Spinal Muscular Atrophy Type 2

This information sheet briefly explains the cause, effects and management of Spinal Muscular Atrophy (SMA) Type 2. It includes sources of further information and support. It is for the families of children diagnosed with SMA Type 2. It may also be useful for healthcare and other professionals.

The glossary at the end further explains the words that appear in bold font.

More information on SMA Type 2 and sources of support is available from SMA Support UK’s route map for SMA Type 2: [www.routemapforsma.org.uk](http://www.routemapforsma.org.uk)

SMA Type 2 is a complex condition; there is a lot of information to take in and every child with SMA is different. Your child’s medical team will always be happy to go over any of this with you.

What is Spinal Muscular Atrophy?

Spinal Muscular Atrophy (SMA) is a rare, genetically inherited neuromuscular condition. SMA may affect crawling and walking ability, arm, hand, head and neck movement, breathing and swallowing. SMA is often grouped into ‘Types’. Types of SMA are based on the age at which symptoms first appear and what physical ‘milestones’ a baby or child is likely to achieve. Milestones can include the ability to sit, stand or walk.

There are four main types of SMA: Types 1, 2 and 3 appear in childhood; Type 4 appears in adulthood and is also known as Adult Onset SMA.

These ‘Types’ are not rigid categories. There is a wide spectrum of severity both between the different types of SMA and between children, young people and adults within each type.
There are also other, even rarer forms of SMA with different genetic causes including SMA with Respiratory Distress (SMARD), Spinal and Bulbar Muscular Atrophy (SBMA) and Distal SMA (DSMA).

**What causes SMA?**

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

SMA affects a particular set of nerve cells called the lower motor neurons\(^1\) which run from the spinal cord out to our muscles. The lower motor neurons carry messages that make it possible for us to move the muscles we use to crawl and walk, to move our arms, hands, head and 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)\(^2\).

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 their 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 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\(^2\). 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 ‘The Genetics of Spinal Muscular Atrophy’: [www.smasupportuk.org.uk/the-genetics-of-sma](http://www.smasupportuk.org.uk/the-genetics-of-sma)

**What is SMA Type 2?**
SMA Type 2 is sometimes called intermediate SMA or chronic infantile SMA. The symptoms of muscle weakness and floppiness (low tone / hypotonia) usually appear between 7 and 18 months of age.

Each child with SMA Type 2 is different. Some children will sit independently whilst others will require some support. Usually children with SMA Type 2 will need supportive aids for standing and a wheelchair to get around.

Sometimes doctors try to indicate the degree of severity within SMA Type 2 by using a decimal classification³, for example 2.1, 2.2, 2.5, 2.9. If you have any queries regarding this please speak to your child’s medical team.

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

**How is SMA Type 2 diagnosed?**

A doctor will diagnose SMA Type 2 after taking a medical history, physically examining your 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.

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.

**What are the effects of SMA Type 2?**

This section describes the effects of SMA Type 2 in general terms. But, it’s important to remember that each child with SMA Type 2 is affected differently and the severity of the condition varies from child to child.

Children’s muscle weakness is usually the same on both sides of their body (symmetrical). The muscles closest to the centre of their body (proximal muscles) are usually more severely affected than the muscles furthest from the centre of their body (distal muscles). This can make it difficult for children with SMA Type 2 to lift their arms and legs but they will still be able to use their hands and fingers. Generally, children with SMA Type 2 find that their legs are weaker than their arms.

As your child grows it may be difficult for their muscles to keep up with their daily activities. If your child has been able to, for example, crawl or roll, they may lose this ability as they get older. They may also become weaker after infections and at times of major growth spurts such as puberty. SMA doesn’t affect a child’s sexual or intellectual⁴ development.

Because a child with SMA Type 2 has weak respiratory muscles it can be difficult for them to cough effectively. This can make them more vulnerable to respiratory (chest) infections.
In SMA Type 2 the muscles supporting the spinal column are weakened. This means that most children will develop a sideways curvature of their spine (scoliosis). Also, because the condition reduces children’s ability to move, some joints may become tight (contracture) restricting their range of movement.

