Huntington's Disease

The genetic disorder, Huntington's Disease is a fatal genetic disorder that has no cure, however there are many scientists who are working on gene therapy in attempts to eradicate this genetic disease.

Huntington's Disease or HD is a fatal genetic disorder that causes the progressive breakdown of nerve cells in the brain. The disease was, "first recognised as an inherited disorder in 1872 when a 22-year-old American doctor, George Huntington, wrote a paper called *On Chorea*." (Phillips) After its recognition as a genetic disorder, scientists began to do research on the symptoms and effects of the disease. One of the first effects was the degeneration of brain cells. This degeneration deteriorates a person's physical and mental abilities and overtime leads to an early death. The disease has a 1 in 2 chance of being passed to the child if the parent is diagnosed with the disease and therefore carries the faulty gene. The symptoms usually begin between the ages of 30 and 50, and it worsens over a 10 to 25 year span. People who are diagnosed never die due to the disease itself, but rather to diseases such as pneumonia, heart failure, or other complications due to their weak physical state. The disease eventually affects a person's ability to walk, talk, and perform normal body functions. Symptoms of the disease include, personality changes (such as mood swings and depression are common) in addition to forgetfulness and impaired judgment, an unsteady gait, and involuntary movements (chorea). Slurred speech, difficulty in swallowing and significant weight loss are also common symptoms of the disease in its early stages. The disease can be divided into three stages that can be identified by a doctor. The three stages consist of a beginning stage that begins with changes in

coordination, and some involuntary muscle movement, such as twitching and convulsions. These are often coupled with lapses in mental capabilities and mood swings. Depression and other mental disorders are common in the initial stages of the disease. As the disease progresses, the muscular degeneration becomes more intense and begins to create problems for the individual when performing simple tasks, such as walking and talking. Occupational and physical therapists can help to regain some control of voluntary movements and to deal with changes in thinking and reasoning. Speech will become increasingly labored and difficulty swallowing may occur. This may require help from a speech language pathologist. The final stage of the disease will result in the affected person becoming completely dependent on their support system and family for everyday tasks. They are at a heightened risk of choking as they are no longer able to regulate the muscles in the throat that control swallowing. They will retain awareness of their family and friends, however will no longer be able to verbally communicate. Throughout the progression of the disease, the affected person will experience significant weight loss due to a decrease in appetite and ability to swallow and chew. Those who suffer from the disease should be supported by family and friends, and they should be gently cared for as their mental health may also be affected, resulting in depression, and loss of will to continue living. The pain felt by those who suffer is incomprehensible, and medications, therapy, and love will help ease their pain and suffering, and will hopefully make them more comfortable. (Huntington's Disease Society of America)

There are no cures for this disease, however certain steps can be taken to ensure that the person afflicted can remain as comfortable as possible as the disease progresses over many years. Exercising early on in the disease can help control movement and ease pain felt by the afflicted

person. There are certain medications such as “the drug tetrabenazine, antipsychotic drugs, antidepressants, and tranquilizers.” (Cunha) These drugs are able to relax muscle tension, calm involuntary movements, and dull pain to help induce sleep. For the mental effects of the disease antidepressants, mood stabilizing drugs, and antipsychotics can be helpful for controlling mental disorders and mood swings that accompany neuron degeneration. (Mayo Clinic Staff) For those who do not wish to take medication there are certain methods of therapy, both physical and mental that can ease strain on both the mind and body. Mental therapy can involve psychotherapy, which consists of a psychiatrist, psychologist, or social worker that assists the afflicted person with behavioral problems, developing healthy coping strategies, providing communication, and establishing relationships and effective communication with family members. (Mayo Clinic Staff) Physical therapy can be used to effectively control muscle movement and tremors that plague many people with Huntington’s Disease. Physiotherapy “integrates both mental and physical exercises to aid patients in learning new strategies to accomplish tasks that become more challenging as the disease progresses.” (Liou) The activities focus on memory, concentration, and other mental skills as patients are taught different approaches to assist in completing daily tasks that may become difficult for them such as walking, speaking, eating, and personal hygiene. Therapists may also be able to determine whether it is safe for a patient to engage in certain activities such as driving and operating other machinery and they may also recommend changes in the patient's workplace in order to ease the complications associated with the disease. (Liou) Although there are no known cures, families with a history of the disease can opt to try and receive genetic testing to know whether they carry the gene. The idea of genetic testing sometimes faces scrutiny as, “many people see no benefit in

knowing that they will someday develop the disease. Others want an end to uncertainty so that they can make informed choices about the future." (Huntington's Disease Society of America) Genetic testing involves scientist that detect the presence or absence of the genetic sequence that causes Huntington's Disease. This all began in 1983, a team of scientists located the first genetic marker for Huntington's disease. This indicated the approximate location of the Huntingtin gene on chromosome 4. This was able to lead to the development of the first pre-symptomatic genetic test for Huntington's which traced the inheritance of markers linked to the Huntington gene. The test requires blood samples from family members, and is not always informative or an available option for families. (Liou) Families who choose to undergo genetic testing often do so to prevent offspring inheriting the gene and developing the disease.

