Spinal Muscular Atrophy (SMA) is a hereditary condition that is passed from parents to their children through their genes. When faced with a diagnosis of SMA many families want to learn more about genetics so that they have a better understanding of the condition, what it means for future pregnancies and for other family members, and what genetic treatment options might be available in the future.

This information sheet is for families of children diagnosed with SMA Types 1, 2 and 3 that are caused by recessive mutations in the SMN1 gene (explained fully later). There are other rarer forms of SMA which are not covered in this information sheet, however, some of the information may still be useful. (You can also read the SMA Support UK leaflet ‘The Genetics of Some Rarer Forms of Spinal Muscular Atrophy’: www.smasupportuk.org.uk/the-genetics-of-some-rarer-forms-of-spinal-muscular-atrophy)

The genetics of SMA is complex and every person with SMA is different. Your medical team will always be happy to go over any of this information with you and they can provide you with genetic information that applies to your individual situation.

As well as families, this information may also be useful for healthcare and other professionals, and members of the general public. It includes questions that families often ask and the glossary at the end further explains the words that appear in bold font.
What are genetic conditions?

**Genetic** conditions are caused by faults in our **genes**.

Our bodies are made up of many millions of **cells**. Nearly all cells have a structure called the **nucleus**, which contains **chromosomes**.

Body cells usually have two copies of each chromosome – one **inherited** from a person’s mother and the other one from a person’s father.

We all have 46 chromosomes in each cell in our body and these are arranged in 23 pairs.

Chromosomes are compact bundles of **DNA**. (See Box 1 for an explanation of DNA.)

A gene is a specific section of DNA. Genes are packaged into chromosomes.

Genes carry the information needed to make **proteins**. Our cells need protein for their structure, survival and to work correctly. We each have approximately 20,000 different genes making different proteins in our bodies. Each protein made by a different gene has its own unique function. The function is determined by the order in which the base pairs are arranged in that particular gene. Usually there are two copies of each gene on each chromosome pair: one inherited from each parent.

Sometimes a gene can contain an unusual change or fault known as a **mutation**. Genetic conditions occur when a mutation within a gene affects how the protein in our bodies is produced and how it works.
Box 1 – an explanation of DNA

DNA is often described as a recipe book, or a set of instructions, because it contains the information needed for a person to grow and develop.

DNA is made up of lots of nucleotides joined together. Each nucleotide contains a phosphate, a sugar and a base. The phosphate and sugar are always the same but the base varies in each nucleotide. The base can be one of four: adenine (A), guanine (G), cytosine (C), or thymine (T).

These bases pair up: A with T, C with G. The order in which these pairs of bases are arranged affects how the ‘recipe book’ information is read. The joined base pairs hold the nucleotides together in strands that twist together to form the DNA double-helix shape.
SMA is an autosomal recessive condition - what does that mean?

People have 23 pairs of chromosomes. 22 of the pairs are non-sex chromosomes, known as autosomes, and they are found in both males and females. The 23rd pair consists of two sex chromosomes (X and Y), which determine your sex. Females have two X chromosomes (XX), and males have an X and a Y chromosome (XY).

Conditions described as autosomal are those in which the faulty gene (mutation) that causes the condition is located on one of the autosomes and not on one of the two sex chromosomes. Autosomal conditions affect both males and females.

We all have some faulty genes. In a recessive condition (like the main types of SMA), a person who carries one faulty copy of the gene and one normal copy will not have the condition.

SMA is an autosomal recessive genetic condition because the Survival Motor Neuron 1 (SMN1) gene responsible for SMA is located on the autosomal chromosome 5 and you must have two faulty copies of the gene for you to have SMA.

What is a carrier?

In a recessive condition, people who have one healthy copy and one faulty copy of a gene do not have any symptoms, but the faulty gene can be passed on to their children. As a result of this they are called carriers.

It is estimated that as many as 1 in 40 people may be a carrier of SMA. When two carriers have a child together there is a chance that their child will have SMA or will be a carrier. Each copy of the gene (healthy or faulty) has the same chance of being passed on. This happens randomly, like the result of a coin toss.

What are the chances that my children will have SMA or be carriers?

The chances of your children being carriers or having SMA will depend on whether you or your partner have SMA or are carriers. The chances stay the same for each pregnancy. Having one child who has SMA or is a carrier does not change the chances for any further children. The following diagrams show what the chances are in different families. For the purpose of the diagrams a ‘non-carrier’ means a person who does not carry the faulty gene and does not have SMA.

