Huntington's Disease Association

Huntington's disease:
A genetic testing guide

Contents

3 The genetics of Huntington's disease

8 What is genetic testing?

10 The predictive testing process

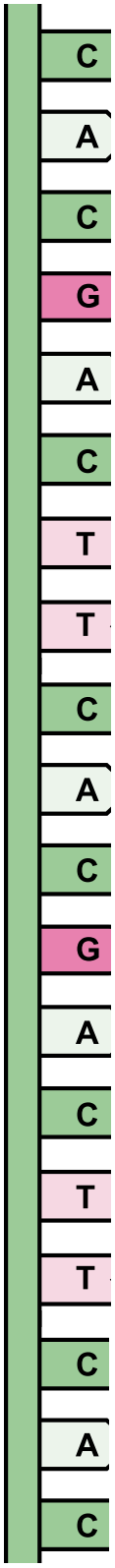
14 Deciding whether to have the predictive test

15 Support from the Huntington's Disease Association

17 Resource library

18 Glossary

The genetics of Huntington's disease



A gene is a DNA section with instructions for making proteins, the building blocks of biological processes. Each human cell has about 25,000 genes, organised into chromosomes- dense structures that store different genes.

We each have 23 pairs of chromosomes; one chromosome from each pair is inherited from each parent. As a result, we generally possess two copies of each gene, with one passed down from each parent.

The gene important to Huntington's disease is HTT, which provides the instructions for a protein called Huntingtin. The gene is located on chromosome 4. Everyone has two copies of the HTT gene – one from each parent. It is only when one of these genes is altered in a particular way that someone will be at risk of developing Huntington's disease.

DNA is made up of four special chemicals: A (Adenine), T (Thymine), C (Cytosine), and G (Guanine). Our amazing cellular machinery reads these chemicals in groups of three, guiding the cell to create amino acids, the essential building blocks of proteins. For instance, the sequence CAG instructs the cell to produce an amino acid called glutamine. Within the HTT gene, there's a specific section where the CAG instruction is repeated several times. This repetition is known as a CAG triplet repeat, which leads to the creation of a chain of glutamines- something we refer to as polyglutamine.

Having CAG triplet repeats is completely normal, and you'll find that the number of repeats can vary a bit from person to person. Since we inherit two copies of the HTT gene, we actually have two different lengths for our CAG repeats.

If a person has two copies of the HTT gene that both contain 26 or fewer CAG repeats, they will not develop Huntington's disease, nor will their children or future generations.

Huntington's disease involves an abnormal CAG repeat expansion in the HTT gene, leading to an excess of glutamines in the protein. This expansion is present from conception and disrupts protein function, accumulating in cells and damaging brain nerve cells over time.

If a person has 40 or more CAG repeats on one copy of their HTT gene, they will develop Huntington's disease at some point in their lifetime.

The onset of symptoms for Huntington's disease can be quite different, even among family members. It's important to note that knowing the size of the CAG repeat isn't always straightforward, and predicting when symptoms will appear based solely on this size can be challenging. Generally speaking, however, larger CAG repeat sizes tend to result in an earlier onset of symptoms. For instance, childhood onset Huntington's disease, known as Juvenile Huntington's Disease, is often linked to larger CAG repeat expansions, usually above 60 CAGs.

It appears that having up to 26 CAG repeats does not seem to be related to Huntington's disease. However, if there are more than 40 CAG repeats, it is associated with an increased risk of developing Huntington's disease. For those with between 26 and 40 repeats, this is often referred to as the 'gray' area, which can understandably lead to some uncertainty.

If a person has 36 to 39 CAG (reduced penetrance) repeats on one copy of the HTT gene, some may develop Huntington's disease symptoms during their lifetime, while others may never show them. When symptoms emerge, they usually occur later, with likelihood increasing as repeat numbers rise.

A child whose parent has a CAG repeat in the 'reduced penetrance' range faces a 50% chance of inheriting a gene from that range. However, this 'reduced penetrance' CAG repeat can occasionally expand over generations, meaning the child might inherit a full expansion of more than 40 repeats.