Due to its incurable nature, many scientists are devoting their research to discovering a way to eradicate this genetic disorder. Scientists have discovered that "the huntingtin mutation is an unstable trinucleotide (CAG) repeat expansion in the ORF of exon 1 of the gene." Which leads to "the expression of an expanded polyglutamine repeat in the huntingtin protein." (Huntington's Disease Society of America) The excess protein causes neuron dysfunction and death, in the striatum and cortex of the brain which interrupts memory, movement, and other daily functions necessary for life. Scientists are studying the behavior of stem cells in people who suffer with Huntington's Disease "in order to explore the role mutant *HTT* plays in neural development and in producing disease phenotypes." (Liou) Scientists are exploring the role it plays in hopes to have a greater understanding of the way the huntingtin mutation affects the human body as a whole. While observing the stem cells, researchers came to the conclusion that the huntingtin mutation has great effect of gene expression and regulatory pathways that are

involved in critical neurological development. The model with stem cells indicates that early disruption of signaling pathways within cells is crucial for determining the changes in development with may help develop treatments for those who suffer with the disorder. (Liou) Scientists and researchers have been using linkage studies in which they look to identify certain genetic markers within a set of DNA similar to the Huntington Gene, although certain markers like eye color, or hair color were unhelpful, "other markers were a tremendous help in locating the Huntington gene, including markers in a region of the Huntington-bearing chromosome called the "non-coding region." The DNA in these regions does not code for proteins, but it still consists of a linear sequence of the chemical components called nucleotides. Using laboratory techniques, researchers found a few regions or "loci" of this DNA where family members with HD all had the very same nucleotide sequence." (Liou) These genetic markers help scientists to identify the specific genes affected and possible genetic therapy to replace affected genes and to someday eradicate the disease.

Huntington's disease is inherited in an autosomal dominant pattern, meaning one copy of the mutated gene is required to have the offspring inherit this disorder. Whenever it is inherited, the offspring only needs to have one parent that is a carrier of the mutated gene to be affected by this disorder. ("Huntington Disease - Genetics Home Reference")

> As the altered *HTT* gene is passed from one generation to the next, the size of the CAG trinucleotide repeat often increases in size. A larger number of repeats is usually associated with an earlier onset of signs and symptoms. This phenomenon is called anticipation. People with the adult-onset form of Huntington disease typically have 40 to 50 CAG repeats in the *HTT* gene, while people with the juvenile form of the disorder

> tend to have more than 60 CAG repeats. Individuals who have 27 to 35 CAG repeats in the *HTT* gene do not develop Huntington disease, but they are at risk of having children who will develop the disorder. As the gene is passed from parent to child, the size of the CAG trinucleotide repeat may lengthen into the range associated with Huntington disease (36 repeats or more). ("Huntington Disease - Genetics Home Reference")

Due to its nature as an autosomal dominant disorder, the chances of a carrier of the mutation producing offspring who will develop the disease is very high. However "approximately 30,000 Americans have Huntington's Disease." (Huntington's Disease Society of America) So while only 1 in 10,000 Americans suffer from the disease, it is still semi-rare, only affecting a small portion of Americans. (Nordqvist)

Huntington's Disease only affects a small portion of Americans directly, however it affects many more indirectly through family and friends who develop this disorder. While scientists continue to search for more genetic information on the huntingtin gene and how to correct or eliminate the mutation, there do not appear to be any major breakthroughs the standard route for treatment consists of medication, and different therapies to make the progression of the disease and its symptoms, easier to control.

Works Cited

Cunha, John P. "Huntington's Disease: Read About Treatment Options." *MedicineNet*. MedicineNet, 2016. Web. 19 Jan. 2017.

"Huntington Disease - Genetics Home Reference." *U.S. National Library of Medicine*. National Institutes of Health, June 2013. Web. 19 Jan. 2017.

Huntington's Disease Society of America. "What Is Huntington's Disease?" *Huntington's Disease Society of America*. N.p., 2017. Web. 14 Jan. 2017.

Liou, Stephanie. "Physical Therapy and Huntington's Disease Treatment and Management." *HOPES*. Huntington's Outreach Project For Education, 26 June 2010. Web. 19 Jan. 2017.

Mayo Clinic Staff. "Huntington's Disease Treatments and Drugs." *Mayo Clinic*. Mayo Foundation for Medical Education and Research, 24 July 2014. Web. 19 Jan. 2017.

Nordqvist, Christian. "Huntington's Disease: Causes, Symptoms and Treatments." *Medical News Today*. MediLexicon International, 29 Feb. 2016. Web. 19 Jan. 2017.

Phillips, Dennis H., Ph.D. "Huntington's New South Wales." *What Is The History Of Huntington's Disease (HD)? | Huntington's NSW*. Australian Huntington's Disease Association, 2001. Web. 15 Jan. 2017.

Works Consulted

Davies, S., and D. B. Ramsden. "Huntington's Disease." *Molecular Pathology* Dec. 2001: 409. *General OneFile*. Web. 14 Jan. 2017.

Wexler, Nancy S. "Venezuelan Kindreds Reveal That Genetic and Environmental Factors Modulate Huntington's Disease Age of Onset." *Proceedings of the National Academy of Sciences*. N.p., 31 Dec. 2003. Web. 14 Jan. 2017.