Please remember that if your child has a rare form of SMA the diagrams may not necessarily apply to you and your family. If this is the case your child’s medical team will be able to give you information about your particular genetic situation. You can also read SMA Support UK’s leaflet ‘The Genetics of Some Rarer Forms of SMA’: www.smasupportuk.org.uk/the-genetics-of-some-rarer-forms-of-spinal-muscular-atrophy
Autosomal recessive family 1: Both parents are carriers

If two carriers have a child together the chances are as follows:

- Child does not have SMA and is not a carrier: 1 in 4 chance (25%)
- Child does not have SMA but is a carrier: 2 in 4 chance (50%)
- Child has SMA: 1 in 4 chance (25%)

Autosomal recessive family 2: One parent is a carrier, the other does not have SMA and is a non-carrier

Their child will not have SMA but they could be a carrier.

- Child has SMA: not possible (0%)
- Child does not have SMA and is not a carrier: 2 in 4 chance (50%)
- Child does not have SMA but is a carrier: 2 in 4 chance (50%)

Autosomal recessive family 3: One parent has SMA, the other does not have SMA and is a non-carrier

Their child will not have SMA but they will be a carrier.

- Child has SMA: not possible (0%)
- Child does not have SMA and is not a carrier: not possible (0%)
- Child does not have SMA but is a carrier: 4 in 4 chance (100%)
Autosomal recessive family 4: One parent has SMA, the other is a carrier

Their child will be either be a carrier or have SMA.

- Child does not have SMA and is not a carrier: not possible (0%)
- Child has SMA: 2 in 4 chance (50%)
- Child does not have SMA but is a carrier: 2 in 4 chance (50%)

Autosomal recessive family 5: Both parents have SMA

All their children will have SMA.

We have had one child with SMA, how can we find out if our next child will also have SMA?

If you already have had one child with SMA then we assume that you and your partner are both carriers of the faulty gene that causes SMA. If you have another pregnancy with the same partner the chance that your next child will have SMA is 1 in 4 (25%), as shown in the autosomal recessive family 1 diagram. The copy of each gene inherited from each parent is random and cannot be predicted. Some couples who are both carriers decide to take that chance while others want to consider alternative options when having children.

One option is prenatal diagnosis, for example amniocentesis or Chorionic Villus Sampling (CVS). If the test shows that the foetus does have SMA then the couple will have the opportunity to decide whether or not to continue with the pregnancy. Another option is pre-implantation genetic diagnosis (PGD), which involves collecting eggs from the woman and fertilising them outside the body (similar to IVF treatment). Each embryo is tested and only embryos that are carriers or do not
have SMA are implanted back into the uterus. A new option, available from September 2016 is Non-Invasive Prenatal Diagnosis (NIPD) which tests the foetus’ DNA in a blood sample from the mother.

As a couple you will want to make a joint personal decision about these options and the healthcare professionals who see you will give you more information to help with this. You can also read SMA Support UK’s information sheet ‘Future Options in Pregnancy’: www.smasupportuk.org.uk/future-options-in-pregnancy

What is genetic counselling?

If you have a child with SMA you should be offered a referral for genetic counselling. You can also request a referral from your General Practitioner (G.P.).

Genetic counselling takes place with a healthcare professional who has expert training in genetics. They will answer any questions you have regarding your genetic circumstances and they will provide you with advice and information. You will be able to go back to them at a later date if you have more questions.

Adults with SMA can also ask for genetic counselling, particularly if they are considering having children.

I’m a carrier, should I suggest that other family members get tested?

As genes are inherited from parents and passed on from generation to generation you share many of your genes with members of your extended family. It is therefore possible that your blood relations may also be carriers of the same faulty gene. You might want to tell your relations about this so that they can make their own decisions about testing. They should also have the option of genetic counselling so that they can obtain information for themselves and make a decision about whether they want to have carrier testing.

More information about the SMA mutation:

What does the mutation that causes SMA do?

People who have SMA have a fault in a gene called Survival Motor Neuron 1 (SMN1). SMN1 is found on chromosome 5 and is responsible for making an essential protein called the Survival Motor Neuron (SMN) protein. SMN protein is found in all the cells in your body and is particularly important for nerve cells called lower motor neurons. These connect your brain and spinal cord to your muscles allowing you to contract your muscles so that you can move. When SMN protein levels are reduced past a certain point the lower motor neurons deteriorate causing muscle weakness and atrophy (wasting).
Carriers of SMA have one normal copy of the \textit{SMN1 gene}. This is usually sufficient for their bodies to make enough of the \textit{SMN protein} for them to live without the symptoms of SMA. However, people who have \textit{inherited} two faulty copies of \textit{SMN1} cannot make enough SMN protein and so they have SMA.