SMA Type 2 can weaken children’s chewing and swallowing muscles (bulbar muscles). Some children find that their tongue or shoulder muscles twitch (fasciculation) and they may have a slight tremor in their hands. SMA Type 2 doesn’t affect bladder and bowel control but children will need help, for example, with transferring from their wheelchair to the toilet, dressing and undressing.

What healthcare and support is needed for SMA Type 2?

The Standards of Care for SMA (SoC) were internationally agreed in 2007. They outline best practice and management for the three more common forms of SMA, which includes SMA Type 2. The sections in the SoC headed ‘sitters’ cover best practice and management for SMA Type 2. Though currently being updated, the SoC remain as key guidelines for doctors and families. You can find out how to obtain your copy in the section ‘Further Resources’ (page 10). Though this is a family version, please be aware it is written in a very clinical way.

Your child should receive care from a multidisciplinary healthcare team, which can feel like an overwhelming number of people but they all have an important role to play. You will have contact with specialists in neuromuscular conditions, respiratory medicine, orthopaedics, physiotherapy, occupational therapy, speech and language therapy, dietetics and a hospital or community consultant paediatrician. If possible one of the team should be your keyworker whose job it is to help co-ordinate services for your family. You can find out more about how these people help in our information sheet ‘Who’s Who of Professionals’: www.smasupportuk.org.uk/whos-who-of-professionals

Children with SMA Type 2 should be seen by their medical team regularly to measure any change in their health and to offer advice and interventions at the right time. The aim is to enable your child to remain healthy and enjoy a good quality of life. At every appointment with your child’s medical team you should be given time to ask questions and then jointly with the team decide what support is best for your child.

- Breathing

Children with SMA Type 2 can have breathing problems such as hypoventilation and their muscle weakness can lead to an increased risk of respiratory (chest) infections. Some may need help with their breathing and coughing. Your child’s medical team will advise you on what is best for your child.

You can read an overview of what good respiratory management involves in the Standards of Care. As each child is affected differently it’s important to discuss any queries you have with your child’s medical team.
- Eating, drinking and nutrition

Children with SMA Type 2 sometimes have difficulty with their chewing, swallowing and nutrition.

Your child’s health visitor, consultant, speech and language therapist or dietician will be able to provide advice and support on eating and nutrition. Occupational therapists and physiotherapists may also advise on positioning, seating or arm supports to help your child to eat independently.

Your child may have problems putting on weight if eating becomes tiring for them or if they have illnesses or infections. Equally, your child may become overweight due to their reduced mobility. If this happens the extra weight can increase the stress on muscles, bones and joints, making physical activity even more difficult. A dietician will be able to advise on a healthy diet that will suit your child.

If your child has difficulty swallowing there is a risk that they may inhale liquids or food into their lungs (aspirate) which can cause chest infections. If this is happening, or your child is not putting on weight, your child’s medical team may suggest alternative ways for them to take in food. This may involve your child’s food going through a tube directly into their stomach (gastrostomy (G) tube).

Children with SMA Type 2 can become constipated which may cause discomfort and can make breathing more difficult. You can discuss how to manage this with your child’s medical team.

Muscle weakness may make it difficult for your child to open their mouth widely. This can cause problems with eating, teeth cleaning and dental care. Regular dental check-ups and getting help with these sorts of problems early may help to prevent complications such as aspiration, when food gets into the lungs.

- Posture, movement and mobility

SMA Type 2 will mean that your child will have difficulties with their posture, movement and mobility. They will need their own exercise routines designed by their physiotherapist to help with this. Routines may include exercises to help maintain their range of motion, reduce any discomfort, stretch any tight muscles and prevent contractures. Regular gentle stretching of their tight joints can help to reduce the pain that contractures can cause. If your child does have any pain, do talk to their doctor and physiotherapist. Your child might enjoy doing these exercises in the bath, or a swimming or hydrotherapy pool as the warm water aids buoyancy.

