

## **“HD” Testing Procedures and the ethical dilemma of “To Test or Not to Test”?**

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### **Introduction**

Huntington’s disease (HD) is an inherited, degenerative brain disease. Huntington’s disease affects both the mind and body. Symptoms generally appear between the ages of 30 and 50 years of age, but have appeared as young as 2 and as old as 70. Each person of a Huntington’s disease affected parent has a 50% chance of inheriting the disorder and is said to be “At Risk”. Huntington’s disease usually progresses over a 10-25 year period. HD causes personality changes, depression and mood swings. HD causes unsteady gait, involuntary movements or chorea, slurred speech, impaired judgment, difficulty swallowing and intoxicated appearance. Approximately 30,000 Americans have Huntington’s disease and approximately 150,000 are at risk of inheriting Huntington’s disease. Huntington’s disease affects all races, ethnic groups and sexes equally. Huntington’s disease does not skip generations; if you do not get HD then you cannot pass it on. If you carry the gene, you will develop the disease if you live long enough, and you can pass it on. (Huntington's Disease Society of America, 2007)

One of the purposes of this research project is to determine if “At Risk” family members of a person with Huntington’s disease are willing or not to obtain information for testing or to participate with drug trials for the treatment of Huntington’s disease prior to the onset of the disease.

There are Huntington’s disease Centers of Excellence in every state in the United States. Each Center of Excellence has Predict HD programs. The Predict HD program is a test group of pre-systematic persons that are “At Risk” of getting HD. One of their parents has been positively diagnosed with HD. The persons in the Predict HD control group attend a center of excellence annually during the same month to be tested for cognitive and gross motor testing. This way there can be a comparative study conducted to determine if there are gross motor or cognitive changes from one year to the next.

This study is going one step further beyond the Predict HD control sample. There has been a control sample of “At Risk” families from a group of selected families within the same geographic region of United States. The ethical dilemma of this research is if the “At Risk” patients want to know if they are positive for HD or not. The researcher conducted personal interview of a case study of persons that are “At Risk” of obtaining the onset of Huntington’s disease.

### **Background of Huntington’s disease**

Huntington disease (HD) is a genetic disorder of the central nervous system with symptoms usually appearing in adults within the third or fourth decade of life, although symptoms can

occur in individuals younger or older than this. Within the same family, the symptoms vary both in their rate of progression and in the age of onset. Symptoms may include involuntary movements and loss of motor control. In addition, personality changes may occur with loss of memory and decreased mental capacity. Symptoms in individuals, as well as confirmation of diagnosis in other family members, are used to determine the diagnosis. Huntington's disease is inherited as an autosomal dominant condition.

The human body contains 100 trillion cells. A nucleus is inside each human cell (except red blood cells). Each nucleus contains 46 chromosomes arranged in 23 pairs. One chromosome of every pair is from each parent. Each chromosome is filled from each tightly coiled strands of DNA. Genes are segments of DNA that contain instructions to make proteins and other building blocks of life.

Each of us has 46 chromosomes which come in pairs; one member of the pair comes from each parent. Therefore, 23 chromosomes are from the mother, and 23 chromosomes are from the father. There are two types of chromosomes: 1) autosomal chromosomes, which are the first 22 pairs, and 2) sex chromosomes that are the 23rd pair (the 23rd pair in females consists of two X-chromosomes, and the 23rd pair in males consists of an X-chromosome and a Y-chromosome). Since Huntington's disease is autosomal dominant, this means the gene involved is on an autosomal chromosome (not one of the sex chromosomes) and recently has been localized on the fourth autosomal chromosome pair (the #4 chromosome). In affected individuals, one gene of this gene pair (the HD gene) is not functioning correctly and expresses itself more strongly, or 'dominates' the other working gene. Since it is not on one of the sex chromosomes, it can affect both males and females. Males and females have the same chance of having affected children.

An affected parent passes either the HD gene, or the other working gene, to his or her offspring. There is a 50% (1 in 2) chance at each pregnancy that a child of an affected parent will receive the gene for Huntington disease. The age of onset, degree and type of clinical symptoms, as well as rate of progression varies with HD.

During a clinic visit with a neurologist or geneticist, it may or may not be possible to clinically determine whether an individual has the HD gene. With increased age and without symptoms, the likelihood of having the gene without evidence of disease decreases, and the risk becomes less than 50%. Therefore, the risk for passing the gene to children decreases. However, if symptoms begin and a diagnosis is made, each child of an affected parent has a 50% chance of having the Huntington's disease gene. Information about the genetics of HD should be shared with children prior to their family planning so that they can receive the most current information.