What is a deletion?

A \textit{deletion} is a type of \textit{mutation} that involves the removal of a small section of DNA. When part or all of a \textit{gene} is missing your body can no longer make healthy \textit{protein}. Instead, a shorter, often less functional protein is made or in some instances no protein at all is made. About 95% of people with SMA have a deletion mutation in both copies of the \textit{SMN1} gene. This is called a \textit{homozygous} deletion.

The other 5% of people with SMA have a \textit{point mutation}. This is when a single base (\textit{nucleotide}) within the DNA is altered. Often they will have the more common deletion mutation in one of their copies of \textit{SMN1} and the point mutation in the other copy. Point mutations in \textit{SMN1} can be \textit{inherited} from a parent or arise as new mutations (called \textit{de novo mutations}), meaning that they have occurred accidentally in the parental egg or sperm that made that particular person. There is then the chance that that person will pass the condition on to their own children.

![Figure 1. Deletion and Point Mutations. Taken from Skirton. H. and Patch, C. (2009) Genetics for the Health Sciences. Oxford: Scion Publishing.](image-url)
What is the \textit{SMN2} gene?

In addition to \textit{SMN1} we possess a second \textit{gene} that is able to produce some functional \textit{SMN protein}. This gene is almost identical to \textit{SMN1} and is therefore called the \textit{SMN2} \textit{gene}\textsuperscript{3}. \textit{SMN2} has an important single base (\textit{nucleotide}) difference from \textit{SMN1}. This causes a small chunk of the gene, called \textit{Exon 7}, to be excluded in the majority of SMN protein that the \textit{SMN2} gene makes. It is estimated that only about 10\% of the SMN protein made from \textit{SMN2} is functional\textsuperscript{11}.

\begin{figure}[h]  
\centering  
\includegraphics[width=\textwidth]{figure.png}  
\caption{People possess two genes able to produce SMN protein. \textit{SMN1} produces all the functional SMN protein we need and is the gene affected in SMA. \textit{SMN2} only makes a small fraction of functional protein (about 10\%). The large majority (about 90\%) of protein produced from \textit{SMN2} is lacking an essential part and is consequently non-functional. Figure adapted from\textsuperscript{10}.}
\end{figure}

\textbf{\textit{SMN2} copy number}

Usually we all have two copies of each gene, one \textit{inherited} from each parent, on each \textit{chromosome} pair. However, sometimes duplication happens resulting in some people having more than the usual one copy of \textit{SMN2} on each chromosome.

The severity of a person’s SMA is dependent on how much functional \textit{SMN protein} their \textit{SMN2 gene} produces. The higher the \textit{copy number} (i.e. the more copies of the \textit{SMN2} gene), the less severe their SMA is likely to be\textsuperscript{12-13}.

Individuals with fewer copies of \textit{SMN2} will on average produce less functional SMN protein and are therefore more likely to develop a more severe form of SMA. However, \textit{SMN2} copy number cannot be used to determine the Type of SMA an individual will have as other genes and differences in
the \textit{SMN2} gene itself can affect how much SMN protein is made. For example, an individual with two copies of the \textit{SMN2} gene could have SMA Type 1 or SMA Type 2.

As \textit{SMN2} copy number analysis is not predictive for individual cases it is not performed for diagnostic or \textbf{carrier testing} purposes for SMA. It is, however, often used in \textbf{clinical trials} to group patients in order to try to identify whether copy number affects the effectiveness of the drug being tested. As \textit{SMN2} copy number and SMA severity do not correlate perfectly the results do have to be treated with caution.

\section*{Types of SMA}

The varying amounts of \textbf{SMN protein} that can be produced from the \textit{SMN2} gene means that there is a wide range in the severity of SMA. For more information on the different types of SMA please see SMA Support UK’s individual information sheets for SMA Types 1, 2, 3, 4 and SMARD. These can be downloaded from the website: \url{www.smasupportuk.org.uk/about-sma} or requested by phone on 01789 267 520 or by e-mail: \url{supportservices@smasupportuk.org.uk}

\section*{Rarer forms of SMA}

As previously stated this information sheet focuses on SMA caused by \textbf{recessive mutations} in the \textit{SMN1 gene}. There are other rarer forms of SMA, some of which are covered in the SMA Support UK leaflet ‘The Genetics of Some Rarer Forms of Spinal Muscular Atrophy’: \url{www.smasupportuk.org.uk/the-genetics-of-some-rarer-forms-of-spinal-muscular-atrophy} You can also ask your medical team if you require further information on any of the rarer forms of SMA.