Regular moderate exercise will also help your child to maintain their fitness and stamina and activities such as swimming and horse riding can be adapted to match their physical ability.
Although your child will lose muscle strength over time, it is important that they maintain activities like supported standing for as long as possible. Standing is good for breathing, blood circulation, bladder, bowels, bones and joints.

As your child’s physical abilities change, an occupational therapist will advise what sort of seating will give them the best, most comfortable support. This will make it easier for them to play with toys, eat independently and join in at home and at school.

A physiotherapist will assess your child and provide appropriate equipment to support their standing and positioning. Some children benefit from having splints (sometimes called orthoses) for support. Types of orthoses include ankle foot orthoses (AFOs) and knee, ankle, foot orthoses (KAFOs). These will be made specifically for your child by an orthotist who will explain how they will help.

Your child’s physiotherapist and occupational therapist will be able to advise you about powered wheelchairs. This should be at around the time that your child would have been learning to walk. This equipment will mean that they will be able to explore and join in much more easily and this will help with their physical, emotional, social and educational development.

As already mentioned, most children with SMA Type 2 develop a sideways curvature of their spine (scoliosis). It is important that the medical team monitors your child regularly so that any increase in curvature is noticed early. The degree of the curvature and your child’s age will be factors in deciding how to manage this. Initially this may be with a spinal brace or jacket but surgery to correct scoliosis may be recommended if the scoliosis is contributing to breathing difficulties, is preventing comfortable sitting or if the curvature has progressed beyond a certain point.

You may be provided with a sleep system which will support your child’s back, arms and legs to make sleeping more comfortable. Your occupational therapist can advise you about sleep systems.

Occupational therapists can also give you advice about other adaptations and equipment that will help with your child’s everyday activities such as writing, playing, washing, dressing, cooking and eating, both at home and at school. With appropriate encouragement, adaptations and support, your child will be able to lead as fulfilling a life as their friends.

- **Emergency health plans**

Your child’s medical team may work with you to develop an emergency health plan. This records the treatment you wish your child to receive if there is an emergency or if their health deteriorates. You should have your own copy so that you can give it to hospital services if you are away from your home area. The plan can be reviewed and you can change your mind about its contents at any time.

**What other help is available?**
A diagnosis of SMA Type 2 with all its complexity has an enormous impact on families. It’s important for you and your child to have emotional support and plenty of time to talk and ask questions. This can be with members of your child’s medical team, your local G.P., health visitor, social worker, psychologist or a counsellor.

To enable your child to fully participate in activities at home, school and in their community, you will need information, advice and support on mobility, education, equipment and sources of funding that will aid their inclusion. You can find out more by talking to your child’s healthcare team, Spinal Muscular Atrophy Support UK (SMA Support UK) and the other people and agencies listed in this leaflet and on the SMA Support UK route map for SMA Type 2: [www.routemapforsma.org.uk](http://www.routemapforsma.org.uk)

SMA Support UK can provide information and support to families affected by SMA in the UK. Our Outreach Workers are able to visit you at home and can discuss with you the health, social, educational, financial and care support that you and your child may be entitled to. We can also put you in touch with our Peer Support Volunteers who have personal experience of living with SMA Type 2. Information about these services is available on our website: [www.smasureportuk.org.uk/how-we-can-support-you](http://www.smasureportuk.org.uk/how-we-can-support-you) or please phone us on 01789 267 520 or email: supportservices@smasureportuk.org.uk

Muscular Dystrophy UK also provides information, support and advocacy services, including grants towards specialist equipment, for people affected by a range of neuromuscular conditions. Their website is: [www.musculardystrophyuk.org](http://www.musculardystrophyuk.org) or you can phone them on 0800 652 6352 or e-mail: info@musculardystrophyuk.org