When a person has a CAG repeat of 27-35 on one copy of their HTT gene, they are said to have an 'intermediate allele'. People with this type of allele won't develop Huntington's disease. In fact, about 6-8% of the general population has an intermediate allele. Overall, there's usually nothing to be concerned about, and these alleles are often discovered by chance. It's worth noting, though, that there is a very small possibility that a child of someone with an intermediate allele might inherit a reduced or full penetrance CAG-repeat expansion.

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

How is Huntington's disease inherited?

Huntington's disease is an 'autosomal dominant disorder.' This means that, while everyone possesses two copies of the HTT gene, it only takes one expanded copy of the gene for a person to develop Huntington's disease.

When a child is conceived naturally by a parent with a CAG triplet expansion, there's a 50% chance that they might inherit the expanded copy of the gene, which means there could be a risk of developing Huntington's disease. Interestingly, some individuals may receive a Huntington's disease diagnosis even without any known

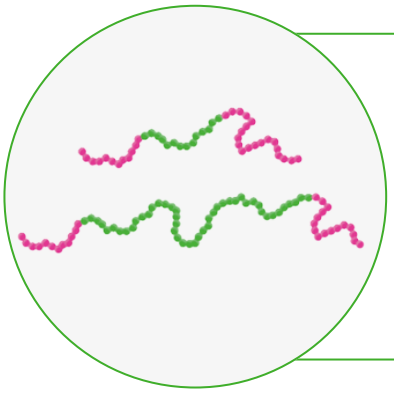
family history of the condition. This can occur for various reasons, such as adoption, lack of knowledge about their family background, or if their parents passed away before any symptoms appeared. Additionally, a new Huntington's disease diagnosis in a family can occur if one parent has a reduced penetrance or intermediate allele, making things a bit more complex but still manageable.

Caused by a faulty gene

The gene that causes Huntington's is often called the huntingtin gene (HTT).

Hereditary

Everyone has two copies of the gene - one inherited by each parent.

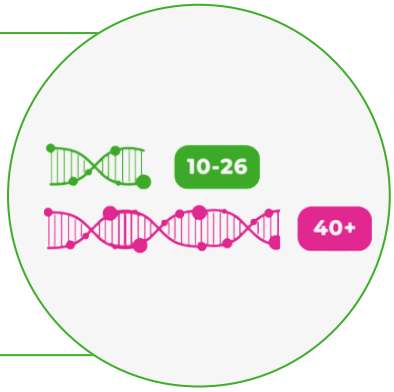


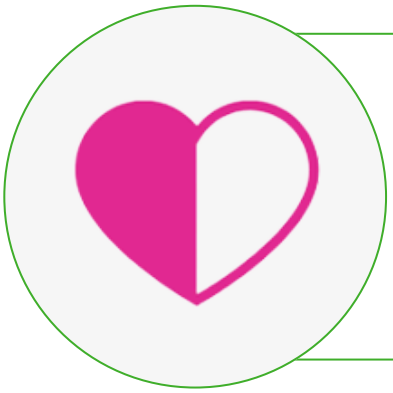
Huntingtin gene

When the huntingtin gene is faulty, the huntingtin protein it produces repeats certain genetic sequences known as CAG too many times. This in turn damages neurons in certain areas of the brain.

CAG repeats

A normal CAG repeat is between 10 and 26. Usually one of your CAG repeats will be in this region. If one of your CAG repeats is over 40, this means that you will go on to develop Huntington's disease.



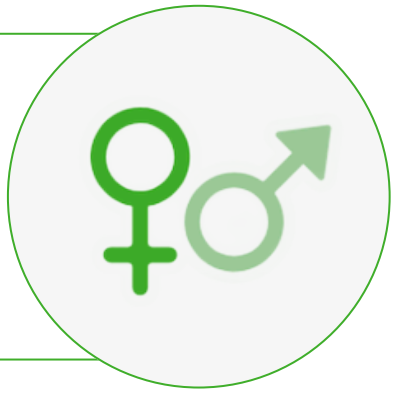


50 / 50 risk

The gene is passed down through the parent's DNA through the egg and sperm. Anyone born to a parent with Huntington's has a 50% chance of inheriting it.

