Muscular Dystrophy UK

Fighting muscle-wasting conditions

Spinal muscular atrophy (SMA)

Overview

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 most common form of SMA is known as '5q SMA' due to its genetic cause. 5q SMA includes the different 'types' or clinical classifications – Types 1, 2, 3 and 4.

How many people are affected by SMA?

Approximately 1 in 40 people carry the faulty SMN1 gene11 - that means there are 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 indicate that approximately one in every 10,000 babies worldwide are born with a Type of SMA, and that Type 1 SMA accounts for approximately 60% of cases11,12 . In the UK in 2017, there were 755,043 live births13-15. This suggests that in that year approximately 76 babies were born with a type of 5q 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 SMA11,12 .

Symptoms

SMA Types 1, 2, 3 & 4

SMA Type 1

The symptoms and effects of SMA Type 1 usually begin from birth or within the first few weeks or months of life. Generally, the earlier the onset of symptoms, the more severe the condition.

Each child is affected differently, but in general, babies with early onset SMA are:

- bright, alert and responsive; their intelligence isn't affected
- able to smile and frown as their facial muscles aren't severely affected
- often described as 'floppy' babies due to their low muscle tone (hypotonia) and severe muscle weakness.
- unable to support or lift their head due to their weak neck muscles
- unable to sit unsupported and have difficulty rolling over
- able to move their hands and fingers but have difficulty lifting their arms and legs

They have:

- breathing muscle weakness, which can cause a weak cry and difficulties with breathing and coughing
- an increased chance of chest infections, which can be lifethreatening
- difficulty swallowing their saliva and other secretions, which may make them sound chesty or make them cough
- difficulties feeding and gaining weight
- an increased risk of fluids or food passing into their lungs (aspiration), which can cause choking and, sometimes, chest infections or pneumonia

It's not possible to predict life expectancy accurately but for most children, without intervention for breathing difficulties, this has previously been estimated as less than two years. Evidence suggests that since the International Standards of Care for SMA introduced more proactive managements in 2007, children have been living longer.

SMA Type 2

The symptoms and effects of SMA Type 2 usually begin between 6 and 18 months of age. Generally, the earlier the onset of symptoms, the more severe the condition.

Each child is affected differently, but in general, children with SMA Type 2 are usually bright and engaging. However, due to SMA, they are likely to experience:

- muscle weakness on both sides of their body
- muscle weakness closest to the centre of their body as these muscles are more severely affected than muscles furthest away
- difficulties moving their arms, but their hands and fingers less so
- difficulties lifting their legs - legs that are weaker than their arms

As they get older, their intellectual and sexual development isn't affected but SMA usually causes them:

- muscle weakness that may make it difficult for them to keep up with their daily activities. For example, if they have been able to crawl or roll, they may lose this ability
- a tendency to become weaker after infections and at times of major growth spurts such as puberty
- weak breathing muscles, making it difficult for them to cough effectively and more vulnerable to chest infections

- muscles supporting the spinal column that are weak meaning that most children will develop a sideways curvature of their spine6 (scoliosis)
- reduced ability to move so that some joints may become tight (contractures) and further restrict their range of movement

Children and adults will need help with daily tasks like washing, dressing and undressing. Though their bladder and bowel control isn't usually affected, they will need help transferring from their wheelchair to the toilet.

SMA Type 2 can weaken chewing and swallowing muscles. For some children, their tongue and shoulder muscles may twitch and they may have a slight tremor in their hands.

Though this is a serious condition that may shorten life expectancy, improvements in care standards mean that the majority of people can live long, fulfilling lives.

SMA Type 3

The symptoms and effects of SMA Type 3a usually begin between 18 months and 3 years.

The symptoms and effects of SMA Type 3b usually begin after 3 years, but before adulthood.

Each child is affected differently, but in general, children with SMA Type 3 are bright and engaging. However, their SMA causes:

- muscle weakness on both sides of their body
- muscle weakness closest to the centre of their body as these muscles are more severely affected than muscles furthest away
- legs that are weaker than arms

As they get older, their intellectual and sexual development isn't affected, but their SMA usually causes them to have:

- difficulties with standing and walking. This usually happens later for children with SMA Type 3b than for children who develop the first symptoms at an earlier age
- difficulties keeping up with daily activities. For example, if they have been able to walk or climb stairs, they may lose this ability. Some children may fall more easily because of their muscle weakness. If they're sitting on the floor they may need help to get up - muscles supporting the spinal column that are weakened. This means that some children develop a sideways curvature of their spine (scoliosis)
- a reduced ability to move due to some joints becoming tight (contractures), restricting their range of movement.
- a tendency to become weaker after infections and at times of major growth such as puberty.