Regional care advisors and sometimes neuromuscular nurse specialists are attached to NHS neuromuscular clinics in various regions of the UK. They provide support and information to children and adults with muscle diseases and their families. They link up with other professionals and services so that people receive the local health and social support they need. Regional care advisors’ contact details are available on Muscular Dystrophy UK’s website: [www.musculardystrophyuk.org/get-the-right-care-and-support/people-and-places-to-help-you/care-advisors/](http://www.musculardystrophyuk.org/get-the-right-care-and-support/people-and-places-to-help-you/care-advisors/)

Children’s hospices throughout the UK also offer a wide range of services and support to children and families, some also offer short breaks. Details of hospice services are available from ‘Together for Short Lives’ on 0808 8088 100 and more information is available on their website: [www.togetherforshortlives.org.uk](http://www.togetherforshortlives.org.uk)

- Financial Support

Families living in the UK may be eligible for a number of financial benefits to help towards the cost of providing the extra care their child may need. This does depend on your individual circumstances.
For further information about financial benefits visit the Gov.UK website [www.gov.uk](http://www.gov.uk) and look at the sections ‘Benefits’ and ‘Carers and Disability Benefits’. The Department of Work and Pensions (DWP) can be contacted on: 0345 608 8545.

**Contact a Family** provide information and support to families who have a child with a disability. This includes information on benefits and grants. They can be contacted on 0808 808 3555 or through their website: [www.cafamily.org.uk](http://www.cafamily.org.uk)

**Disability Rights UK** publishes free factsheets on a range of benefits and the ‘Disability Rights Handbook’ annually. For further information visit: [www.disabilityrightsuk.org](http://www.disabilityrightsuk.org)

**Turn2Us** is a charity which helps people access money available to them through welfare benefits, grants and other help. They can be contacted on 0808 802 2000 or through their website: [www.turn2us.org.uk](http://www.turn2us.org.uk)

Your health visitor, **neuromuscular** care advisor, family support worker, social worker or outreach worker may be able to help you with applications for financial benefits.

There are also a number of charities that may assist you with the cost of general household goods, specialist equipment and holidays / days out. Please contact SMA Support UK for more information or see the SMA Type 2 route map: [www.routemapforsma.org.uk](http://www.routemapforsma.org.uk)

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### Genetic Counselling

As a parent with a child with SMA you should be offered a referral for **genetic counselling** to help you understand how SMA is passed on and what the chances are of other people in your family being affected. Genetic counselling also provides you with the opportunity to discuss your choices for any future pregnancies.

As your child and any siblings grow up they can also ask for genetic counselling, particularly if they are considering having children.

For more information on the genetics of SMA, the chances of having a child with SMA and the tests that can be carried out, please see our leaflet ‘The Genetics of Spinal Muscular Atrophy’: [www.smasupportuk.org.uk/the-genetics-of-sma](http://www.smasupportuk.org.uk/the-genetics-of-sma)


### Is there a treatment or cure for SMA Type 2?

Although there is currently no cure for SMA, this does not mean that nothing can be done. As we have outlined above, there are a range of options aimed at managing symptoms, reducing complications of muscle weakness and maintaining the best quality of life.
There is also 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). For more up to date information on this, please go to: [www.smasupportuk.org.uk/the-uk-expanded-access-programme-for-nusinersen-for-children-with-sma-type-1](http://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](http://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.
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 potential opportunity. If this is of interest to you, you can sign up 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

Further Resources

Standards of Care for Spinal Muscular Atrophy (TREAT-NMD)
This booklet describes best practice management and treatment for the more common forms of SMA. It is used by doctors but is also available to families. A hard copy can be requested from SMA Support UK. It can also be downloaded from the TREAT-NMD website: www.treat-nmd.eu/sma/care/family-guide/

Other publications
Any family with a child with SMA Type 2 may contact supportservices@smasupportuk.org.uk or phone 01789 267520 for a free copy of each of the following publications:

