

Genetic Testing



Huntington's Disease

Family Guide Series

Juvenile Onset HD

Family Guide Series

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HOW TO USE THIS GUIDE

This guide was created to help individuals and families understand the purpose and process of genetic testing for Huntington's Disease and, through this knowledge, to be better able to make a very personal, very significant choice.

In this booklet, we are sharing what we know about HD and what it may mean to discover that you or a loved one has the disease. Once you understand the issues involved, you can use the guide as a starting point for conversations with family and friends.

Whatever you may decide about genetic testing for HD after reading this guide, we want you to know that you are not alone in facing the challenges presented by HD. There is an informed, welcoming community of HD professionals and families that you can turn to for support.

Genetic testing for HD can affect an individual's quality of life in both positive and negative ways. Reading this guide is just the beginning of the decision-making process. We strongly encourage you to work with a genetic counselor or other HD professional while considering this option.

I. Huntington's Disease and the HD Gene

What is Huntington's Disease?

Huntington's Disease (HD) is a hereditary brain disorder which leads to both physical and mental disabilities that increase over time. 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 involuntary movements like twitching, but each person who has HD is affected differently and early symptoms vary from person to person.

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

If you have a parent with HD, you have a 50% chance, or one in two, of having inherited the gene that causes HD. Each child born to a person who has HD, regardless of gender, has the same chance of being born with the HD gene. Men and women are equally affected, so that either parent may pass on the HD gene to any offspring.

Will 50 percent of the children of a person develop the disease?

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 that causes the disease in order to one day develop this disorder.

What if neither of my parents have HD?

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 possible reasons for this. Perhaps the parent who had the gene for HD died at an early age, before the symptoms appeared. It may be that other family members had HD but were misdiagnosed as having Parkinson's disease or another disorder with HD-like characteristics. It is also possible that the parent carried the genetic mutation for HD in what is called the "indeterminant range of the CAG expansion for HD" (this is explained further on), in which case the parent did not develop the disease, but could still pass it on to the children. There may also be cases of questionable paternity.

If I was born with the 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.

The HD Gene

How do genes work?

A gene is the basic unit of inherited traits

passed to an individual from his or her parents. Genes are made up of long chains of DNA (deoxyribonucleic acid) which lie on chromosomes found in every cell of the body. Some of this DNA determines what the gene does in the body, and some of it determines when and how the gene becomes active. Knowing that you have a particular gene does not tell you when the gene may become active.

Tell me about the HD gene

What we call the "HD gene" is actually a variation in a gene that is found in every human being. In fact, each person has two copies of the gene. The variation that indicates HD is found at one end of the gene and involves what is called CAG repeats. A CAG repeats is a set of nucleotides (the building blocks of DNA) that is repeated over and over at the end of the gene. The three nucleotides in the repeat are Cytosine, Adenine, and Guanine (CAG). In people who have inherited the variation associated with HD, there are 40 or more CAG repeats. No one with 35 or fewer CAG repeats has been known to develop HD symptoms. In between is the "indeterminant" range of 36-39 CAG repeats, where the individual may or may not develop the symptoms of HD within a normal life-span*. If either one of an individual's two copies of this gene has a long enough CAG repeat, they will develop the disease.

Can the number of CAG repeats change over time?

The number of CAG repeats does not change throughout an individual's life.

* Information provided by Martha Nance, M.D., HD Genetic Testing Group

II. Genetic Testing

What is Genetic Testing?

Genetic testing is a biochemical way of determining the presence of a particular gene in an individual. A blood test is 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 four categories of testing for the HD gene:

1. Presymptomatic testing, for people at risk for HD but showing no symptoms, is the type of testing which will be discussed in greatest detail in this booklet.
2. Confirmatory testing determines whether a person showing possible HD symptoms actually has 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).
4. Prenatal Genetic Diagnosis (utilizing in vitro fertilization).

What is involved in getting tested?

Ideally, the testing process involves several sessions with various professionals, both before and after testing, depending on the needs of

the individual and the staff composition at the facility. These sessions typically include genetic counseling, discussion of the results, and follow-up. The genetic test itself is a blood test.

The purpose of genetic counseling 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 interview will usually reveal whether symptoms are present; if so, a neurological exam will be scheduled. If the person is found to have the HD gene, but is not symptomatic at the time of the interview, a neurological exam is suggested within about 6 months. This will determine if any early symptoms of HD are present and will establish a baseline for future assessments and treatments.

