Huntington's Disease Association

Huntington's disease:

A genetic testing guide

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The genetics of Huntington's disease

A gene is a piece of biological information that a person inherits from their parents. It is present in every cell of the body and tells cells what to do. Genes control cells by producing proteins and different genes make different proteins.

A gene is usually attached to a chromosome - a threadlike structure of DNA that stores many different genes. Each cell in the human body contains around 25,000 genes stored on 23 pairs of chromosomes.

The Huntington's gene determines whether a person could develop Huntington's disease and is stored on chromosome pair four. The Huntington's gene provides the code for the Huntington's protein. Everyone has two copies of the Huntington's gene – one inherited from each parent. However if a person inherits a faulty copy of the gene from a parent they will develop Huntington's disease.

DNA is made up of four chemicals - A (Adenine), T (Thymine), C (Cystostine) and G (Guanine). The code for the Huntington's gene contains three of these chemicals C, A and G which are repeated over and over again in a particular sequence causing an expansion.

If a person has Huntington's disease, this means they have inherited an expanded copy of the Huntington's gene from a parent. If there are too many CAG repeats on one copy of the gene, the protein that is produced is 'faulty' and can damage nerve cells in the brain. It is a bit like adding too much of one ingredient in a recipe.

If a person has a Huntington's gene with 26 or fewer CAG repeats, they will not develop Huntington's and neither will their children or future family generations.

If a person has 40 or more CAG repeats, they will develop Huntington's at some point during their lifetime. The symptoms of Huntington's can begin to show at any age and some people don't show symptoms until late adulthood.

If a person has a Huntington's gene containing between 36 and 39 CAG repeats this is called the 'reduced penetrance' range. Some people in this range will develop symptoms of Huntington's, but others won't develop symptoms at all. If symptoms do develop, the age at which symptoms start tends to be much later.

The child of someone with a CAG repeat in the 'reduced penetrance' range has a 50% risk of inheriting a gene within the 'reduced penetrance' range. Occasionally, the CAG can expand into full penetrance, with more than 40 repeats.

Someone with a CAG repeat of 27-35 is known as having an 'intermediate allele'. People with an intermediate allele will not develop Huntington's disease. Around 6% of the general population carry an intermediate allele. There is often nothing to worry about, however, there is a very small chance that the child of someone who carries an intermediate allele could inherit a reduced or full penetrance gene.

Huntington's status		CAG repeat length
Unaffected	Normal	
	Intermediate	
Affected	Reduced penetrance	
	Full penetrance	

Huntington’s is what’s known as an ‘autosomal dominant disorder’. This means that you only need one copy of the faulty gene to develop the disease.

Every child conceived naturally to a parent who has the faulty gene has a 50% chance of inheriting the gene and the disease. In exceptional cases, where both parents have the faulty gene, the child has a 75% chance of inheriting it. In some rare cases, if one parent has two faulty Huntington's genes, all of their children will develop Huntington's disease.

It is possible to be diagnosed with Huntington’s disease, even if there is no family history of Huntington’s. This could happen if a person is adopted and doesn’t know their family history, or if their parents died early, before symptoms had developed. This can also happen if one of their parents carried a reduced penetrance or intermediate allele.

What is genetic testing?

There are two types of genetic testing - predictive testing and diagnostic testing.

Predictive testing

If somebody knows that they are at risk of Huntington's disease they can have a blood test to tell whether they have inherited an expanded copy of the Huntington's gene.

The test measures the number of repeats in both copies of the Huntington's disease gene.

In a few cases, the test result is not clear and a definitive answer is not possible. This is because the number of CAG repeats is in the reduced penetrance range.

A person usually must be 18 years old or older to have a predictive test, however if a person under 18 years old is thinking about getting the test they can seek advice from their local genetics team.

If the test shows that a person does have the faulty gene then it is said to be a positive test. If the test shows that both Huntington's genes are within the normal range, then the test is said to be negative and the person will not go on to develop the disease.

Diagnostic testing

Diagnostic testing is used when a person of any age has symptoms of Huntington's disease already. It is undertaken with the appropriate consent, by doctors who think their patient may have Huntington's disease or Juvenile Huntington's disease. A blood test is also usually taken to confirm the diagnosis.

The predictive testing process

Testing is available at regional Genetics Clinics, which are located throughout England and Wales. Generally, appointments can be made through the GP.

Visiting a genetics clinic does not come with any obligation to have the test. Staff at the clinic are available to discuss any concerns that a person may have. Each clinic will follow an agreed counselling protocol before a person is able to take the test. This usually means that a person must attend at least three sessions, in which they have the opportunity to ask questions and to consider the implications of having the test. It is possible to withdraw from the testing process at any time.

