

Presymptomatic Testing for Huntington's Disease: The Role Of Genetic Counseling

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Genetic counseling is a crucial component of presymptomatic testing for Huntington's disease (HD). It includes a discussion of the clinical aspects of HD, the molecular genetics and inheritance of HD, motivations for testing, possible ramifications of testing as well as assessment of an individual's support system and psychological health. The role of genetic counseling in presymptomatic testing for HD is well recognized. In 1994, The Huntington's Disease Society of America guidelines recommended pretest genetic counseling, psychological screening, and neurological evaluation.¹ Subsequently, many laboratories began to require counseling prior to presymptomatic testing. In our center counseling involves four separate visits, the third of which is a full neurological evaluation. This allows an individual time to assimilate information and make a thoughtful decision regarding testing. This article will review the process of genetic counseling for presymptomatic HD testing.

CLINICAL ASPECTS

Genetic counseling begins with a review of the clinical aspects of HD, a degenerative neurological disorder which includes motor, cognitive, and emotional disturbances. Motor abnormalities include both involuntary and abnormal voluntary movements. Progression of motor abnormalities results in severe rigidity and joint contractures. Cognitive losses are progressive and typically begin with a decrease in cognitive speed and flexibility as well as impaired concentration. Psychiatric disturbances in HD are common. Typical symptoms include depression, irritability and apathy.² Although some families are knowledgeable about the symptoms, others are less so. This may be due to a lack of involvement with

affected family members, attributing symptoms to individual personalities, or a negative family history of HD. Individuals contemplating presymptomatic genetic testing should understand the symptoms and progression of HD, so that they can determine how this disease may impact their lifestyles, goals and relationships.

At this time no cure exists, although symptomatic treatment is available. Both high potency neuroleptics and Dopamine depleting agents have been used to reduce chorea.² The psychiatric symptoms associated with HD have been treated with tricyclic antidepressants, selective serotonin reuptake inhibitors and monoamine oxidase inhibitors.² Unfortunately, no treatment has been proven to reduce cognitive abnormalities.² Prior to presymptomatic testing, individuals should understand that symptomatic treatment exists, but none of these treatments ameliorate the disease.

INHERITANCE

During genetic counseling, it is explained that HD is inherited in an autosomal dominant fashion; that is, each offspring of an affected individual is at 50% risk for the condition. For counseling purposes, the risk reduces with age when an individual is asymptomatic. Therefore, a 25 year old and a 55 year old, both with an affected parent, have an age adjusted risk of 49% and 25% respectively.⁷ Individuals undergoing presymptomatic testing for HD must understand their risk for the condition. Additionally, if they are affected, it is possible that their age at onset will be earlier than in their parents.

MOLECULAR GENETICS

A discussion of the molecular genetics of HD is also crucial. The gene

Abbreviations Used:	
HD	Huntington's Disease
PCR	polymerase chain reaction

associated with HD, IT15, was identified in 1993.³ Individuals with HD have an expanded CAG trinucleotide repeat in one copy of the IT15 gene, usually greater than 39 CAG repeats.⁴ Normal individuals have less than 27 CAG repeats in each copy of their IT15 gene.⁴ It is important for individuals to understand that an intermediate range of CAG repeats may or may not result in HD for the individual, although it is possible for future generations to inherit an expanded CAG repeat associated with HD.⁴ This is due to meiotic instability which results in an expansion of CAG repeats from one generation to the next.

In HD, a CAG trinucleotide repeat of greater than 26 has been associated with meiotic instability.⁴ An expansion is more likely to occur when paternally inherited.⁵ The CAG repeat size is loosely associated with age at onset where the larger size repeat is associated with a younger age at onset.⁶ This association can not be used to predict age at onset for specific individuals, since individuals can have the same CAG repeat size but have different ages of onset.⁶

THE DNA TEST

The next topic for counseling is the molecular testing. The direct gene test uses polymerase chain reaction (PCR) to determine the CAG repeat length in each copy of the IT15 gene.⁴ This test is highly accurate. Direct gene testing can determine whether an individual has a CAG repeat length in the HD range, in the indeterminate range, or in the normal range. If a

CAG repeat length in the HD range is identified, that individual will develop HD during his/her lifetime. As mentioned, genetic testing cannot predict age at onset, severity of symptoms or disease progression. The children of an individual with a CAG repeat length in the HD range are at 50% risk for the condition. If a CAG repeat length in the indeterminate range is identified, then the exact risk to develop HD may be unknown. The children or grandchildren of an individual with a CAG repeat length in the indeterminate range may be at risk for HD due to an expansion of the repeat. If the CAG repeat length in both copies of the IT15 gene is normal, the individual and his/her children are not at risk for HD. A review of possible results is crucial to ensure that each individual understands the implications of each result as well as the possibility of an indeterminate result.