- SMA Type 2 and Me – an illustrated book written for children
- Smasheroo – an illustrated book for young children affected by SMA Type 2 or SMA Type 3
- Tilly Smiles – Tilly has SMA Type 2 and she and her family have written this book to inspire others

Further copies may be ordered from the shop on SMA Support UK’s website: www.smasupportuk.org.uk/merchandise

SMA Support UK Information
Leaflets and other resources may be downloaded from the SMA Support UK website: www.smasupportuk.org.uk/about-sma Hard copies may be requested by phoning 01789 267 520 or emailing the support services team on: supportservices@smasupportuk.org.uk

The UK SMA Patient Registry
This leaflet describes the work of the Registry and how to sign up. A hard copy may be requested from SMA Support UK. It can also be downloaded from: www.treat-nmd.org.uk/registry
Please help us keep on producing information like this.
We receive no government funding and rely on public support.
You can sign up as a reviewer and / or make a donation.

Contact us on office@smasupportuk.org.uk or phone 01789 267 520
Or
Go to: www.smasupportuk.org.uk/donate

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

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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 from 8.30am to 6pm Monday to Friday to offer free information and emotional support.

If they can’t help you, they are more than happy to signpost you to specialist services close to you, or to other people who can help.

www.musculardystrophyuk.org
Glossary of Terms

Amino acid
The individual building blocks of proteins. There are 20 different amino acids that are naturally incorporated into proteins. The specific order of the amino acids determines the structure and function of a protein.

Amniocentesis
The removal of a sample of amniotic fluid (the fluid around an unborn baby) for prenatal testing. Cells in the fluid can be tested for certain genetic disorders.

Amniotic fluid
The fluid surrounding a foetus in the womb.

Anterior
Front or forward.

Anterior Horn
The front part of the spinal cord where the cell bodies of the lower motor neurons are located. Long, slender projections of the motor neurons called axons migrate out from the anterior horn in large bundles of nerves in order to reach muscles.

Antibodies
Proteins made by the body to protect itself from "foreign" substances such as bacteria or viruses.

Aspiration
Passage of food, fluid or vomit into the airway / lungs.

Atrophy
The wasting or shrinkage of a part of the body. SMA is called Spinal Muscular Atrophy because the lower motor neurons within the spinal cord degenerate, which leads to the wasting of skeletal muscles.

Axon
The long, slender main projections of a nerve cell. Axons carry electrical impulses away from the cell body (where the nucleus is) to its target, such as muscles.

Bulbar muscles
Muscles around the mouth and throat. When these muscles are affected, swallowing and speaking may become difficult.

Carbon dioxide
A gas that is produced as a waste product of **cells** using oxygen to make energy. It is removed from the body by breathing out.

**Cell**
The basic building block of all known living organisms. Cells come in many different forms such as motor neurons (a type of nerve cell), keratinocytes (main cell type of the skin), or erythrocytes (red blood cells).

**Central nervous system**
The central nervous system consists of the brain and the **spinal cord**. The CNS is connected to other **tissues** and organs in the body, such as skeletal muscles, by the **peripheral nervous system** (PNS).

**Chorionic villus sampling (CVS)**
CVS is a way to test if an unborn baby has SMA. A sample of chorionic villous **cells** (placental tissue) is removed using a needle. This is usually done between the eleventh and fourteenth week of a pregnancy. The cells can then be genetically tested for SMA.

**Chromosomes**
Chromosomes are compact bundles of **DNA**. Humans have 46 chromosomes in each **cell** (with a few exceptions, including sperm and egg cells). They inherit 23 from their mother and 23 from their father to make 23 pairs.

**Clinical**
The observation and treatment of patients, rather than laboratory studies that do not directly involve patients.

**Clinical trial**
A trial done on humans, usually to test a treatment or intervention, or to find out more about a disease. (See also **Phase 0**, **Phase 1**, **Phase 2**, **Phase 2a** and **2b**, **Phase 3** and **Phase 4 clinical trials**.)

