the last ten years there is evidence of improvements in prognosis and “Even in Type 1, the most severe form of SMA, there has been an increase in survival as a result of a more proactive approach”\(^6\).

It’s important to remember that each child with SMA Type 1 is affected differently and the severity of the condition varies from child to child.

In general, babies with early onset SMA:

- have low muscle tone (hypotonia) and severe muscle weakness and are often described as ‘floppy’ babies

- are unable to support or lift their head, have difficulty rolling over and are unable to sit unsupported due to muscle weakness

- have difficulty lifting their arms and legs, while still being able to use their hands and fingers

- may have a weak cry and their weak breathing muscles cause difficulties with breathing and coughing. This can also increase the chance of respiratory infections which can be life-threatening

- have difficulty swallowing their saliva and other secretions which may make them sound chesty or make them cough. Issues with swallowing can make it difficult to feed and gain weight. There is an increased risk of fluids or food passing into the lungs (aspiration) which can cause choking and, in some cases, chest infections or pneumonia

- facial muscles are not severely affected, so babies can frown and smile

- the brain is unaffected and babies with SMA Type 1 are often described as bright, alert and responsive
How is it diagnosed?

A doctor will diagnose SMA Type 1 after taking a medical history, physically examining a child and by taking a blood sample for DNA testing. The blood sample is tested for a deletion mutation in the *Survival Motor Neuron 1 (SMN1)* gene on chromosome 5. The result of this test is usually available within 2 – 4 weeks, but can sometimes take longer.

If there is any uncertainty about the diagnosis, further tests such as an electromyogram (EMG) may be discussed but these are not usually needed to confirm SMA.

It’s recommended to routinely assess the number of *SMN2* (backup) copies. Although this isn’t necessary to reach diagnosis, and cannot predict severity for any one child, but is an important influencing factor. Also, it is sometimes used as a criterion for enrolment in clinical trials.

Approximately 60% of children diagnosed with a form of childhood onset SMA have SMA Type 1. It is sometimes referred to as ‘Werdnig-Hoffman Disease’ or ‘severe infantile SMA’ or early onset SMA.

Symptoms of SMA Type 1 usually begin and are diagnosed before six months of age. For a number of reasons, however, some children may not be diagnosed with SMA Type 1 until they are around one year old. These children are likely to have a different experience from children who are diagnosed much younger. Their diagnosis is sometimes given as ‘strong Type 1’ or ‘SMA Type 1 / Type 2’. These children may reach the physical milestone of being able to sit independently and have experiences more similar to children who have SMA Type 2. SoC information relating to ‘sitters’ and SMA Support UK’s information relating to SMA Type 2 / sitters may be relevant for these children.

Any queries about a diagnosis and terms used can be discussed with the child’s medical team.

Is there a treatment or cure?

Although there is currently no cure for SMA, this does not mean that nothing can be done. There are a range of options aimed at managing symptoms, reducing complications of muscle weakness and maintaining the best quality of life. For more on this please see the next section on health care and support our information sheet, ‘Looking After your Baby with Spinal Muscular Atrophy Type 1’.

- **Nusinersen/ Spinraza™**

  The first (and currently, the only) potentially available drug treatment for SMA is called nusinersen. Essentially, the drug is designed to modify the product of the *SMN2* gene to produce more functional SMN protein.
In collaboration with researchers, nusinersen was developed by Ionis Pharmaceuticals and Biogen Idec, which have run clinical trials with infants and children affected by SMA Types 1, 2 or 3. There have not yet been any clinical trials of nusinersen with anyone with SMA Type 4. On June 1st, 2017, the European Commission approved nusinersen for marketing under its brand name Spinraza™ as a treatment for those with 5q SMA. This is a broad term, that includes SMA Types 1, 2, 3 and 4.

Currently in the UK, nusinersen is only available if the medical team and family agree that an infant with SMA Type 1 is eligible and may potentially benefit from the treatment. This is possible in Scotland via the NHS and in the rest of the UK via what is called an Expanded Access Programme (EAP).

Deciding if this is a treatment you want to request is a very personal decision. Our information sheet ‘Nusinersen for children with SMA Type 1: Information for Families’ talks more about this and also gives more information about the treatment itself and the EAP eligibility criteria.

To find out more about how nusinersen works and the clinical trial results, please explore this section of our website: http://www.smasupportuk.org.uk/nusinersen Here, you will also find out how the UK drug approval system works, what stage nusinersen has reached, and the collaborative efforts being made to widen access to the treatment.

**What healthcare and support is there?**

Whatever path you are on, advice and support is available so that your baby and you have the best care possible.

The 2017 Standards of Care for Spinal Muscular Atrophy (SoC) provide a summary of guidelines for health professionals covering the three more common forms of SMA, which includes Type 1. The sections in the SoC headed ‘non-sitter’ covers best practice and management for SMA Type 1 (but please note as above that for some, SoC information relating to ‘sitters’ and SMA Support UK’s information relating to SMA Type 2 / sitters may be relevant).