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 may 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.

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, it is helpful if the at risk person has either genetic testing results from an affected family member or family history that suggests a clear pattern typical of HD, supported by medical records if

they are available. 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.

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 \$315 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. Several laws are in place to help people against this type of discrimination. Most states have laws in effect to prohibit medical insurance from using genetic test results to determine coverage, premiums, or cancellation. Most states also have laws in effect to prohibit employers from requiring genetic testing or using genetic testing results to determine compensation, employment, or promotion. In the spring of 2008, a Federal law, GINA, was passed with the same protections against medical insurance and employment discrimination as those listed above. The law regarding medical insurance and the law regarding employment go into effect in 2009. This law does not address the possibility of discrimination based on genetic test results for life insurance, long term care insurance, or disability insurance. Therefore, there may

still be reasons to do as others have done in the past and wait until the results are received before seeking reimbursement from the insurance company. In the past, people typically did this only if the result was negative. It is suggested that all decisions regarding insurance, be made by the at risk individual prior to beginning the testing process.

Are the results of the test always accurate?

The accuracy of positive or negative results is almost 100 percent. To make sure the correct gene is being tested, documentation of an HD diagnosis or a positive test result in the family is required. 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 exactly 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.

How will I know if 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.

Presymptomatic Testing

Tell me about presymptomatic testing for HD

The genetic test for the HD gene is performed on a blood sample. While the actual procedure is simple, the decision to have the test is not.

The Huntington's Disease Society of America recommends that persons who wish to undergo presymptomatic testing for HD do so at one of our Centers of Excellence, or at a testing center with specific training in working with HD. A list of these testing centers is available from HDSA on our website or by phone.

Confirmatory Testing

What is confirmatory testing?

Confirmatory testing is used to verify a neurologist's suspicion that a person has HD. It is often performed when an individual has symptoms which appear to be those generally associated with HD. Although a neurologist or other physician may believe a confirmatory test is in order, the individual and his or her family are the ones who must make the decision, with a full understanding of what the results may mean.

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.

Testing in Children and Pre-Natal Testing

Should children be tested?

Testing of children (those under 18 years of age) is strongly discouraged. 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 insurance companies, employers, and perhaps (consciously or unconsciously) by their parents. Since there are no treatments that delay or halt the progression, there is little practical reason for children to be tested. This may change as new treatments are developed.

If a child is exhibiting symptoms of juvenile HD, a neurologist who is familiar with HD should be consulted first. HDSA Centers of Excellence have neurologists who are extremely knowledgeable about HD. After the child's symptoms are evaluated and the parents consulted, only then should genetic testing be considered as a confirmatory measure.

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.

Can I conceive children in a way to know their HD status?

Couples who are concerned about passing the HD gene onto their children, and would like to decrease that chance, should consult a genetic counselor to discuss *In Vitro Fertilization with Prenatal Genetic Diagnosis*. IVF with PGD is a way to test embryos for the HD gene before implantation to create a pregnancy with an embryo that is free of the HD gene.

The Decision to Test

Should I be tested for HD?

The decision to undergo genetic testing is an intensely personal one that cannot be taken lightly. Testing should never be forced on an at-risk individual. There are no "right" or "wrong" answers. Each individual will have to take his/her own circumstances into consideration before making the decision.

Typically, 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 that will cause HD. This is why we recommend that the genetic testing process include follow up counseling, as is done at HDSA Centers of Excellence and other centers that follow HDSA guidelines.

Persons whose test is negative are often puzzled at their conflicting emotional responses to their news. Overall, we have found that most people adjust well to the results, positive or negative, after some time has passed.

Why wouldn't I want to be tested?

Quite a number of individuals at risk for HD ultimately choose not to be tested for the gene. Their reasons for this decision are often based on the fact that the test cannot predict the age of onset, fears of possible discrimination in the workplace or community, and currently, there are no effective treatments or a cure for the disease.

Things to Consider

The following are some of the issues to think about and/or 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.

Friends

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.

Is There a "Right" Time to be Tested?

Although all of us face stresses in our daily lives, it is recommended that one 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) or during a pregnancy, unless the at risk person is considering terminating the pregnancy.

Should I Get Tested With My Siblings?

While siblings often decide together to pursue genetic testing, separate appointments are required so that each at risk person's situation can be independently considered.