MOTIVATIONS FOR TESTING

The counselor should explore the individual's motivations for testing.

Presymptomatic testing for HD has a profound effect on the individuals tested. It is crucial that they receive genetic counseling and support services from professionals knowledgeable about both the genetic test itself and the ramifications of testing.



Individuals who seek presymptomatic testing for HD fall into one of four general categories: young adults, older at risk parents, newly at risk individuals and clinically affected individuals.⁸ Young adults often use testing information to make life decisions. Older at risk parents may not want to know

their status, but consider testing to clarify the risk of their adult children. Newly at risk individuals have not been previously aware of their at risk status. Therefore they often pursue testing to reassess their plans for the future. Some individuals have not yet realized they are clinically affected and present for presymptomatic testing. These individuals may have an idea that they are affected and may be looking for confirmation while others are surprised. Identifying an individual's motivations for testing allows the genetic counselor to determine whether those motivations are based on accurate information and expectations. In addition, the genetic counselor is able to assess and discuss the potential impact of testing.

IMPACT OF DETERMINING HD STATUS

Prior to testing, genetic counselors discuss the effect of test results on life decision making. Since many individuals pursue testing in order to use the results for future planning, it fol-



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lows that testing has a potentially enormous impact. Individuals may choose not to have a family because they are concerned about the risk for HD in children and/or they are concerned about how HD will affect their parenting abilities. Additionally, they may alter their financial and educational decisions. This discussion should help the individual realize how positive or negative test results will impact his/her decisions.

Since presymptomatic testing can have significant psychological ramifications,^{9,10} the counselor should discuss possible ramifications prior to testing. Often an individual has already decided whether they will develop HD. A test which reveals an unexpected result may cause psychological distress. In addition, some individuals who test positive become extremely anxious and hypervigilant for symptoms.⁸ Individuals have attempted suicide after learning their HD status. This discussion allows the individual to assess the possible psychological ramifications of testing. In addition, it allows the genetic counselor to explore with an individual the possible effects of determining their status as well as the risk for adverse psychological events including suicide.

Since determining the HD status of an individual can affect relationships with family members and friends,^{11,12} a discussion of how relationships may be affected is warranted. Individuals who test positive may be concerned about their spouse's response to the result. Parents may feel guilty when their adult child tests positive, even though they had no control over the outcome. When one sibling tests negative, s/he may feel guilty for escaping HD, while the sibling who tested positive did not. Relationships with friends can change as well. Friends may feel as though they do not know what to say or how to be supportive. Some friendships may be strengthened while others are lost. At the end of this discussion, an individual should understand the impact testing has on relationships. In addition, a plan to deal with possible effects can be constructed.

Genetic counseling must include a discussion about the possibility of discrimination by insurance companies and employers. Health care providers and patients have been concerned about the potential for denial, cancellation or re-

fusal to renew insurance policies based on genetic test results. In addition, concerns have been raised about varying premiums or conditions based on genetic information. The true risk for this discrimination is unknown, but most individuals who opt for testing pay for services out-of-pocket to reduce this risk. In addition, concerns have been raised about the risk for job loss related to genetic information. Again, the true risk is unknown at this time, but individuals should understand the potential risk prior to determining their HD status.

Despite preparation and careful decision making, the initial impact of a test result can be overwhelming. Some individuals may feel as though they are in a state of shock. It is the role of the genetic counselor to discuss possible reactions to test results as well as ways to deal with this initial reaction. At the time of disclosure, genetic counselors must determine whether an immediate mental health counseling referral is appropriate. Many individuals do not require referral although follow-up with a genetic counselor and/or a mental health counselor is recommended.

CONCLUSIONS

Presymptomatic testing for HD has a profound effect on the individuals tested. It is crucial that they receive genetic counseling and support services from professionals knowledgeable about both the genetic test itself and the ramifications of testing. Presymptomatic testing is known to impact specific areas of an individual's life. Therefore a detailed discussion of these issues should be undertaken prior to testing. As our ability to perform new genetic tests has grown, we have seen that testing can bring both substantial benefits and concerns. The examination of these possible effects allows individuals to determine whether they will truly benefit from testing.

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