Some children, young people and adults will need help with daily tasks like washing, dressing and undressing. Though their bladder and bowel control isn't affected, some may need help getting to and sitting on the toilet.

Most people with SMA Type 3 don't have breathing problems and their life expectancy isn't affected9 . Most can live long, fulfilling lives.

SMA Type 4

The symptoms and effects of SMA Type 4 begin in adulthood.

Each person is affected differently, but in general, symptoms can include:

- tired, aching muscles
- a feeling of heaviness
- numbness
- cramp
- a slight shaking of the fingers and hands
- fatigue SMA Type 4 progresses steadily and slowly over time causing increased muscle weakness with age. This may impact on daily living activities such as walking, dressing and bathing.

SMA Type 4:

- rarely affects swallowing or breathing
- doesn't affect intelligence, and life expectancy is normal.

It's important not to confuse SMA Type 4, which affects the lower motor neurons, with Motor Neurone Disease (MND) - also known as Amyotrophic Lateral Sclerosis (ALS). MND affects both the upper and lower motor neurons. Though SMA is also classed as a motor neuron disease, it isn't MND. Whereas MND is almost always life-threatening, SMA Type 4 isn't.

Causes

What causes SMA?

The SMN1 gene

All types of 5q SMA affect the nerve cells called lower motor neurons. These are found within the spinal cord and transmit signals to muscles. These nerve cells carry electrical signals from the brain to activate the muscles used for movement such as crawling and walking. These signals control movement of arms, hands, head and neck as well as breathing and swallowing. For these nerve cells 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 5q 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 means these specialist nerve cells in the spinal cord deteriorate. This restricts the delivery of signals from the brain to their muscles, making movement difficult. The muscles then waste due to lack of use - this is known as muscular atrophy.

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 while SMN2 can make some functional SMN protein, it cannot fully make up for the faulty SMN1 gene in people with SMA.

Unlike most genes, the number of copies of SMN2 on each chromosome can vary from one person to the next; this can be between 0 – 8 copies. At the population level, the severity of SMA is linked to how much SMN protein is made; there is therefore a general relationship between the number of SMN2 copies (“SMN2 copy number”) and the likely severity of SMA symptoms. Having more SMN2 copies is generally associated with less severe SMA symptoms. However, at the individual level, accurate predictions cannot be made about the Type or severity of SMA based on the SMN2 copy number alone. This is likely to be because other genetic and possibly environmental factors have an influence on the disease.

How do people inherit 5q SMA?

5q SMA is passed from parents to their children through faulty SMN1 genes. It usually follows an autosomal, recessive pattern of inheritance. This means that:

- 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 have 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.

In around 2% of cases of SMA, the mutation is new in the affected person, most likely due to an error in making the egg or sperm cell from which they were conceived. This is called a de novo mutation.

Diagnosis

How is SMA diagnosed?

Any child or adult with suspected SMA will be physically examined. This may be by their GP, paediatrician, neurologist or neurological specialist who will ask about their medical history and concerns. A GP may have met few children or adults with SMA so may make an immediate referral to a specialist neuromuscular centre. Once SMA is suspected, a blood sample for DNA testing will be arranged. The blood sample is tested for a deletion mutation in the Survival Motor Neuron 1

(SMN1) gene on chromosome 5. It is also now recommended that the number of SMN2 copies is also assessed as this can be a helpful indicator of what effects the condition will have. Clinical trials of new treatments often have entry criteria that specify the number of SMN2 copies someone must have to be eligible to take part.

The SMN1 deletion test result is usually available within 2 – 4 weeks. Other tests may take longer.

If there's any uncertainty about the diagnosis, further tests such as an electromyogram (EMG) which records the electrical activity of muscles may be discussed, but this isn't usually needed to confirm 5q SMA.

Treatment

Is there a treatment or a cure for SMA?

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 1,2 .

Nusinersen / SpinrazaTM

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 (EC) approved nusinersen for marketing under its brand name SpinrazaTM as a treatment for those with 5q SMA. Following any EC marketing approval, it's up to each country to decide who can be prescribed the drug.

Currently in the UK, nusinersen is only available in Scotland if the medical team and family agree that an infant with SMA Type 1 is eligible and may potentially benefit from the treatment.

Disclaimer

If you have feedback about this factsheet or want to request references, please email info@musculardystrophyuk.org.

Here for you

The friendly staff in the care and support team at the Muscular Dystrophy UK's London office are available on 0800 652 6352 or info@musculardystrophyuk.org.

Version: 1 / Date published: 1 September 2018 / Original author: SMA Support UK Information Production Team / Updated: 1 January 1970 / Updated by: / Date of review: 1 September 2021