\section*{Possible treatments for SMA}

There is extensive research taking place into the genetics of SMA. Alongside improved understanding of the condition this had led to the development of potential treatments. Some of these are being tested in clinical trials and may potentially be licensed in the UK.

For information and the latest updates on current clinical trials please see the web links in the further information and resources section of this leaflet.

SMA Support UK notifies the SMA community of the publication of any research updates and developments via its website, social media and monthly E-news. You can sign up for mailings at: \url{www.smasupportuk.org.uk/sign-up-for-mailings}
Common questions

Q: My partner is a carrier of SMA and we are thinking of having children. Where can I get tested to see if I am a carrier too?

A: Ask your General Practitioner (G.P.) to refer you to your regional genetics centre. The main genetics clinics are usually in large regional cities, but outreach clinics may be held in other smaller hospitals across the region.

Q: In a family with SMA who will be able to have genetic testing?

A: Staff at your regional genetics centre can give you specific advice about who might need to be tested. Close family members will be seen first to identify who might be carriers. The process might include drawing a family tree.

Q: There is a history of SMA in my family, when should my partner and I have genetic testing?

A: Having genetic counselling before pregnancy will give you and your partner more time to think about genetic testing and the possibly difficult decisions this can raise. But, do not be afraid to seek genetic counselling if you are already pregnant.

Q: What is the waiting time for a genetics appointment?

A: You will usually be offered an appointment within 18 weeks.

Q: A member of my family has been diagnosed with SMA. I am pregnant and I don’t know if I am a carrier. How do I get a quick referral to genetic services?

A: Contact your General Practitioner (G.P.) to ask for an urgent genetic counselling referral. If this is not possible you can contact your local genetic service directly (a list of centres is available on the British Society for Genetic Medicine website www.bsgm.org.uk). You and your partner may be offered testing if appropriate.

Q: I have no family history of SMA, can I still be tested?

A: Genetic testing is not usually available on the NHS to people with no personal family history or connection to SMA.
Q: Can I have a genetic test for SMA without having genetic counselling?

A: This is generally not possible via the NHS. Genetic counselling will give you the most up-to-date and accurate information enabling you to make informed choices about the options available to you.

Q: How long will it take to get the results of a genetic test for SMA?

A: It usually takes 1 to 2 months to test for a known family alteration or common gene change. It may take longer for rarer types of SMA.

Q: How many copies of the SMN2 gene can an individual have?

A: Theoretically quite large numbers are possible, but highly unlikely. It has been reported that some individuals have 4-8 copies of the SMN2 gene but 1-2 copies is more usual.

Q: I have been tested for SMA and the test has come back negative but my consultant still thinks I have SMA. Is this possible?

A: In a small number of cases the genetic basis is more complex and further genetic testing may be necessary. Your doctor will advise you depending on your symptoms and the tests you have had so far.

Q: My son has SMA symptoms but the test has come back negative. Is it possible that he has SMA?

A: Routine testing for SMA will confirm the diagnosis in the majority of people but sometimes further genetic testing may be needed. Your doctor will advise you depending on your son’s symptoms and the tests he has had so far. This may include investigations for other conditions that can present in a similar way to SMA.

Q: My daughter has been diagnosed with SMA. I’m worried that her brother and sister might develop SMA too. Should they be tested?

A: It is important for you to discuss this with the healthcare professionals involved and your family. Your decision may be influenced by the type of SMA your daughter has and whether you already have worries about the health of your other children.

Q: My sister’s son has been diagnosed with SMA. I have a 4 year old daughter and I’m worried that she might develop SMA too. Should I have her tested?

A: You could have carrier testing at a genetic centre to see whether or not your children have a chance of having SMA. Once you have your result you can discuss with your healthcare professionals
and your family whether or not to test your daughter. Genetic centres would not usually offer carrier testing in childhood as it removes the child’s right to make an informed decision when they are older.

