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.’ Further information on SMA Type 1 and sources of support is available from SMA Support UK’s online route map for SMA Type 1 (see further resources for details).

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) causes progressive loss of movement and muscle weakness as a result of muscle wasting (atrophy). The condition may affect crawling and walking ability, arm, hand, head and neck movement, breathing and swallowing.

SMA is often grouped into ‘Types’ based on the age at which symptoms first appear and whether a child will achieve their physical developmental ‘milestones’, including the ability to sit, stand or walk.

There are four main types of SMA. In Types 1, 2 and 3 symptoms begin in childhood. Individuals with SMA Type 4 have symptoms that begin in adulthood; this is sometimes also called ‘Adult Onset SMA’.

Although SMA is often referred to by these ‘Types’ they are not rigid categories. There is a wide spectrum of how severely individuals are affected, both between the different types of SMA and between children, young people and adults within each type.

What causes SMA?

Usually, signals from the brain are sent via the spinal cord along the nerve cells and through to muscles. This makes it possible for us to consciously contract the muscles and to make them move.

SMA affects a particular set of nerve cells called lower motor neurons which run from the spinal cord out to the muscles. The lower motor neurons carry messages that make it possible for us to move the muscles used to crawl and walk, move our arms, hands, head, neck, and to breathe and swallow.
For our lower motor neurons to be healthy we need to produce an important protein called the Survival Motor Neuron (SMN) protein. Our ability to do this is controlled by a gene called Survival Motor Neuron 1 (SMN1)\(^1\).

We all have two copies of this SMN1 gene, one from each parent.

- People who have two faulty copies of the SMN1 gene have SMA.
- People who have one faulty copy of the SMN1 gene are carriers of SMA. Carriers usually do not have SMA or any symptoms of SMA.
- People who have two healthy copies of the SMN1 gene do not have SMA and are not carriers.

SMA is passed from parents to their children through their SMN1 genes. When two people who are carriers have a child together, their child may inherit two faulty SMN1 genes, one from each parent. If this happens then their child will have SMA.

Having two faulty SMN1 genes means that a child is only able to produce very low amounts of the SMN protein. This causes the lower motor neurons in their spinal cord to deteriorate. Messages from their spinal cord do not efficiently get through to their muscles which makes movement difficult. Their muscles begin to waste due to lack of use and this is known as muscular atrophy.

In addition to SMN1, we possess a second gene that is able to produce some functional SMN protein. This gene is almost identical to SMN1 and is called the SMN2 gene\(^1\). However, SMN2 only makes a small fraction of functional protein (about 10%).

For more information on the inheritance of SMA and how SMN2 is linked to the severity of an individual’s SMA, please see our leaflet: ‘The Genetics of Spinal Muscular Atrophy’.

**Diagnosis**

The current internationally accepted standards of care for SMA\(^2,3\) describe the clinical classification of SMA Type 1 as a condition with symptoms which begin at age 0 – 6 months and where the physical milestone of sitting unsupported has never been achieved. These standards and classification are currently being reviewed\(^4\).

SMA Type 1 is the most severe form of SMA. Approximately 60% of children\(^5\) diagnosed with childhood onset SMA have SMA Type 1. It is sometimes referred to as ‘Werdnig-Hoffman Disease’ or ‘severe infantile SMA’.

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. Sadly, SMA Type 1 is a life-limiting condition. It is not possible to predict accurately life expectancy for babies diagnosed at a very early age, however without intervention this is usually less than two years.
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 muscle tests such as an electromyogram (EMG) or a muscle biopsy may be discussed but these are not usually needed to confirm SMA.

Some children may not be diagnosed with SMA Type 1 until they are around one year old. These children are likely to have a very different experience and life expectancy from children who are diagnosed much younger. Their diagnosis is sometimes given as ‘strong Type 1’ or ‘SMA Type 1 / Type 2’. These children tend to live longer and may have experiences more similar to children who have SMA Type 2. SMA Support UK’s information relating to SMA Type 2 may be relevant for these children.

To reflect the wide spectrum of severity of infants with SMA a decimal system of classification has been suggested (e.g. 1.1, 1.2, etc) as well as an alphanumeric system (e.g 1a, 1b, etc)\(^7\). Any queries regarding a diagnosis and terms used can be discussed with the child’s medical team.

**What are the effects of SMA Type 1?**

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 diagnosed at an early age:

- 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

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 our information sheet, ‘Looking After your Baby with Spinal Muscular Atrophy Type 1’.

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.

• **Nusinersen/ Spinraza™**

The first (and currently, the only) potentially available 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. To find out more about how nusinersen works and what the clinical trial results have been, please explore this section of our website: [www.smasupportuk.org.uk/nusinersen](http://www.smasupportuk.org.uk/nusinersen).

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.

As of 1st December 2017, access to nusinersen in the UK is still only possible for children with SMA Type 1, through what is called an Expanded Access Programme (EAP). Biogen is funding the drug for free through this EAP and NHS England is funding the administration costs of the scheme.

To access the EAP both the child’s medical team and the child’s parents/guardians have to agree that it will be of potential benefit and that the child is eligible for the treatment. 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.
Biogen is reviewing whether it will continue funding this programme. For more up to date information, please go to: www.smasupportuk.org.uk/the-uk-expanded-access-programme-for-nusinersen-for-children-with-sma-type-1

Nusinersen’s future availability in the UK will depend upon the outcome of reviews by regulatory authorities of the evidence gained from clinical trials in each subtype of SMA. These authorities also review the costs of provision and consider submissions from the patient community. The authorities include the National Institute for Health and Care Excellence (NICE), NHS England, the Scottish Medicines Consortium and other authorities in the devolved nations. For an update on what stage any reviews have reached and whether the reviews are considering the funding of nusinersen treatment for specific types of 5q SMA only, or for all types of 5q SMA please go to: www.smasupportuk.org.uk/where-uk-access-has-got-to.

• Other developments

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.smasupportuk.org.uk/research We alert people to new postings via our social media and monthly E-news. You can sign up for mailings at: www.smasupportuk.org.uk/sign-up-for-mailings

What healthcare and support is there?

Healthcare and support are discussed in detail in the information sheet ‘Looking After your Baby with Spinal Muscular Atrophy Type 1’.

The Standards of Care for Spinal Muscular Atrophy (SoC)\(^2\) describe best practice and management for 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. Though currently being updated\(^4\), the SoC remain as key guidelines for doctors and families. You can find out how to obtain a copy on page 7 in 'Further Resources'.

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.

**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’.

**Further Resources**

**SMA Support UK information:**

You will find a wide range of leaflets and resources in this section of the website: [www.smasupportuk.org.uk/about-sma](http://www.smasupportuk.org.uk/about-sma)

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

The SMA Type 1 route map can be found at: [www.routemapforsma.org.uk](http://www.routemapforsma.org.uk)

**Standards of Care for Spinal Muscular Atrophy (TREAT-NMD)**
Contact SMA Support UK for a hard copy or download a copy from the Treat NMD website: www.treat-nmd.eu/sma/care/family-guide/. Though this is a family version, please be aware it is written in a very clinical way.

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