Affects men and women

Both sexes are at risk and can inherit the disease. There is evidence to suggest that when passed through the father the gene has a higher chance of expanding into a higher CAG repeat.



30 - 50 average onset of symptoms

The symptoms of Huntington's disease affect the person's mind, mood and movement. Although the movement is the most obvious symptom, the mental symptoms can be the most difficult to manage.

Testing for the gene

You can find out if you carry the faulty gene by taking a blood test known as a predictive test. You need to be 18 years old to take the test. Not everyone wishes to find out.

What is genetic testing?

A genetic test for Huntington's disease typically involves a blood test to collect a sample of DNA, which is then analysed to count the number of CAG repeats on each copy of the gene. There are two types of genetic testing diagnostic testing and predictive testing.

Diagnostic testing

Diagnosing Huntington's disease involves looking for certain clinical features, but confirming it with genetic testing can really help. This type of testing is done for anyone showing symptoms of the disease, no matter their age. Doctors who suspect their patient might have Huntington's disease or Juvenile-onset Huntington's disease carry out this testing with the individual's consent, ensuring a caring and respectful approach.

The test usually focuses on examining the HTT gene closely. If they are still unsure about the diagnosis or if there isn't any known family history of Huntington's disease, they may consider a more comprehensive genetic test, like whole genome sequencing. It's important to note that the time it takes to get results from these two testing methods can differ quite a bit. Targeted HTT genetic testing generally takes around two to three months for results, while whole genome sequencing results may take up to a year.

Predictive testing

If someone understands that they might be at risk for Huntington's disease because of their family history, even if they don't show any symptoms yet, they can still explore the option of genetic testing. This testing can help them find out if they've inherited a CAG triplet repeat expansion.

The test is a simple blood test, and while the results usually take about one month to six weeks to come back, it's really important to also include predictive test counselling with a Clinical Geneticist or Genetic Counsellor to better understand the potential implications of those results.

The predictive testing process

You can find testing options at various Regional Genetics Clinics across England and Wales, typically requiring a referral from a GP. If you're under 18 and thinking about a predictive test, you can talk about your risk of Huntington's disease and seek guidance from your local genetics team.

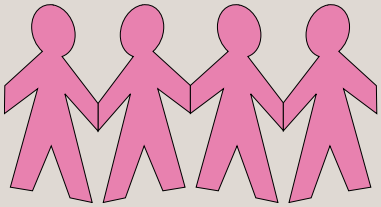
Visiting a genetics clinic provides an opportunity to explore your options for predictive testing. You won't feel pressured to proceed; instead, you can have open conversations about the advantages and disadvantages that suit your unique situation. The staff are dedicated to ensuring you feel supported throughout your journey, particularly if you're considering genetic testing. Each clinic adheres to a set of international guidelines for predictive test counselling, which means your genetic testing will usually occur over several appointments. Remember, it's perfectly okay to change your mind at any stage of the testing process.

After deciding to move forward with genetic testing, you can expect the results to be ready within about four to six weeks. It's completely normal to feel a bit stressed during this time. Typically, the results are shared either in person or through a video consultation, and you'll have follow-up appointments available. No matter the outcome we're here to support you every step of the way.

A typical testing journey

Initial session

1



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.

2

The doctor or genetic counsellor provides information about Huntington's disease, the genetic test process and possible results.

3

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.

4

The person will be given the chance to identify someone who will support them through the process.

5

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.

6

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 session

1

A review of the information discussed at the first session is undertaken.

2

The doctor / genetic counsellor, in accordance with genetic testing guidelines, may consider a neurological examination or recommend additional psychological appraisal.

3

The person and genetic counsellor will discuss preparing for the results.

