Huntington’s Disease

*Epidemiology*

Huntington’s Disease (HD) is a genetic disorder inherited in an autosomal dominant pattern1. If a parent has the HD gene, their child will have a 50% chance of having the disorder1,2. Unfortunately, because the age of onset is delayed until the adult years, the gene is often passed on to children before recognition of symptoms in the adult3. The HD gene exists on the short arm of chromosome four2,4. Genetic testing can be performed with 95% accuracy; however 100% accuracy is currently unavailable due to the use of genetic markers instead of the actual gene1,5. Researchers are still searching for the marker on the opposite side of the gene which would increase the testing accuracy to 99% as well as potentially create a better understood pathogenesis of the disorder, leading to possible prevention1. There is a high prevalence of HD in European countries. Four to eight people are affected for every 100,0004. Harper also notes that prevalence is high in India and central Asia4. Annual prevalence rates in America range from zero cases in Alaska, Idaho, and North Dakota to 4.09 cases per million people in South Dakota. Mortality rates are highest in the Northwest states and lowest in the South6. Prevalence is higher among Caucasians than African Americans6.

*Pathology and pathophysiology of disorder/condition*

HD is primarily characterized by cell death in the striatum, but other areas of the CNS such as the hypothalamus, brainstem, and cerebral cortex are also affected3. The gene mutation on the short arm of chromosome four consists of a repeat of the nucleotide sequence CAG over 36 times. In an individual without HD, this sequence would repeat between 11 to 34 times2. This lengthening of the gene creates the protein Huntington which damages nerve cells throughout the CNS2. Post-mortem studies show complete atrophy of the caudate nucleus and cerebral cortex. Severe neuronal loss and gliosis is noted in the caudate nucleus more than the putamen, though both are affected1. In severe cases of this disorder, individuals have lost up to 30% of their brain weight5. Associated pathology includes decreased number of neurotransmitters and enzymes as well as atypical receptor sites3. Barbeau found that individuals with HD were found to have decreased amounts of the neurotransmitter GABA and GAD in the striatum and globus pallidus7. The role of GABA is to modulate the amount of dopamine in the brain. Without GABA, dopamine is uncontrolled, therefore producing the choreic movements1. Levels of Choline acetyltransferase, met-enkephlin, and homovanillic acid are also decreased in most cases7. Some peptides that were decreased or missing were substance P and angiotensin-converting enzyme7. Studies show an increase in the amount of Somatostain and Neuropeptide Y in the striatum and globus pallidus in subjects with HD as compared to the control subjects1,5. Somatostain acts as a catalyst to dopamine, increasing its presence and effects1. Cross et al found a decrease in dopamine D-1 and D-2 receptors8.

Presentation of this disorder varies slightly for each person; however, there are two main forms: choreic and rigid3. Those expressing the choreic form of HD will present with abnormal involuntary movements and impaired intellect or dementia3. Weiner and Goetz describe these choreic movements as “short, rapid, continual, purposeless, and uncoordinated”1. Common physical demonstration includes facial grimacing and twisting and jerking of the core and extremities3. These individuals will commonly attempt to mask these involuntary movements by following the chorea with a purposeful movement or by chewing gum1. Those presenting with the less common, rigid form of HD, also known as the “Westphal variant”, demonstrate hypo-kinetic muscular rigidity as well as mental deterioration3,9. Their clinical picture is dominated by slowed movements, tremors, and a kyphotic posture3,9. This form of HD is commonly developed in the adolescent years9.

*Disease progression*

HD is a progressive disorder that continues to increase in severity as one ages. The age of onset varies and can be as early as age two, but is generally between the age of 35-421,2. Most individuals live their first three decades without any symptoms. Onset is commonly characterized by occasional irregular movements of the face and extremities such as facial grimacing or “piano playing” fingers1. There is commonly a mild change in personality and deterioration of intellect2. In the middle years of the disorder, motor impairments such as dysphagia, dysarthria, and gait abnormalities are more prominent. The individual is often experiencing both voluntary and involuntary movement dysfunctions. Involuntary choreic movements occur in 90% of patients diagnosed with HD and is exacerbated by stress, anxiety, and/or depression2. The voluntary motor impairments are often more debilitating. Some examples are occulomotor disturbances, delayed motor initiation, clumsiness, lack of motor coordination, disturbed fine motor control, and ataxic gait2. During the final stages of the disease, chorea fades and is replaced by slow, rigid movements and dystonia2. Communication is often limited due to impaired speech. Patients often require a percutaneous endoscopic gastronomy tube for feeding due to impaired swallowing. These individuals are nonambulatory and dependent upon others for all tasks. In the last days, weight loss occurs independent of calorie intake and sleep is difficult to achieve2.

There is a staging system for HD that categorizes patients according to their ability to participate in their vocation, financial responsibilities, social roles, and self-care activities3:

Stage 1: Patient is diagnosed with HD, but is not yet demonstrating any symptoms and is able to participate in all functions of life without difficulty.

Stage 2: Patient is still employed at their work place, but has been given decreased responsibilities. He or she is able to complete activities of daily living independently.

Stage 3: Patient is unemployed and needs assistance with managing household activities, but is able to complete some activities of self-care.

Stage 4: Patient is unemployed and no longer able to participate in any household activities or personal ADL’s. He or she can only complete activities with assistance from family members.

Stage 5: Patient is completely dependent upon others for daily living.