**Contracture**
A tightness in the connective **tissue** and tendons around a joint that results from weakness and inability to move a joint through its full range of motion.

**Deletion mutation**
Genetic material (part of the **DNA**) missing from a **chromosome** or **gene**.

**Diagnosis**
Identifying a disease from its signs and symptoms or from its genetic cause. A **clinical diagnosis** is given when a doctor sees enough signs or symptoms to be confident that a person has the disease in question. In **genetic disorders**, a genetic diagnosis is given when a **genetic test** has been performed and the fault in the **gene** that is known to cause the disease is found. Doctors who are experts in SMA can usually diagnose the condition with a high degree of accuracy from the clinical signs and symptoms alone. However, genetic tests are usually
recommended for all genetic disorders to increase certainty, to make sure any treatment is correctly targeted and to enable the family to have prenatal testing in future pregnancies if they wish.

**Distal**
Anatomical term meaning situated away from the centre of the body, towards the extremities. Distal muscles, such as those found in the hands and feet, are typically less affected by the more common forms of SMA compared to proximal muscles, such as those involved in breathing.

**DNA (Deoxyribonucleic acid)**
DNA is the molecule that contains the genetic instruction manual to build all known organisms. DNA is often compared to a set of blueprints, a recipe, or a code, since it contains the instructions needed to construct other components of cells, such as proteins.

**Electromyogram (EMG)**
A test that assesses the electrical activity of the muscles and the nerves controlling the muscles. It is used to help diagnose neuromuscular disorders. There are two kinds of EMG: intramuscular and surface. An intramuscular EMG involves inserting a needle electrode, or a needle containing two fine-wire electrodes, through the skin into the muscle. A surface EMG involves placing an electrode on the surface of the skin.

**Embryo**
The name given to the developmental stage from fertilised egg up until about eight weeks of pregnancy when the embryo becomes a foetus.

**Enzyme**
A protein which initiates, facilitates or speeds up a chemical reaction. Almost all of the processes that occur in our body require enzymes. Examples include the digestion of food and the growth and building of cells.

**Fasciculation**
A small involuntary muscle twitch which can occur in any muscle in the body.

**Foetus (fetus)**
The term used for an unborn baby after the eighth week of development until birth.

**Gastrostomy / Gastric tube (G Tube)**
Feeding tube placed in the stomach in a surgical procedure. Sometimes referred to as a PEG (percutaneous endoscopic gastrostomy).

**Gene**
A section of DNA that carries the information to produce a specific protein. Genes are the unit of heredity that are passed from one generation to the next. We usually possess two copies of each gene, one inherited from each of our parents. When genes are altered through mutation, this can affect the structure and function of the proteins that they produce, leading to disease.
Genetic counselling
Information and support provided by a genetic specialist to people who have genetic disorders in their families or are concerned about a genetically transmitted condition. Genetic counselling helps families understand things like how the condition is passed on, what the chances are of children being affected, and which other family members may be at risk of carrying the affected gene. It also helps affected teenagers / young adults to understand their future choices.

Genetic disorders
Conditions resulting from alterations to an individual’s genes. Genetic disorders can be caused by defects in one or more genes, or whole chromosomes.

Genetic testing
The examination of an individual’s genes to identify any faults that could cause a genetic disorder.

Genetics
The study of genes and inheritance.

Heredity
The passing of traits (characteristics) through the inheritance of genes from one generation to the next.

Hypotonia
Decreased / low muscle tone, sometimes described as floppiness.

Hypoventilation
A reduced rate and depth of breathing (too shallow or too slow), which leads to an increase of carbon dioxide in the body.

Inheritance
The process by which an individual acquires traits (characteristics) from his or her parents.

Molecule
Two or more atoms chemically bonded together. For example, water is a molecule made up of two hydrogen atoms and one oxygen atom bonded together (H₂O).