4

There may be additional appointments based on a person's individual wishes and circumstances.

Blood test

A blood sample for DNA will be taken at some point following one of the appointments. The DNA might be stored for testing at a later date or testing might start as soon as the DNA sample arrives in the laboratory.

The results

At a follow up appointment (usually a month to six weeks after the genetic test has been requested) 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. You will find stories of others who have been through the testing process on our website and social media.

Deciding whether to have a predictive test

Choosing the right time to have a predictive test is a significant and personal choice, and it's important to take various factors into thoughtful consideration.

Genetic counselling offers valuable support for individuals to make the best choices for themselves. After their sessions, individuals might feel ready to take the test, decide that it's not the right time for them, or even opt to take the test later on when they feel more prepared.

If someone decides to take the predictive test, it's important to consider not just the emotional effects the results might have on them and their loved ones, but also how these results could influence other aspects of their lives. For instance, a positive gene result could impact things like life insurance and job opportunities. There are specific careers, like those in the armed forces, where being at risk of Huntington's disease might present challenges during the recruitment process.

A predictive test can't indicate when symptoms will develop or what they may be, but it can confirm if a person is likely to develop Huntington's disease.

Genetic test results affect individuals differently. Some feel relief in knowing their likelihood of developing the disease, enabling them to plan ahead. Many use the results to motivate their lives, raise awareness, or engage in research opportunities. However, everybody reacts differently and some people struggle with the knowledge.

Some people prepared for a positive Huntington's disease test may struggle to accept that they will not develop the condition. They might feel guilt when a close relative is affected. The Huntington's Disease Association also offers support to those who test negative.

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** or **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** or **info@hda.org.uk**

Website

Our website offers practical advice and sources of help and support, it has pages on genetics and starting a family. 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**

Mailing list

We send out monthly newsletters and keep people updated about events, news and research via email. You can join our mailing list via the website. **https://www.hda.org.uk/information-and-support/keep-up-to-date/**

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.

Huntington's Disease Association

0151 331 5444

Info@hda.org.uk

www.hda.org.uk

Supporting via advice support, resources, and an online forum

Huntington's Disease Youth Organization (HDYO)

info@hdyo.org

en.hdyo.org

Supporting via advice, support resources, and an online forum

NHS - GP finder tool

www.nhs.uk/service- search/find-a-gp

Supporting via advice referrals

Glossary

Genetic testing can be a difficult topic to understand. To help, we've put together this glossary explaining the key terms found within this guide:

DNA	Stands for Deoxyribonucleic Acid. This is the molecule that holds the genetic instructions that make up all living organisms.
CAG	Is a term given to a specific DNA sequence: Cytosine, Adenine and Guanine.
HTT	This is the Huntingtin gene.
Glutamine	This is the most prominent amino acid, and is crucial for functions such as gut health and immune system support.
Reduced penetrance	Refers to someone who has a genetic variant, or mutation, that may or may not show the associated trait or disease.
Allele	This is a specific form of a gene.
Neuron	This is a cell that sends both electrical and chemical signals around the body.
Genome sequencing	This process reads the sequence of A, T, C and G chemicals that make up our DNA.
Clinical Geneticist	Someone who examines a patient and their medical history to understand whether an underlying genetic disorder is present.
Genetic Counsellor	Someone who guides a patient through the genetic testing process by explaining key concepts and the implications of a diagnosis.
Psychological appraisal	A process that assesses a patient's mental health and psychological wellbeing.

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**

www.hda.org.uk

@hda_tweeting
@hdauk
@hdauk
@hda_uk
Huntington's Disease Association

Huntington's Disease Association

Liverpool Science Park IC1,
131 Mount Pleasant,
Liverpool, L3 5TF

Registered charity no. 296453

A company limited by guarantee.
Registered in England no. 2021975

Design and print by the Huntington's Disease Association Published May 2025 Third edition

Please note this information is correct at time of design. Visit the website to check for the most up to date information.

Inspired by our community