**Further information and resources**

**Genetics and Genetic Testing**

- Cure SMA (America) (formerly Families of SMA)  
  [www.curesma.org/sma/causes-diagnoses/genetics](http://www.curesma.org/sma/causes-diagnoses/genetics)
- Genetic Alliance UK  
  [www.geneticalliance.org.uk/information](http://www.geneticalliance.org.uk/information)
  Tel: 0207 704 3141

**Pre-implantation Genetic Diagnosis (PGD) information**

- Genetic Alliance UK  
  [www.geneticalliance.org.uk/information/services-and-testing/preimplantation-genetic-diagnosis-information-for-patients](http://www.geneticalliance.org.uk/information/services-and-testing/preimplantation-genetic-diagnosis-information-for-patients)
  Tel: 0207 704 3141

**Clinical trial process information**

- TREAT-NMD - Neuromuscular Network information about clinical trials and research. TREAT-NMD can be contacted on: 0191 241 8605.  
  [www.treat-nmd.eu/research/overview](http://www.treat-nmd.eu/research/overview)
- Clinical Trials.gov - American website which explains what clinical trials are.  
  [http://clinicaltrials.gov/ct2/info/understand](http://clinicaltrials.gov/ct2/info/understand)
- Cure SMA - American website for families, formerly called Families of SMA.  
  [www.curesma.org/research/our-strategy/clinical-trials](http://www.curesma.org/research/our-strategy/clinical-trials)

**Current clinical trials in SMA**

TREAT-NMD is a network for the **neuromuscular** field that provides an infrastructure to ensure that the most promising new therapies reach patients as quickly as possible. Current SMA trials are listed on their website: [www.treat-nmd.eu/research/clinical-research/sma-current-trials](http://www.treat-nmd.eu/research/clinical-research/sma-current-trials)

TREAT-NMD can also be contacted on: 0191 241 8617.

Clinical Trials.gov – American website which lists SMA clinical trials.  
Research progress

SMA Support UK:
- Research progress - overview and highlights: www.smasupportuk.org.uk/research-progress
- Drug treatments that have been successful in clinical trials: www.smasupportuk.org.uk/drug-treatments-proven-to-be-effective-for-sma

The UK SMA Patient Registry

The Patient Registry is a database of genetic and clinical information about people affected by SMA. It is used to find participants for clinical trials and to help specialists gain more knowledge about SMA. Information about the work of the Registry and how to sign up can be obtained from SMA Support UK or downloaded from: www.treat-nmd.org.uk/registry
The registry can also be contacted on: 0191 241 8605.

SMA Support UK information

SMA Support UK leaflets can be requested on 01789 267 520 or downloaded from: www.smasupportuk.org.uk/about-sma

Online resources

- Route maps for Spinal Muscular Atrophy Types 1, 2, 3 and Adult Onset SMA: www.routemapforsma.org.uk

Other publications

The following books can be ordered from SMA Support UK: www.smasupportuk.org.uk/merchandise

- Smasheroo – an illustrated book written by a parent for children with 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
- SMA Type 2 and Me – an illustrated book written for children with SMA Type 2
- Type 3 SMA and Me – a book written for children with SMA Type 3
Glossary of Terms

Allele
An alternative form of a single gene. For instance, people can have different alleles for the ability to tongue-roll – the recessive non-rolling allele or the dominant tongue-rolling allele.

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 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.

Anterior Horn Cell
The nerve cells that make up the anterior horn of the spinal cord. Also known as lower motor neurons, these cells are the main cell type affected in SMA.

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

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.

Autosomal inheritance
Inheritance of a faulty gene on one of the autosomes - the chromosomes other than the sex chromosomes. Autosomal inheritance usually affects both males and females equally.

Autosomal recessive inheritance
When a genetic disorder is recessive, two faulty copies of a gene, one from each parent, must come together for the disease to occur. If a person has only one faulty copy, they do not usually have the symptoms of the disease, but are known as carriers because they can pass on the faulty
gene to their children. A disease is autosomal when the faulty gene is found on one of the autosomes. SMA is usually an autosomal recessive condition.

**Autosome**

Any of the 22 pairs of chromosomes found in the human body that are not involved in the determination of sex. They are identical in both males and females. Each pair of autosomes (one from the father, one from the mother) contain genes for the same traits (characteristics).

**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.

**Carrier**

This term relates to autosomal recessive inheritance and X-linked recessive inheritance patterns. A person who has both a faulty copy and a healthy copy of a gene is a carrier. Carriers usually have no symptoms due to the healthy copy of the gene, but they may pass on a condition to their children. In the case of SMA, carriers have one faulty copy of the *Survival Motor Neuron 1 (SMN1)* gene and one healthy copy of *SMN1*. Two individuals who each carry the *SMN1 mutation* have a 25% (1 in 4) chance of having a child with SMA for each pregnancy. A child must inherit two copies of the faulty *SMN1* gene to develop SMA, one copy from each parent.