Motor neurons
The nerve cells that connect the brain and spinal cord to skeletal muscles allowing conscious muscle contraction (movement). They act as a message delivery system: electrical signals originating in the brain are fired down the spinal cord along upper motor neurons; the electrical signals continue along lower motor neurons, which project out to skeletal muscles to control movement. Lower motor neurons are located in the anterior horn of the spinal cord and are the main cell type affected by SMA. In SMA, low levels of the Survival Motor
Neuron (SMN) protein cause the deterioration of lower motor neurons leading to muscle weakness and atrophy.

Muscle biopsy
Removal of a small amount of muscle tissue for analysis.

Mutation
A permanent change in the DNA sequence of a gene that can be inherited by subsequent generations. Dependent upon the type of mutation and where it occurs within the gene, it might have no effect on the protein produced, or it might disturb the protein’s function causing a genetic disorder such as SMA.

Nerve cells
Also called neurons, nerve cells allow the quick transmission of electrical signals throughout the body. Different types of nerve cell make up the nervous system which functions to allow us to perceive and react to our surroundings. For example, the brain sends a signal along the nerves to tell a muscle to contract (move). Nerve cells are important for both involuntary (unconscious) functions like the beating of the heart and voluntary (conscious) functions like moving your arm.

Neuromuscular
Anything that relates to the nerves, muscles, or the neuromuscular junction.

Neuromuscular Junction (NMJ)
The specialised connection, known as a synapse, between the lower motor neurons and skeletal muscle fibres. The NMJ allows signals from the nerves to get through to the muscles enabling them to contract (move).

Nucleus
The control centre of a cell that contains the DNA wrapped up within chromosomes.

Orthopaedic
Relating to the musculoskeletal system: the body’s muscles and skeleton, including the joints, ligaments, tendons, and nerves.

Orthoses (also orthosis and orthotics)
Devices or aids manufactured to prevent or assist movement of the spine or limbs or to provide support for joints and muscles. For example: splints, spinal jacket / brace, ankle-foot orthoses (AFOs), knee ankle-foot orthoses (KAFOs).

PEG (percutaneous endoscopic gastrostomy) feeding tube
A feeding tube placed through the skin of the abdominal wall into the stomach. The tube is placed by a procedure which uses an endoscope camera. In some cases it may be carried out using sedation without the need for a general anaesthetic.
Peripheral nervous system (PNS)
Consists of the nerve cell extensions found outside of the central nervous system (CNS). The PNS acts to connect the CNS with the muscles and internal organs. The lower motor neuron axons and their connections with the muscle (neuromuscular junctions) are found within the PNS.

Phase 0 clinical trial
A very early clinical trial conducted on a small number of people. The purpose of phase 0 trials is to discover the therapeutic potential of a drug and to evaluate whether the drug development is worth continuing further. Unlike the phase 1 clinical trials, phase 0 trials are not used to evaluate in detail the drug dosage, treatment safety or side effects.

Phase 1 clinical trial (also written as phase I)
Phase 1 clinical trials are the first stage of testing a drug or treatment on humans. Researchers will test a new drug or treatment on a small group of people, often healthy volunteers rather than patients. This phase is used to evaluate the treatment’s safety, to determine how much of the drug it is safe to give, and to identify any side effects. After a Phase 1 clinical trial, it is usually not possible to give an answer about whether or not the drug is effective, as this is not what this phase of trial is designed to discover.

Phase 2 clinical trial (also written as phase II)
Phase 2 clinical trials are designed to test how well the drug or treatment works as well as to continue safety assessments on a larger group of people. Only one third of experimental drugs successfully complete both phase 1 and phase 2 clinical trials.

Phase 2a and Phase 2b clinical trial (also written as phase IIa and IIb)
Phase 2 clinical trials are sometimes divided into Phase 2a and Phase 2b. Phase 2a is designed to assess how much drug should be given. Phase 2b is designed to study how well the drug works when different amounts are given.

Phase 3 clinical trial (also written as phase III)
A Phase 3 clinical trial is designed to test a new drug on a larger number of people after it has been shown to be effective in a phase 2 clinical trial. Phase 3 trials allow researchers to gain a more in-depth understanding of the effectiveness of the drug and to further assess the benefits / risks of the drug.