The gene for Huntington's disease on the fourth chromosome has been characterized in recent years. The chromosome is composed of genes, and each gene is composed of a string of molecules called nucleotides. The nucleotides are adenine (A), cytosine (C), guanine (G), and thymine (T). The gene is made up of a series of three nucleotides which form the structure of

DNA in the gene. Each gene has its own unique sequence of base pairs. In Huntington's disease, the DNA sequence, CAG (cytosine-adenine-guanine), is part of this sequence. This sequence may be duplicated many times in individuals, up to 26 times in the general population. The duplication of this segment is called a "trinucleotide repeat" in which these three nucleotides (CAG pattern) are repeated over and over. Individuals with Huntington's disease may have from 40 to over 100 repeated CAG segments. Specific laboratory and clinic evaluations are needed to interpret other repeat levels, which may be referred to as indeterminate, intermediate, non-penetrant, or reduced penetrance, with meiotic instability. It is not known how this repeated sequence causes Huntington's disease, but research to develop therapies to treat Huntington's disease is ongoing. (Debra Collins, 2007)

### **The Cause of Huntington's disease**

Huntington's disease is inherited as an autosomal dominant disorder with complete penetrance resulting from a mutation on chromosome 4. The nature of the mutation is an expansion of CAG repeats at the end of the gene. Although the nature of the gene product (the protein huntintin) is not fully understood, it is known to be expressed ubiquitously and needed for normal cell survival. The expansion of the CAG repeats causes a region of polyglutamine on the huntintin protein that enhances the function of a cysteine protease called apopain. Since this protease is known to play a role in apoptosis (a type of programmed cell death), it is thought that the huntintin mutation leads to inappropriate apoptosis and destruction of cells. Why this cell destruction is differentially targeted to the basal ganglia and cerebral cortex is not understood. (*Neurosciences Journal*, 1998)

### **Huntington's disease Testing Procedures**

The importance of the testing procedures cannot be emphasized enough. The Huntington's Disease Society of American has developed a very clear and concise procedure for testing for "At Risk" persons and Huntington's disease. The rationale for such strict procedures is due to the fact that the incidence of "Suicide" is very high for people that obtain a positive test for having a 40 CAG repeat or higher, which shows that a person will have onset of Huntington's Disease during some stage of their lives.

The procedure will begin with a Pre and Post test counseling will be incorporated in any pre-symptomatic testing program. While the HD gene discovery alters some aspects of the test, the personal, family and ethical issues remain unchanged and the importance of counseling is therefore not diminished. The decision to take the pre-symptomatic test should always be an informed, carefully considered and freely chosen personal decision. Under no circumstances should an individual be coerced into testing. The testing program should include the following components: (1) Initial telephone contact/pre-screening interview (2) Three pre test, in-person sessions for genetic counseling, neurological evaluation and psychological evaluation (suicide prevalent) (3) Blood drawn is sent to a HD Center of Excellence for testing (4) Fourth session for disclosure of results.

The participant should be accompanied to all testing sessions by a companion (spouse, close friend, not a sibling). Excluding prenatal non-disclosing testing of exceptional circumstances, there should be at least one month's interval between the pre test sessions and the final decision to take the test. Minors should not be tested unless there is a medically compelling reason to do so. Test results should not be divulged to anyone other than the participant without his/her consent. Test results should be given in person; results should never be given over the telephone or by mail. Confirmatory testing may be offered to an individual with clear symptoms of HD and a documented family history.

A clinical neurological examination remains the definitive means of diagnosis. Individuals or couples considering prenatal testing should seek genetic counseling prior to conception. Laboratories are not to accept anonymous DNA samples for testing. The time line for testing will vary from individual to individual; some individuals may need more visits to complete the testing process. It is estimated that the entire testing process may take from 3-4 months, but the time frame may vary from person to person.

### **Ethical Dilemma of “To Test or Not to Test” Case Study**

There were two different families from the upper Midwest district of the Huntington’s Disease Center of Excellence that were contacted and interviewed. They were posed the question of the “Pro’s and Con’s of being tested.” Over 300 family members were at risk due to the size of the families. There were 100 of the different family members interviewed and posed the questions: (1) Why get tested for HD? (2) Why Not to be tested for HD?

### **Case Study Research Outcomes**

From the research interviews, the researchers obtained data on being tested for Huntington disease or not to be tested. There were several areas of discussion ranging from whether or not to be tested. Based upon the outcomes, there were  $n=53$  participants that were willing to be tested and 41 who were not willing to be tested. There were  $n=6$  participants who were undecided. The next area of interest was posed from the participants that responded that they were willing to be tested. These participants were willing to find out to properly prepare themselves for possible financial situations that could arise.

The participants responded that some of their financial reasons were based upon having a proper savings set aside 30%, having disability insurance in place 6%, obtainment of long term health insurance 57% and making decisions on career motives 32%.