A baby with SMA Type 1 and their family should receive care and support from a multidisciplinary healthcare team. This can feel like an overwhelming number of people but they all have an important role to play. In the team there are likely to be specialists in neuromuscular conditions, palliative care, respiratory medicine, orthopaedics, physiotherapy, occupational therapy, speech and language therapy, dietetics and a hospital or community consultant paediatrician. In addition, care and support may also be provided by a General Practitioner (GP), community nurse and health visitor. One of the team should act as a keyworker, whose role it is to help co-ordinate services. There is more about how these people can help in the information sheet ‘Who’s Who of Professionals’.

Children’s hospices offer a wide range of services and support to children with life-limiting conditions and their families throughout the UK. Families of infants with SMA Type 1 should be offered access to a hospice and, if appropriate, palliative care services.
Ideally the goal of care is to enable a baby with SMA Type 1 to enjoy a good quality of life at home with their family with minimum hospital admissions. Parents should have the opportunity to discuss the range of care options available with their medical team so that they can jointly decide what support is most appropriate for their child.

Healthcare and support are also discussed in more detail in the information sheet ‘Looking After your Baby with Spinal Muscular Atrophy Type 1’, which combines information about practical daily care issues along with tips and suggestions that have worked for other families.

**Genetic counselling**

Parents with a child with SMA should be offered a referral for genetic counselling. A referral can also be requested by a GP.

Genetic counselling takes place with a healthcare professional who has expert training in genetics. They will explain how SMA is inherited and what the chances are of other family members also being affected. Genetic counselling also provides the opportunity to discuss options and choices for any future pregnancies. Genetic counsellors can also be contacted at a later date to discuss any further questions.

There is more information on the genetics of SMA, the chances of having a child with SMA and the tests that can be carried out in the leaflets ‘The Genetics of Spinal Muscular Atrophy’ and ‘Future Options in Pregnancy’.

**Research and further developments**

There is a considerable amount of research into SMA taking place around the world. This research will not only improve our understanding of the condition but will also help to develop effective treatments.

One area of extensive research is the genetics of SMA and the underlying mechanisms that lead to damage of the nerve cells. The UK is a significant contributor to this, with several UK centres involved in clinical trials and international collaborations. This has led to very encouraging breakthroughs in developing treatments that increase the production of SMN protein by addressing the genetic fault.

The **UK SMA Patient Registry** is a database of genetic and clinical information about people affected by SMA. As new treatments for SMA are being developed they need to be tested in clinical trials. Researchers wanting to find people interested in joining a clinical trial contact the Patient Registry which then contacts the people who have registered to let them know about the opportunity. If this is of interest to you, you can register with the Patient Registry.

The Registry also helps specialists gain more knowledge about the condition and the number of people affected by SMA. This information helps to develop and improve worldwide standards of care for people with SMA.
You can find out more by looking at their website: www.treat-nmd.org.uk/registry e-mailing: registry@treat-nmd.org.uk or phoning: 0191 241 8640.

SMA Support UK’s website also notifies the SMA community about latest developments with other drug treatments, the science behind them and what clinical trials and other research is going on: www.smasuresearch.uk/research We alert people to new postings via our social media and monthly E- news. You can sign up for mailings at: www.smasuresearch.uk/sign-up-for-mailings

Further Resources

SMA Support UK information:

You will find a wide range of leaflets and resources in this section of the website: www.smasuresearch.org.uk/about-sma

The leaflet ‘Looking after your baby’ and other information related to SMA Type 1 is in this section: www.smasuresearch.org.uk/type-1

The SMA Type 1 route map can be found at: www.routemapforsma.org.uk

Standards of Care for Spinal Muscular Atrophy (2017)

You can read about and download the 2017 internationally agreed Standards of Care from here: http://www.smasuresearch.org.uk/international-standards-of-care-for-sma

Version 1.7
Author: SMA Support UK Information Production Team
First published: April 2017
Updated: May 2018
Next full review due: April 2020

Please help us keep on producing information like this.
We receive no government funding and rely on public support.

You can sign up as an information publication reviewer by contacting us by email: office@smasuresearch.org.uk or phoning: 01789 267 520

Or to make a donation go to: www.smasuresearch.org.uk/donate

If you have any feedback about this information, please do let us know at: supportservices@smasuresearch.org.uk
References


Other sources used


Roper, H. and Quinlivan, R. on behalf of workshop participants (2010) ‘Implementation of “the consensus statement for the standard of care in spinal muscular atrophy” when applied to infants with severe type 1 SMA in the UK’, Archives of Disease in Childhood, 95(10), pp. 845-849.


We are grateful to the writers and reviewers who assist us in our information production. A list of who this includes may be viewed on our website: www.smasupportuk.org.uk/our-writers-and-reviewers-panel or requested from supportservices@smasupportuk.org.uk

Whilst every effort is made to ensure that the information in this document is complete, correct and up to date, this cannot be guaranteed and SMA Support UK shall not be liable whatsoever for any damages incurred as a result of its use. SMA Support UK does not necessarily endorse the services provided by the organisations listed in our information sheets.