Once somebody decides that they want to have the test, they have two separate blood samples taken, so that the result can be double-checked. The DNA which is extracted from the blood is then analysed in a specialised laboratory.

It can take time for a clinic to confirm a result, so it is not uncommon to wait around four weeks for a result. This can, understandably, be a stressful time. The result will always be delivered in a face to face appointment. After the result, follow-up counselling should be available.

A typical testing journey

Initial session

- The person provides details of their family history to the doctor or genetic counsellor at the session who then attempts to confirm the diagnosis history by checking the results of prior family tests.
- The doctor or genetic counsellor provides information about Huntington's disease, the genetic test process and possible results.
- The person will discuss with the genetic counsellor their reasons for requesting a test at this stage in their life and their approach to the possible outcomes. There will also be a chance to discuss, if wanted, the reproductive options available if the person wants to avoid the possibility of passing the disease on to the next generation.
- The person will be given the chance to identify someone who will support them through the process.
- The person will be encouraged to think about and discuss the impact any result will have on their family or friends. This can be particularly important in relation to other family members who may not wish to be tested themselves but where the test could also reveal their status.
- The person will be encouraged to consider financial implications and other issues such as life insurance and employment.

Reflection period

- The initial session is followed by a summary letter and then a period of reflection. If the person wants to continue with the process, a second session is then arranged.

Second / third session

- A review of the information discussed at the first session is undertaken.
- The doctor / genetic counsellor, in accordance with genetic testing guidelines, may consider a neurological examination and a psychological appraisal to better evaluate the person. This, however, is not a requirement for participation in predictive testing.
- The person and genetic counsellor will discuss preparing for the results.

Blood test

- A date is arranged for a blood sample to be taken. Results will not be be provided on the day.

The results

- At a follow up appointment (usually a month after) there will be a face to face discussion to discuss the results of the test.

Follow up sessions

- Relevant follow up sessions are arranged as required after results are given.

Advice and support

- Whatever the result, it is important that the person accesses the help, support and advice available. At the Huntington's Disease Association, we have a number of helpful information guides and Specialist Huntington's disease advisers who can provide support and put the person in touch with others who may have gone through similar experiences. There are Huntington's Disease Association branches and support groups who meet up and down the country as well as online communities.

Deciding whether to have a predictive test

Deciding whether or not to have a predictive test and when to have it is an important decision and there are many things to carefully consider. Only the person can decide whether to be tested or not.

Genetic counselling can help people to make the right decision for them. They may decide after counselling that they want to take the test, that they would prefer not to take the test or even that they want to take the test but at a later date.

If a person does choose to have the predictive test, in addition to the emotional impact the result may have on themselves and their family, they should also think about how the result could affect other parts of their life. A positive result may have an impact on things like life insurance and job opportunities. There are certain occupations, such as the armed forces, where being at risk of Huntington's may act as an obstacle to recruitment.

A predictive test cannot show when a person will begin to develop symptoms, or what those symptoms may be, but it can usually confirm whether or not that person is going to develop Huntington's.

The genetic test result, regardless of the outcome, can affect people differently. Some people find relief in knowing that they will go on to develop the disease rather than continuing at 50% risk, allowing them to plan ahead. Many people who test positive, use the result as their motivation to live their life to the full before Huntington's symptoms take hold and raise awareness of the disease.

Other people who have lived at risk and have mentally prepared themselves for a positive test result and a life with Huntington's, can find it difficult to adapt to the news that they won't go on to develop it. They may also experience feelings of guilt that they have escaped the disease when a loved close relative is affected.

Starting a family

Somebody who has Huntington's or is at risk of Huntington's may wonder what their options for having children are. As Huntington's is a genetic disease, it is likely that the person may be concerned about the possibility of passing on an expanded copy of the gene to their children.

Sometimes it can be difficult for children growing up when their parent has Huntington's.

If somebody with Huntington's decides that they would like to have children, then there are several avenues that they can consider.

If a person feels that it is important to have a child that is biologically theirs they can try to conceive naturally and accept the risk of the child inheriting the genetic condition.

Another option is to try to conceive naturally and, if successful, undergo a test called prenatal diagnosis (PND), to find out if the developing fetus is affected. In most cases, this test is only carried out if the person would consider ending the pregnancy if the fetus is found to have an expanded Huntington's gene.

Another option is to seek preimplantation genetic diagnosis (PGD). PGD uses IVF (in vitro fertilisation); a procedure in which a woman takes drugs to enhance egg production. She then has the eggs removed from her ovaries and fertilised with sperm to create embryos in a laboratory. The eggs are then returned to the woman's body in the hope of a pregnancy.