**Carrier testing**

A genetic test to find out if a person is a carrier of a faulty gene.

**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 (CNS)**

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.

Copy number (of a gene)
The number of copies of a particular gene a person has. In SMA, the copy number is mainly important in the context of the Survival Motor Neuron 2 (SMN2) gene. While SMA is usually caused by a mutation in the Survival Motor Neuron 1 (SMN1) gene, there is evidence that having more copies of the SMN2 gene may help to make SMA less severe, although other factors also play a role.

De novo mutation
An alteration in a gene that arises for the first time in one family member as a result of a mutation in an egg or sperm cell of one of the parents, or in the fertilised egg itself. Neither parent will have the mutation themselves.

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.

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.

Dominant inheritance
A method of genetic inheritance where having a single faulty copy of a gene is enough to cause a genetic disorder, even though a healthy copy of the gene is also present. We inherit one copy of each gene from our mother and one from our father. Individuals with a dominant condition have a 50% chance of passing on the altered gene, and the resulting genetic disorder, to their children.
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.

Exon
Genes are divided into regions called exons and introns. Exons are the sections of DNA that provide the code that enables proteins to be produced.

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

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.

Genotype
Genotype can refer to a person’s or an organism's entire genetic makeup, or the alleles at a particular genetic location.
Heredity
The passing of traits (characteristics) through the inheritance of genes from one generation to the next.

Homozygous
Having two identical alleles of a gene on both chromosomes in a pair. In other words, homozygous refers to a genotype consisting of two identical alleles of a gene for a particular trait (characteristic). For example, someone with two copies of the dominant tongue-rolling gene (allele) is said to be homozygous for this gene. Individuals who are homozygous for a trait are referred to as homozygotes.

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

Intron
Genes are divided into regions called exons and introns. The protein-coding exons are interspersed with introns, which have structural and regulatory roles.

In vitro fertilisation (IVF)
A process by which eggs are fertilised by sperm outside the womb. The fertilised egg is then transferred into the womb to try to establish a successful pregnancy.

Messenger RNA (mRNA)
An intermediate molecule between DNA and proteins. It acts as a template that can be read by the ribosomes in order to produce proteins.

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.

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).

Nucleotide
The individual building block of our DNA and RNA. A nucleotide consists of a base, one of four chemicals: adenine (A), cytosine (C), guanine (G) and thymine (T), plus a molecule of sugar and one of phosphoric acid. Within DNA, A pairs with T, and C with G. Within RNA the thymine is replaced by uracil (U).

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

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.

Point mutation
A type of genetic mutation that causes a single building block of DNA (nucleotide) to be replaced with a different one.

Pre-implantation genetic diagnosis (PGD)
The technique used to test very early embryos for a specific genetic disorder before they are implanted into the womb. Couples undergo standard in vitro fertilisation (IVF) during which eggs are fertilised by sperm outside the womb. The embryos are grown in the laboratory until they have grown into a ball of cells. A small sample of these cells is then removed for genetic testing.

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**.

Recessive
**Autosomal recessive** describes a form of **inheritance** in which two faulty copies of a **gene** are required in order for a person to be affected by a **genetic disorder**. This means that a faulty copy of a gene is inherited from each parent. **Survival Motor Neuron 1**-associated SMA is an autosomal recessive condition. In X-linked recessive conditions, two faulty copies of the gene are needed for the genetic disorder to show in females, but only one faulty copy in males. This is because X-linked recessive conditions are caused by **mutations** in genes found on the X chromosome, but that are missing from the Y chromosome. Males have one X and one Y chromosome, while females have two X chromosomes.

Ribosome
Ribosomes read **messenger RNA (mRNA)** and use it as a template to build **proteins** within a **cell** by connecting **amino acids** together.

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, for example **messenger RNA (mRNA)**.

Sex chromosomes
The X and Y **chromosomes** determine the sex of an individual. Females have two X chromosomes; males have an X and a Y chromosome.

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

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.

**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 material (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


Version 1.6
Author: SMA Support UK Information Production Team with Rachel Thompson, SMA Patient Registry Curator 2012-2013 and Dr James Sleigh, SMA Support UK Research Correspondent
Published: September 2014
Updated: January 2017
Full review due: September 2017

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We would like to thank Claire Dolling (Principal Genetic Counsellor) and colleagues at the Clinical Genetics Unit, Birmingham Women’s NHS Foundation Trust for their assistance with the ‘Common questions’ section of this information sheet.

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