Phase 4 clinical trial (also written as phase IV)
Phase 4 clinical trials evaluate the long term risks and benefits of a drug or treatment after it has become available on the market. They are designed to detect any rare or long-term effects in a much larger number of people and over a longer time period than was possible during the Phase 1, 2 and 3 clinical trials.

Prenatal testing
The genetic testing for diseases or conditions in a foetus or embryo. This is done by removing a sample of fluid or tissue by procedures such as amniocentesis or chorionic villus sampling (CVS).
**Protein**
Proteins consist of chains of *amino acids* arranged in very specific orders. The order of amino acids within a chain is determined by the genetic code (*DNA*). Different *genes* have the "instructions" for making different proteins. Proteins are the building blocks of our bodies and are essential for the structure, function, and regulation of *cells*, *tissues* and organs. Examples of different proteins include *enzymes*, *hormones*, *antibodies* and the *survival motor neuron (SMN)* protein.

**Proximal**
Anatomical term meaning situated close to the centre of the body. Proximal muscles, such as those found in the hips, shoulders and neck, are more affected than *distal* muscles in most forms of SMA.

**Rare Disease**
The European Union (EU) considers diseases to be rare when they affect not more than 5 per 10,000 persons in the EU.\(^\text{10}\)

**Respiratory**
Relating to breathing.

**RNA (ribonucleic acid)**
RNA is very similar to *DNA* in that it carries genetic information. It plays an important role in the creation of *proteins*. There are different types of RNA that have different roles.

**Scoliosis**
Sideways curvature of the spine.

**Sensory nerves (sensory neurons)**
*Nerve cells* responsible for converting external stimuli, for example sound, light and smell into internal signals. This is how we feel, see, smell and hear.

**Skeletal muscle**
Consciously controlled muscle that attaches to bones allowing movement. Examples include the biceps, triceps, and thigh muscles.

**Spinal**
Relating to the spine.

**Spinal cord**
The bundle of nervous *tissue* within the spine. It includes *nerve cells* and extends out from the brain. The brain and spinal cord make up the *central nervous system* (CNS).
**Survival Motor Neuron 1 (SMN1)**

The **gene** that when **mutated** or deleted can lead to the development of SMA. For our lower **motor neurons** to survive and thrive we need a certain amount of the full-length **SMN protein** produced by the **SMN1 gene**.

**Survival Motor Neuron 2 (SMN2)**

The **gene** that can have an impact on the severity of SMA because it is able to produce a small amount of functional **SMN protein**. In people with a fault in the **SMN1 gene**, this can be important because the more copies of **SMN2** that someone has, the more functional SMN protein they can produce. Individuals with more severe forms of SMA, for example Types 1 and 2, usually have fewer copies of the **SMN2 gene** than those with SMA Type 3.

**Survival Motor Neuron (SMN) gene**

A **gene** that produces the **Survival Motor Neuron protein**. **Mutations** in the **SMN1 gene** are the cause of some forms of SMA. There are two types of **SMN genes**, **SMN1** and **SMN2**.

**Survival Motor Neuron (SMN) protein**

Produced from both the **SMN1** and **SMN2 genes**, the SMN protein is required for the survival of lower **motor neurons**. If there is no SMN protein in a **cell**, the cell will die. Of all the different cell types, the lower motor neurons seem to be most affected by low levels of SMN protein.

**Symmetrical**

The same on both sides of a central point.

**Tissue**

A collection of **cells** that work together to perform a common function. For example, organs are formed from multiple tissues.

**Virus**

Viruses consist of genetic materials (**DNA or RNA**) surrounded by a protective coat of **protein**. They are capable of latching onto **cells** and getting inside them. Some viruses (like the cold virus or flu virus) cause people to become ill. But, their ability to get inside cells also means that certain viruses can be used to deliver treatments into the cell.

**References**