Participants who responded that they were willing to be tested based upon curiosity were  $n=41$  (77%) and  $n=13$  (23%) for other reasons. Participants who also responded to be tested based on fertility reasons were  $n=23$  (43%) and those not concerned with fertility reasons  $n=30$  (57%).

Participants who responded for future health reasons that a positive result would change their lifestyle  $n=30$  (68%); would force the participants to change their diet  $n=7$  (16%); would participate in drug trials  $n=8$  (18%).

There was an extensive dialogue on the fact that several participants would change their career paths and would be making decisions on whether to obtain higher education degrees. The results from changing their career paths were  $n=37$  (70%) and  $n=16$  (30%) would not make any changes based upon a positive HD test result.

The centers of excellence have extensive collaborations and partnerships with several drug trials and Huntington's disease research opportunities. Based upon the findings from the research interviews it was found that  $n=40$  (75%) would become an advocate for Huntington's disease research trials. It was found that  $n=13$  (25%) would not become an advocate for Huntington's disease research and would rather be anonymous in advocating for the disease.

Huntington's disease has a very high prevalence for suicide; therefore, pre-testing procedures require a level of pre and post test counseling based upon the outcomes. The participants responded that  $n=14$  (34%) would require extensive post test counseling so they would not be at a high risk of suicide. There were  $n=27$  (66%) that felt they were not at risk of suicide based upon a positive HD test result.

One of the symptoms of Huntington's disease is the onset of depression as one of the pre-symptomatic symptoms. Even though a positive HD result may not have onset until later in life, there was a concern with the effects of depression on the participants with a positive test result. The participants responded that a positive result would create sadness and possible symptoms  $n=38$  (93%). There were  $n=3$  (7%) that the participants would not have sadness or depressive symptoms due to a positive test result.

Other variables of esteem and insecurities were discussed within the interviews with the participants. It was found that for  $n=31$  (76%) a positive test result would increase insecurities within life paths and esteem. There were  $n=10$  (24%) that felt that a positive test result could not change their life esteem, security, and confidence to live life the same as they would have before their HD positive test result.

Sometimes in life, "Ignorance is Bliss;" some people would rather not know if they have a pre-symptomatic condition. Based upon this concept,  $n=27$  (66%) felt that they would not want to know the results based upon the fact that it could change specific aspects of their lives. It was found that for  $n=14$  (34%) knowing the positive test results would not change the pattern of their lives.

Since Huntington's disease is based upon a 50/50 chance of having the gene passed down from generation to generation, there are specific variables of conditions of whether or not to be tested. It could be a situation in which a distant cousin was found positive, and you could be curious. But if a sibling was found positive, there was discussion of whether it would change

the outlook on getting tested or not. Based upon these circumstances, it was found that  $n=71$  (71%) would get tested if a sibling received a positive test result. There were  $n=20$  (20%) that felt they still would not get tested for Huntington's disease. There were  $n=9$  (9%) that were undecided and felt that it would be a situational decision based upon the decision of their immediate family members.

### **Implications from outcomes of research**

Having this data allows our research team the opportunity to analyze data to strategically place resources in the needed areas. It will also allow us to provide resources and provide family support and needed networks for providing family support. The data will provide the important information for properly educating family and spouses on Huntington's disease. There is also an incredible need for further study. There will be additional studies to follow up on the addition of sources for the respondents that were willing to seek opportunities for drug trials and to participate in the centers of excellence "Predict HD" research group. With the addition of data and information, we can help provide the proper support systems for families to help families in need to help them care for their loved ones in a very positive environment. Eventually we can work toward a cure for this terrible disease.

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### **Biographical Sketch**

Dr. Patrick Wempe is an Assistant Professor in the Health, Physical Education, Recreation & Athletic Training (HPER/AT) Dept. Dr. Wempe has been teaching at Henderson State since the fall of 2005. Dr. Wempe received his undergraduate degree in Recreation/Recreation Therapy from the University of South Dakota. Dr. Wempe worked professionally within the Veterans Administration system as a recreational therapist. Dr. Wempe received his Master's Degree in Exercise Physiology/ Cardiac Rehabilitation from the University of South Dakota. Dr. Wempe received his Ed. D in Adult and Higher Education from the University of South Dakota and specialized within student services and academic achievement. Dr. Wempe taught at the University of South Dakota for five years prior to coming to Henderson State. Dr. Wempe is married to Tricia Wempe (Assoc. Director of Student programs and Dir. of Student Recruitment at Ouachita Baptist University). The Wempes have two children; Angelmaa (6) is currently in the 1<sup>st</sup> grade at Perritt Elementary. Angelmaa is adopted from the country of Mongolia. The Wempe's second daughter's name is Gabriella; she is a participant of the Henderson State University Pre-School 4 year old program. The Wempes reside in Arkadelphia.