

Genetic Testing for Huntington's Disease

A Guide for Families
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I. Huntington's Disease and the HD Gene

What is Huntington's Disease?

Huntington's Disease (HD) is a hereditary degenerative brain disorder which leads to both physical and mental disabilities. Symptoms usually appear between the ages of 30 and 50, but the disease may strike those as young as two or as old as 80. Initial symptoms may include difficulty in concentration, depression or twitching, but each person who has HD is affected differently and early symptoms vary from person to person.

Testing is available to determine whether a person has the gene for HD. The decision about whether or not to be tested for HD is one which requires careful consideration. This booklet will answer the most common questions regarding testing.

How do I know if I am at risk for Huntington's Disease

Huntington's Disease is inherited in an autosomal dominant pattern. This means that every child born to a person who has HD, regardless of gender, has a 50 percent, or one-in-two, chance of inheriting the gene that causes HD. Men and women are equally affected, so that either parent may pass on the HD gene to any offspring.

Does that mean that exactly 50 percent of the children of a person with HD will develop the disease and 50 percent will not?

No, each child has the same 50 percent risk of having inherited the gene for HD regardless of whether or not any brothers and sisters have it.

Can I get HD in any other way?

No, you cannot "catch" HD from another person. You must be born with the gene for HD in order to one day develop this disorder.

In some cases, a person may develop what appears to be HD even though there is no known family history of the disorder. There are many reasons why this may be. Perhaps the parent who had the gene for HD died at an early age, before the symptoms appeared, or maybe other family members had HD but were misdiagnosed as having Parkinson's disease or another disorder with HD-like characteristics. In cases like these, doctors may recommend genetic testing to confirm or rule out a diagnosis of HD.

If I was born with the HD gene, then why don't I have HD now?

We inherit our genes from our parents and therefore we are born with them. Some genes are "turned on" only at later stages of our lives. A good example is the gene for baldness. Many people are born with this gene but it is only in adulthood that it is activated and that people begin to lose their hair. Also, people who have the same gene for baldness may begin losing their hair at different ages.

Has the gene been identified?

Yes, the gene for HD was found in 1993.

How does this gene work?

Each person has 23 pairs of chromosomes in all of the cells of his/her body. Genes lie on these chromosomes and are made up of deoxyribonucleic acid, or DNA. It is estimated that humans have about 100,000 genes which influence development, growth and functioning of the body, and are passed down from parents to children.

The gene for HD lies on the short arm of chromosome four. It is actually a segment of DNA which contains a strip of repeated "trinucleotides" at one end. Nucleotides are the building blocks of DNA. The trinucleotide repeat involved in HD is cytosine-adenine-guanine, or CAG.

Everyone has two copies of the gene for HD.

If all people have the gene for HD, why do only some develop the disease?

Whether a person will or will not develop Huntington's Disease can be determined by the number of CAG (or trinucleotide) repeats contained within their copies of the HD genes. People who have inherited the gene which causes HD have a higher number of repeats, usually above 40. No one with 35 or fewer CAG repeats has been known to develop HD symptoms. Individuals who have an HD gene with 36-39 repeats may or may not develop the symptoms of HD within a normal lifespan.

The number of CAG repeats may change as the gene passes from parent to child - so that the child may have slightly more or fewer repeats than the parent. The tendency for an increased number of repeats is more common when the gene is passed from father to child than when a mother transmits the HD gene.

HD is inherited in a dominant fashion. This means that a person need have only one copy of the gene with a high number of repeats in order to develop the disease.

It is important to note that the number of repeats is significant only in determining whether a person will or will not develop HD. The number of repeats is not known to be correlated with the course of the disease, and a particular repeat number does not predict a specific age of onset. The exception to this is that a very high number of repeats is indicative of the juvenile form of HD with age of onset prior to age 20.

** Information provided by Marba A. Nance, MD, HD Genetic Testing Group.*

II. Genetic Testing

How can I be tested?

A blood test is now available that can determine, in almost all cases, whether a person has the HD gene. This test cannot, however, predict when symptoms will begin or the course of the disease.

There are three categories of testing:

1. **Presymptomatic testing**, for people at risk for HD, is the type of testing which will be discussed in greatest detail in this booklet.
2. **Confirmatory testing** determines whether people showing possible symptoms actually have the HD gene.
3. **Prenatal testing** is used to determine whether a fetus has the HD gene. This can be done by amniocentesis or chorionic villus sampling (CVS).

What does presymptomatic testing entail?

The Huntington's Disease Society of America recommends that at-risk persons who wish to undergo presymptomatic testing do so at an HD testing center. The testing centers involve teams of professionals who are knowledgeable about FM. A list of these testing centers is available from HDSA.