Getting Help With the Decision

How do I decide?

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

HDSA Centers of Excellence 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.

Support during the testing process

It is strongly encouraged that you bring a support person with you to all testing sessions. The partner should be a spouse, companion or a close friend. The partner will be able to provide moral support during appointments, when awaiting test results, upon receiving the results, and thereafter. It is not advisable to bring a sibling or another person who is at risk for HD, so that the support person can focus fully on the needs of the person being tested.

III. Resources

Choosing a Testing Center

We believe that the genetic testing process is far more than a blood test. HDSA recommends that individuals considering genetic testing should do so through an HDSA Center of Excellence or a genetic testing center which follows HDSA genetic testing guidelines.

HDSA Centers of Excellence

The HDSA Center of Excellence program serves as the cornerstone of HDSA's commitment to care. These 21 facilities provide a vast array of medical and social services to HD families in addition to genetic testing and work in collaboration with HDSA chapters, affiliates, regions and support groups to form a seamless national network of resources and referrals for those affected by HD and their families.

To find a Center of Excellence, call 800-345-HDSA or visit www.hdsa.org, click on "Living With Huntington's Disease", then click on "Family Care", then click on "Centers of Excellence".

Other HD testing centers

HDSA also publishes a list of testing centers that follow the HDSA genetic testing guidelines.

The list is available free of charge by calling 800-345-HDSA. It can also be found on the national web site by visiting www.hdsa.org, clicking on "Living With Huntington's Disease", then clicking on "Family Care", then clicking on "Genetic Testing Centers".

Where Can I go for Information and Support?

Huntington Disease Society of America

HDSA is a national non-profit voluntary health agency dedicated to finding a cure for Huntington's Disease. We provide vital support, information and educational services to improve the lives of those affected by HD, offer resources and guidance for HD families through our national network of volunteer-based chapters and affiliates, as well as through our HDSA Centers of Excellence for Family Services. HDSA, through its support for the Coalition for the Cure and other researchers, also promotes and directs significant research to find treatments and, ultimately, a cure for HD.

Publications

HDSA publishes and distributes a wide variety of informational materials including *The Marker* magazine, *Toward a Cure* newsletter, and books, booklets, brochures and videotapes covering care, treatment, research, and related topics. These publications are available for download from the national website by visiting www.hdsa.org, clicking on "Living With Huntington's Disease", then clicking on "Family Care", then clicking on "Publications".

HDSA Chapters and Affiliates

With over 38 chapters and affiliates throughout the country, the Huntington's Disease Society of America (HDSA) is often the first place people go for information or assistance in coping with the effects of HD. HDSA chapters and affiliates can provide information about local resources, including knowledgeable physicians and other health-care professionals, genetic testing centers, support groups and long-term care facilities. In most cases, a chapter social worker is available for information and support.

To find a chapter or affiliate, please contact HDSA at 800-345-HDSA or visit www.hdsa.org, click on "About Huntington's Disease Society of America", then click on "Find Your Local HDSA Chapter, Affiliate or Regional Office".

IV. Research

What is Being Done to Find Treatments or a Cure for HD?

Research is the key to finding treatments and a cure for HD. HDSA, through its support for the HDSA Coalition for the Cure and other researchers, promotes significant research to find treatments and, ultimately, a cure for HD. There have been many exciting breakthroughs in our basic understanding of the disease since the identification of the gene that causes HD in 1993.

HDSA maintains an ultimate goal of developing treatments effective in preventing or delaying the onset and progression of the disorder. In order to expedite the movement of basic research into effective treatments, HDSA has developed a "pipeline" of drug discovery that takes a systematic, comprehensive approach to maximizing the opportunities to achieve our goal – an effective treatment for HD. In 2008, tetrabenazine (Xenazine) was approved by the FDA as the first drug for HD specifically designated to treat the chorea associated with the disease.

How Can I Help?

For more information about how you can help or to find out more about HDSA, please contact the Huntington's Disease Society of America
505 Eighth Avenue, New York, N.Y. 10018
National website - www.hdsa.org
Call: (800) 345-HDSA
Email: hdsainfo@hdsa.org.

We look forward to hearing from you.

The Huntington's Disease Society of America (HDSA) is dedicated to:

- promoting and supporting research to find a cure for HD
- helping people and families affected by the disease, and
- educating the public and healthcare professionals about HD

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