GENETIC TESTING AND HUNTINGTON DISEASE (HD)

What is Huntington disease?

Huntington disease (HD) is a hereditary, neurodegenerative illness with physical, cognitive and emotional symptoms.

What Causes Huntington disease?

HD is a genetic disorder. It is caused by a mutation in the gene that makes the huntingtin protein. There is a section of the huntingtin gene whereby DNA code repeats itself over and over again. This is known as a "CAG repeat" and each individual has a different number of repeats. In people with HD, the CAG sequence is repeated too many times. This "expansion" causes cells to manufacture a harmful protein called mutant huntingtin. The mutant huntingtin protein causes damage to certain parts of the brain – specifically the caudate, the putamen and, as the disease progresses, the cerebral cortex. As the brain cells are damaged, symptoms of HD develop.

Each child of a parent with HD has a 50% chance of inheriting the expanded CAG repeat and being at-risk of HD. Males and females have the same risk of inheriting HD.

What is Genetic Testing for HD?

First, it is important to note that genetic testing can take several weeks to be completed. Test results for HD can be complex. It is recommended that they are reviewed with a genetics specialist in order to fully understand what it means for an individual and their family.

Genetic testing for HD is done on a sample of blood. The test is completed in a specialized laboratory to determine the number of CAG repeats in both copies of an individual's HD gene. Everyone has two copies of the HD gene and it is common for a person to have two different CAG repeat sizes (one inherited from their mother and one inherited from their father).

What is the Predictive Testing Process?

Predictive testing is genetic testing done to determine whether someone will develop HD in the future. It is available through medical genetics clinics in most major regions in Canada. The process may vary somewhat between regions, but usually consists of multiple appointments with genetic counselling and a blood test. The time involved to complete predictive testing can vary from several weeks to several months.

Huntington Society of Canada • 20 Erb St. W - Suite 801 • Waterloo, ON N2L 1T2
1-800-998-7398 • info@huntingtonsociety.ca • www.huntingtonsociety.ca

What Should I Consider?

The decision to undergo genetic testing is a very personal one and many people with a family history of Huntington disease choose not to take the test. Others may want to know whether they will eventually develop symptoms so they can make plans regarding career, financial, insurance, family planning and other life issues.

Possible test results include:

"Gene Mutation Negative" or Normal

The number of CAG repeats is 26 or less. This individual will not go on to develop Huntington disease and their children are not at increased risk either.

Intermediate

The number of CAG repeats is between 27 and 35. This individual will not go on to develop HD themselves. In some cases, their children will have a small risk for developing HD.

"Gene Mutation Positive – Reduced Penetrance range"

The number of CAG repeats is between 36 and 39. This individual is at-risk of HD, but in most cases, the symptoms do not start until late in life. Some people with CAG repeats in this range will not develop any symptoms of HD at all even if they live to an old age. Their children have a 50% chance of inheriting HD and in some cases may be at risk of inheriting a larger CAG repeat number than their parent.

"Gene Mutation Positive – Full Penetrance range"

The number of CAG repeats is 40 or more.This individual will go on to develop symptoms of Huntington disease at some point in their life. It does not necessarily mean that they have signs of HD already but it predicts that they will have symptoms in the future. The result does not provide information as to the exact age when an individual will start to have symptoms or what those symptoms will be. Their children have a 50% chance of inheriting HD.

Unaffected		**Affected**	
Normal ≤26 CAG	Intermediate 27-35 CAG	Reduced Penetrance 36-39 CAG	Full Penetrance ≥40 CAG

Huntington Society of Canada • 20 Erb St. W - Suite 801 • Waterloo, ON N2L 1T2
1-800-998-7398 • info@huntingtonsociety.ca • www.huntingtonsociety.ca

GENETIC TESTING AND HD

Genetic Testing Can Serve Two Purposes:

1. Diagnostic Testing: done to confirm a diagnosis of Huntington disease in individuals who have symptoms of the disease.
2. Predictive testing: refers to a process whereby an individual with a family history of Huntington disease wishes to know whether or not they have inherited the expanded HD gene, even though they currently have no symptoms.

What is Genetic Counselling?

The goal of genetic counselling for HD is to help individuals better understand the potential impact of future genetic testing so that they can make an informed decision and/or to better understand the results of completed genetic testing. Anyone considering genetic testing should have genetic counselling. Both genetic counselling and genetic testing (if deemed appropriate) are covered by provincial health insurance. In some provinces, some or all sessions may be able to be done by videoconference. Check with a Huntington Society Resource Centre Director for more information.

Questions That Would be Addressed with a Genetic Counsellor:

- What are the possible results of my genetic test?
- What would the result mean for me, my partner and my family?
- If I choose not to proceed with genetic testing right now, can I start the process again at a later date?
- Can I receive my test results in the future months or years (when I'm ready)?
- Who should I share my genetic test result with? Parents? Spouse? Children? Employer? Anyone?
- Can I leave the test results for my future adult children if I do not want to know them?
- How do I share my genetic test result with others?
- How do I protect myself from genetic discrimination?
- Can a positive genetic test result impact my ability to get insurance?
- How might a positive genetic test result impact my future planning?
- What are my reproductive and family planning options?
- What do I need to know about research in HD?
- If my test shows that I will develop symptoms, what resources are there in my local area?
- Where do I go if I need additional help and support?

Huntington Society of Canada • 20 Erb St. W - Suite 801 • Waterloo, ON N2L 1T2
1-800-998-7398 • info@huntingtonsociety.ca • www.huntingtonsociety.ca

How do I Arrange for Genetic Counselling?

Anyone with a personal or family history of Huntington disease and who is of the age of majority is eligible for genetic testing. Most genetics clinics require a referral from your family doctor (or another health care professional involved in your care). To find a genetics clinic near you, contact the Huntington Society of Canada by visiting www.huntingtonsociety.ca or the Canadian Association of GeneticCounsellors website at www.cagc-accg.ca.

For More Information

For more information and personal perspectives on predictive genetic testing for Huntington disease, visit https://en.hdyo.org/a/53-genetic-testing. For more information on other related topics, visit www.huntingtonsociety.ca.

Thank you to the authors: Meghan Ferguson, MSc, CCGC, CGC and M. Jill Beis, MSc, CCGC with some updates by Emily Alderman, MSc, CCGC, CGC
Information also taken from Huntington Disease Youth Organization https://en.hdyo.org/

Huntington Society of Canada • 20 Erb St. W - Suite 801 • Waterloo, ON N2L 1T2
1-800-998-7398 • info@huntingtonsociety.ca • www.huntingtonsociety.ca