The testing procedure involves sessions with various professionals. It typically includes one session devoted to each of the following: - genetic counseling; a neurological exam; a psychological interview; discussion of the results; and follow-up. The genetic test itself is a blood test.

The purpose of these sessions is to ensure that the person about to undergo testing understands the implications of this knowledge and is prepared to receive the results. The neurologic exam will determine if any early symptoms of HD are present. If the person is found to be symptomatic, he/she will be offered the option of discontinuing the testing procedure.

The person may withdraw from the testing process at any time.

The sessions of the testing process are usually spread out over one month or more and require repeat visits to a testing center. Exceptions are sometimes made if a person lives

far away from the center or in other circumstances. Decisions concerning scheduling of appointments can only be made by those who will perform the testing.

Should I bring a friend with me?

It is strongly encouraged that you bring a support person/partner with you to all testing sessions. The partner should be a spouse, companion or a close friend. It is not advisable to bring a sibling or another person who is at risk for HD.

The partner will be able to provide moral support during appointments, when awaiting test results, upon receiving the results, and thereafter.

Are blood samples from my family members necessary for testing?

No, you do not need to obtain blood samples from others in your family. However, the testing centers do encourage you to have available either a blood sample from a family member who has HD or the results of his or her genetic test. This is to ensure that the illness in the family is indeed HD. Some people are misdiagnosed as having HD when, in fact, they have another neurological disorder. Therefore it is important to establish that the affected family member has HD. This type of testing is usually reimbursable by insurance.

How much does it cost?

The cost of testing varies from center to center. Some centers are research facilities and will perform the test free of charge for those involved in their studies, some have sliding fee scales, and others charge anywhere from \$600 to \$1,500.

Will health insurance pay for testing?

You need to check with your insurance provider to see if they cover presymptomatic testing. However, before doing so, you should weigh the risks and benefits of submitting a claim. Unfortunately, genetic discrimination does exist. Though unusual, it is possible for an insurance company to deny health coverage or to cancel an existing policy should a person be found to carry the HD gene. A positive test result may also be considered a "pre-existing condition" which could make it difficult to obtain future health insurance coverage. In a number of states, laws do exist which prohibit genetic discrimination by insurers, and a similar federal law is being considered.

Many people choose to wait until they have the results of their genetic test before seeking reimbursement from their insurance company. They then do so only if they do not have the gene.

Are the results of the test always accurate?

The accuracy of positive or negative test results is almost 100 percent provided that another family member is known to have the gene for HD. Test results cannot determine if a person will develop HD if the number of CAG repeats falls into the intermediate range. Also, positive test results cannot predict when the symptoms of HD will begin.

Are the test results confidential?

Test results should be kept confidential and should only be given to another person with your written permission. On an initial call to a testing center, you should ask how confidentiality is ensured.

If the test results cannot tell me when the disease will begin, how will I know when I am beginning to show symptoms?

HD can only be diagnosed by a neurologist. A neurological exam can determine if you have symptoms of HD.

Should I be tested for HD?

The decision to undergo genetic testing is an intensely personal one and one that cannot be taken lightly. Testing should never be mandated or forced upon an at-risk individual. There are many factors to consider and there are no "right" or "wrong" answers. Of course, everyone will have his/her own circumstances to take into consideration. The following are some of the issues to think about and/or to discuss with those who are closest to you:

Spouse

Will your relationship with your spouse or significant other change once your test result is known? Does he/she want you to take the test? How will a positive or negative result impact your future together?

Siblings

Relationships with siblings are sometimes strained by learning a test result. There is often guilt felt by siblings who do not carry the gene (although they had no control over which gene they inherited). Those who have the gene may express anger toward brothers and sisters who do not.

Children

Children often factor heavily in the testing decision. Many people undergo presymptomatic testing before planning a family. Others use the result to decide if they will have more children. Those who already have children worry about the impact of a positive test result. They may ask themselves questions such as: How will I tell the children that they may have inherited the gene from me? How will I explain to them that I will one day show the symptoms of HD? How will this affect their lives?

Parents may feel guilty for having had children knowing that HD was in their family (even if they were not aware of their own risk for inheriting the gene at the time they had children).

Parents

Your relationship with your parents may also be affected by the test result. Parents may feel guilty for passing on the gene. An unaffected parent may be upset by the thought of having to watch his/her child live with HD. A parent may also have mixed emotions in the event that one child tests negative for the HD gene while another tests positive or begins to show symptoms.

Freinds

Friends are among those to whom we turn for support. You may choose to tell a close friend (or friends) about your decision to be tested for HD. Should you choose to be tested, make certain that you share your decision only with people you trust will not discuss it with others.