In the case of PGD, after the fertilised embryos have developed for a few days, one or two cells are removed from each one. The genetic material (DNA and chromosomes) from the cells are then tested for a particular disorder, in this case Huntington's. An unaffected embryo would then be transferred into the woman's uterus. If the pregnancy is successful, the baby should not be affected by the Huntington's it was tested for. Any additional unaffected embryos can be stored for the future.

PGD is an option for parents to have an unaffected child to whom they are both biological parents but it is not always an easy option.

Like all IVF, it is a physically and emotionally demanding process, especially for the woman, and it may not result in a pregnancy. It requires a highly skilled technical team and laboratory set up, which means only a few places deliver this service.

The NHS Commissioning Board will pay for cycles of PGD for couples where the risk of conceiving a child affected by a serious genetic condition is 10% or more and who wish to avoid the birth of an affected child, in accordance with the criteria outlined in Clinical Commissioning Policy.

Referral to a clinic that carries out PGD can be done by a person's clinical geneticist or genetic counsellor after an initial clinical consultation. The test can be funded privately, although it is possible to apply for NHS funding.

Before treatment can start, a person will be asked to give consent for treatment, including aspects such as storage and use of embryos. They will then need to agree to some laboratory testing and preparatory investigations, including health history, ultrasound scan, blood tests, semen analysis, and more.

Preparation time will vary, but on average it will take 5-12 months after the initial consultation before a couple will start treatment. Once in a treatment cycle, the process takes about 9-12 weeks.

Another option for conceiving a child is through the use of donated eggs, sperm or embryos. This means the child is not genetically related to the parent with Huntington's. In the case of a donated embryo being used, the child will not be related to either of the parents. This option has the advantage of giving parents the opportunity to experience pregnancy and childbirth, and to raise a child from the very beginning of its life. Going down this route may still require IVF to assist with conception.

More information about clinics, PGD and other assisted conception techniques can be found by visiting the Human Fertilisation and Embryology Authority website at:

- www.hfea.gov.uk

Information can also be found on the Genetic Alliance UK website at:

- www.geneticalliance.org.uk

Adopting a child is another option that somebody with Huntington's may choose. Various organisations can help match somebody who wants to adopt with the right child for them. These include local authorities, as well as charities. The adoption process can be long and difficult, but some people may decide it is the best option for them.

When someone has the Huntington's gene or is showing symptoms, the agency will consider the implications for the child, the person's health and their ability to look after a child. It is important that somebody with Huntington's disease thinks carefully about whether they'd be able to take on the responsibility of having a child.

More information about adoption is available from Adoption UK at:

- www.adoptionuk.org

Support from the Huntington's Disease Association

Specialist Huntington's Disease Advisers (SHDAs)

Our Specialist Huntington's Disease Advisers have a background in health or social care and are knowledgeable about Huntington's disease. They operate throughout England and Wales and support the person with Huntington's, their carers and any professionals involved in their care. To get in touch with your local Huntington's Disease Adviser, contact us at:

- 0151 331 5444
- info@hda.org.uk

Specialist Huntington's disease Youth Engagement Service (HDYES)

At the Huntington's Disease Association, we have a Youth Engagement Service (HDYES) operated by youth workers who work with young people whose families are affected by Huntington's. This confidential service is for anyone aged 8-25 living in a family affected by the disease. To get in touch with your local Specialist Youth Adviser, contact us at:

- 0151 331 5444
- info@hda.org.uk

Website

Our website offers practical advice and sources of help and support, including downloadable information guides. It also holds information about events and activities that you can attend and details of local branches and support groups. Additionally, the website hosts an online message board for people to access peer support, information and advice.

- www.hda.org.uk
- hdmessageboard.com

Membership

Huntington's Disease Association membership is free for people with Huntington's and their families and it is easy to join. If you become a member, you'll receive a bi-annual newsletter with up-to-date information on events and research. To find out more about becoming a member, please contact us or take a look at our website.

Resource library

The following charities, organisations and public bodies have been mentioned throughout this guide. Their details have been summarised and grouped below for easy reference.

Organisation	Contact details	Support
Huntington's Disease Association	0151 331 5444 info@hda.org.uk www.hda.org.uk	Advice Support resources Online forum
Huntington's Disease Youth Organization (HDYO)	info@hdyo.org en.hdyo.org	Advice Support resources Online forum
NHS - GP finder tool	www.nhs.uk/service-search/find-a-gp	Advice Referrals
Human Fertilisation and Embryology Authority	www.hfea.gov.uk	Information about PGD and assisted fertility techniques
Genetic alliance	www.geneticalliance.org.uk	Information about PGD and assisted fertility techniques
Adoption UK	www.adoptionuk.org	Information about adoption

Notes

Get in touch

For advice and support
or to speak to a
Specialist Huntington's
Disease Adviser

email **info@hda.org.uk**

phone **0151 331 5444**

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We'll be there