Spinal Muscular Atrophy – Key Information

This information sheet is written for anyone wanting to know more about Spinal Muscular Atrophy (SMA).

What is Spinal Muscular Atrophy?

Spinal Muscular Atrophy (SMA) is a rare, genetically inherited neuromuscular condition. It causes progressive muscular 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 four main types of SMA:

- **SMA Type 1**: symptoms begin between the ages of 0 and 6 months. It is the most severe form of SMA. Babies are unable to sit without support. Sadly, without intervention most children with SMA Type 1 rarely survive beyond two years of age, usually due to breathing difficulties.

- **SMA Type 2**: symptoms begin between the ages of 7 and 18 months. Children with SMA Type 2 are unable to stand without support. Though this is a serious neuromuscular condition that may shorten life expectancy, improvements in care standards mean that the majority of people can live long, fulfilling lives.

- **SMA Type 3**: symptoms begin after 18 months of age. Children can stand and walk, although this will become more difficult and they will need more support with this over time. Life expectancy for children diagnosed with SMA Type 3 is not affected and most people can live long, fulfilling lives.

- **SMA Type 4**: symptoms begin in adulthood and include mild to moderate muscle weakness in the arms and legs and some difficulty walking. SMA Type 4 is not life-threatening.

These ‘Types’ are not rigid categories. There is a wide spectrum of severity both between the different types of SMA and between individuals within each type. There are also other even rarer forms of childhood and adult-onset SMA.

For more information about diagnosis and the different types and rarer forms of SMA, visit: [www.smasupportuk.org.uk/about-sma](http://www.smasupportuk.org.uk/about-sma)
What causes the main types of SMA?

- **The SMN1 gene**

The main types of SMA affect the nerve cells called lower motor neurons which run from the spinal cord to the 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:

1. Brain sends signals along the spinal cord via lower motor neuron nerve cells
2. *SMN1* genes don't produce enough SMN protein to keep these cells healthy in people who have SMA
3. Lower motor neurons in the spinal cord deteriorate
4. Signals can't efficiently get through to the muscles making movement difficult
5. 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.

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\(^5\)\(^-\)\(^7\); individuals with more *SMN2* copies typically have a less severe form of SMA than those with fewer copies.

**How do people get SMA?**

SMA is an autosomal, recessive, inherited neuromuscular condition. It is passed from parents to their children through faulty *SMN1* genes:

- People who have inherited two faulty copies of the *SMN1* gene (one from each parent) have SMA.

- People who have inherited one faulty copy and one healthy copy of the *SMN1* gene (one from each parent) are carriers of SMA. Carriers usually do not have SMA or any symptoms of SMA.

- People who have inherited two healthy copies of the *SMN1* gene (one from each parent) do not have SMA and are not carriers.

When two SMA carriers have a child together, for each pregnancy there is a:

- 1 in 4 (25%) chance that the child will inherit both faulty copies of the *SMN1* gene and will develop SMA.

- 1 in 2 (50%) chance that the child will inherit one faulty copy and one healthy copy of the *SMN1* gene and will be a carrier.

- 1 in 4 (25%) chance that the child will inherit two healthy copies of the *SMN1* gene and will not be a carrier or have SMA.

For more detailed information, please see our information sheet: **The Genetics of SMA**

[www.smasupportuk.org.uk/the-genetics-of-spinal-muscular-atrophy](http://www.smasupportuk.org.uk/the-genetics-of-spinal-muscular-atrophy)
How many people are affected?

Approximately 1 in 40 people carry the faulty SMN1 gene\(^8\) - that’s around 1.6 million carriers in the UK.

The incidence is the number of new cases of a condition or disease at any one time. Recent studies estimate that approximately one in every 10,000 babies worldwide are born with a type of SMA\(^8,9\).

In the UK in 2015, there were 777,167 live births\(^10\)-\(^12\). This suggests that in that year approximately 78 babies were born with a type of SMA.

The prevalence is how many people are living with a condition or disease in a population at any one time. Recent studies suggest between 1 and 2 people in every 100,000 worldwide have a type of SMA\(^8,9\).

Based on this, it is estimated that between 650 and 1300 people have SMA in the UK at any one time. Previous estimates by clinicians have suggested an upper limit likely to be 2,500. As there is no central information source, the exact numbers are unknown.

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. These are outlined in the internationally agreed Standards of Care for SMA\(^13,14\). These are currently being updated\(^15\).

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 encouraging breakthroughs in developing treatments.

- **Nusinersen / Spinraza\(^\text{TM}\)**

The first (and currently the only) potentially available treatment for SMA is called nusinersen. Essentially the drug targets the SMN2 gene to produce more 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 1\textsuperscript{st} 2017, the European Commission approved nusinersen for marketing under its brand name Spinraza\textsuperscript{TM} as a treatment for those with 5q SMA\textsuperscript{16}. This includes SMA Types 1, 2, 3 and 4.

Currently, the only way to access the treatment in the UK is through what is called an Expanded Access Programme (EAP). This EAP is only available to children with SMA Type 1 where both the child’s medical team and the child’s parents/guardians have agreed that it will be of potential benefit and that the child is eligible for the treatment.

Nusinersen’s future availability in the UK depends on the National Institute for Health and Care Excellence (NICE), NHS England, the Scottish Medicines Consortium and other authorities in the devolved nations recommending that the NHS funds the drug in England, Scotland, Wales and Northern Ireland. At this stage, it is not known if the funding of nusinersen treatment will be considered for specific types of 5q SMA only, or for all types of 5q SMA.

To find out more about nusinersen and any updates on what progress there has been towards further access in the UK, please go to: www.smasupportuk.org.uk/nusinersen

- **Other research developments**

SMA Support UK’s website also notifies the SMA community about the 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 here: www.smasupportuk.org.uk/sign-up-for-mailings

**References**


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