Most people will have a strong emotional response (either immediate or sometime **in** the future) when they are told whether they do or do not carry the gene. However, most people adjust well to the results after some time has passed.

Where can I find help in making this decision?

There are different resources available to aid you in making your decision.

The HD testing centers are staffed by professionals with the knowledge and expertise to help you decide whether or not to take the test. If you want long-term counseling, an HDSA chapter social worker or the staff at the HD testing center may be able to provide you with a referral to a knowledgeable professional.

You may also consider joining a support group. There are HD support groups in virtually every state and some groups are specifically for those who are at risk. Your local HDSA chapter or the HDSA national office can help you locate a support group in your area.

It is often helpful to read how others arrived at their decisions. Two publications which discuss this are *Experiences of Predictive Testing for HD* (a collection of personal accounts - available from HDSA as part of the Testing Packet) and *Mapping Fate: A Memoir of Family, Risk, and Genetic Research* by Alice Wexler (published in 1995 by Random House).

Another helpful resource is *Walking the Tightrope: Living at Risk for Huntington's Disease* by Randi Jones, Ph.D. This book provides professional insights and practical guidance for people at risk for HD.

Is there a "right" time to be tested?

Although all of us face stresses in our daily lives, one should not undergo testing at the time of a particularly stressful event (a death in the family, divorce, diagnosis of HD in a loved one, or some other traumatic experience).

Should children be tested?

Testing of children (those under 18 years of age) is strongly discouraged. If a child is exhibiting symptoms of HD, a neurologist who is familiar with HD should be consulted. Genetic testing may then be recommended as a confirmatory measure in some cases.

Given that each person should decide for him- or herself whether or not to be tested, minors should wait until they can arrive at this decision for themselves. Testing of children may also expose them to discrimination by health insurance companies, employers, and perhaps (consciously or unconsciously) by their parents.

Is prenatal testing available?

It is possible to determine if a fetus is carrying the gene for HD. The prenatal procedures currently available are amniocentesis and chorionic villus sampling (CVS). It is advisable for a couple to discuss prenatal testing options with a genetic counselor prior to becoming pregnant. If an at-risk partner wishes to be tested for the HD gene, it is recommended that the testing process be completed before conception.

If the parent who has a 50 percent risk for HD does not wish to undergo testing but the couple wants prenatal testing, then *nondisclosing* testing can be performed. Nondisclosing testing is performed by linkage analysis. Linkage analysis compares the chromosomes obtained from the blood samples of several family members to those of the fetus. In this way, the risk that the fetus is carrying the gene for HD can be estimated. A genetic counselor should be consulted well before conception since blood samples from family members must be obtained and analyzed in this type of testing.

What is confirmatory testing?

Confirmatory testing is used to "confirm" a neurologist's suspicion that a person has HD. It is a type of genetic testing which is often performed by a neurologist when a patient has symptoms which appear to be those generally associated with HD.

It is important to bear in mind that, even though a person may be aware that he or she has some of the symptoms associated with HD, hearing this suspicion confirmed can often have a significant psychological effect.

III. Resources and Research

How can I find out where testing centers are located?

The HDSA publishes a list of testing centers which is available free of charge.

Is any research being done to find treatments or a cure for HD?

The key to better treatments and an eventual cure is research. There have been many exciting breakthroughs in recent years, including finding the gene for HD in 1993. In 1995 huntingtin-associated protein (HAP 1), a protein which works along with huntingtin (the protein which is expressed by the HD gene), was discovered. Research is underway to determine how these proteins, and possibly others, are tied to the symptoms of HD.

An international coalition of scientists, known as the Huntington Study Group (HSG), was formed in 1993 to conduct clinical and basic scientific research in a coordinated, systematic fashion. HSG sites combine research facilities with teams of professionals who have expertise in treating HD. The Group has begun to test new drugs which could potentially lead to effective treatments for HD.

In 1997, the Huntington's Disease Society of America established the HDSA Coalition for the Cure, a consortium of 14 top laboratories in North America and Europe. Coalition investigators focus on four key areas of study: animal models, cell models, biochemistry and cell biology. Through HDSA funding, semi-annual meetings and the sharing of data and ideas, the Coalition is accelerating the pace of HD research.

While there is currently no cure for HD, treatments are available which can lessen the severity of some of the symptoms. A neurologist or psychiatrist who is knowledgeable about HD can prescribe appropriate medications, and physical, occupational and speech therapists should also be consulted in the early stages of HD to be optimally effective.

Where can I go for more information?

Additional publications about Huntington's Disease, genetic testing, and related issues may be obtained from the Huntington's Disease Society of America, 158 West 29th Street, 7th Floor,

New York, NY 10001-5300, (800) 345-HDSA or (212) 242-1968.

Visit HDSA web site: www.hdsa.org