Lifespan after diagnosis ranges from 10-30 years1,2. When the disease progresses to the end days, patients typically pass away from heart disease or pneumonia due to debility, choking due to aspiration, or brain injury due to falls1,3. Reed and Chandler note that 7.8% of males and 6.4% of females with HD commit suicide10.

*Effects on systems*

Neuromuscular: HD has the largest effect on this system. HD affects both voluntary and involuntary movements, with effects from impaired voluntary control affecting individuals more than the effects of the involuntary movements. Some common presentations of the impaired control of voluntary movement are akinesia, bradykinesia, incoordination of movement, loss of small motor control, and impaired force modulation11.

Musculoskeletal: Cell death in the CNS can lead to decreased muscle innervation and therefore weakness. This occurs most commonly in the postural muscles of the trunk and upper back, the neck extensors, and the intrinsic muscles of the hands and feet11. Weakness in the neck extensors may lead to a forward head posture and rounded shoulders. Weak intrinsic muscles of the foot decrease one’s ability to find stability in standing, therefore reducing balance. Decreased strength also leads to decreased mobility which eventually leads to a generally decreased health status11.

Cardiopulmonary: It is not uncommon for patients to experience dyspnea either due to fatigue, respiratory muscle weakness, or the development of a sedentary lifestyle. Clearing secretions may be difficult due to muscle weakness and incoordination which often leads to pneumonia11.

Integumentary: In the later stages of HD, patient’s ability to control voluntary movements progressively decreases, therefore limiting their ability to relieve pressure. This increases one’s risk for development of skin breakdown in the form of pressure ulcers11.

*Activity, participation and quality of life*

Akinesia may be portrayed as a lack of interest or attention due to the delay of movement11. This can also slow initiation of a righting reaction in a startling situation or on uneven ground11. Because of this, falls are a common problem in individuals with HD. The lack of movement coordination affects one’s ability to walk, chew, and even breathe. They will often present with a wide based gait with flexed knees and kicking with each step. It is common to bump into objects while walking11. Fine motor control is impaired leading to difficulty using tools and utensils, typing, and grasping objects. These individuals often have difficulty with fine motor skills such as buttoning a shirt or using a remote control11,12. Hand-eye coordination is impaired, making driving or playing sports a difficult task. Decreased motor control impairs one’s ability to produce intelligent speech and may cause drooling, choking, and difficulty eating11. Lastly, force modulation is affected, causing normal movements to become large bursts of motion such as vaulting up from a chair instead of controlled standing11.

The cognitive effects of HD are a large hindrance to participation in social and vocational roles. These patients are often affected with decreased concentration, memory, and impaired multi-tasking11. Common cognitive presentations include short term memory loss, attentional disorders, difficulty with initiation and conclusion of an activity, perseveration, and signs of impulsivity11. These factors can easily affect one’s ability to perform their occupational duties, remain efficient during a schedule, manage finances, and maintain healthy relationships. Loss of short term memory affect’s one’s ability to remember scheduled appointments such as physical therapy, obligations, and household tasks such as turning off the oven or finishing the laundry. Behavioral changes occur frequently in this population as well including irritability, impulsiveness, and lack of attention1. These can affect one’s ability to make wise daily decisions without assistance and participate in healthy conversations with others1.

Quality of life is largely affected for patients with HD. Ho and colleagues found that there was a direct correlation between decreased functional capacity and increased depression with decreased health-related quality of life13. They demonstrated that motor function and cognitive changes were less predicative of changes in quality of life13. Helder et al performed a study that showed a positive correlation of the total motor score, mental state, and time since diagnosis with one’s score on the Sickness Impact Profile14. This shows that we can predict with fairly good confidence that the lower the score on the total motor score and mini mental state and the longer the duration of the disease, the less one’s overall well-being will be14. In general, most patients with HD have moderate to severe functional limitations leading to an effect on quality of life according to the results of the Helder study14. The Robert Wood Johnson Foundation demonstrated that quality of life can be improved in this population when palliative care is initiated in the early stages of the disease15. Hocaoglu, Gaffan, and Ho have developed a quality of life measure for patients with HD known as the “Huntington’s Disease health-related quality of life questionnaire” (HDQoL) which has good psychometric properites including good test-retest reliability (0.8), cronbach’s alpha greater than 0.7, minimal skewness, and very little ceiling and floor effects16.

*APTA Guide Patterns*

The APTA *Guide to Physical Therapist Practice* is a source of many practice patterns. Those related to the evaluation and treatment of HD are18:

4C: Impaired Muscle Performance
5A: Primary Prevention/Risk Reduction for Loss of Balance and Falling
5B: Impaired Neuromotor Development
5E: Impaired Motor Function and Sensory Integrity Associated with Progressive Disorders of the Central Nervous System.
6B: Impaired Aerobic Capacity/Endurance Associated with Deconditioning
6C: Impaired Ventilation, Respiratory/Gas Exchange, and Aerobic Capacity/Endurance Associated with Airway Clearance Dysfunction
7A: Primary Prevention/Risk Reduction for Integumentary Disorders

 *Intervention*

There is currently no cure for HD. All treatments are palliative in nature. The most common treatment is pharmacological. Haloperidol and Fluphenazine are prescribed to reduce chorea; Amitriptyline and Mirtazapine are prescribed for depression; L-dopa and Pramipexole are prescribed for rigidity; Risperidone is prescribed for psychosis; and Olanzapine, Haloperidol, and Buspirone are prescribed for symptoms involving behavior2. Unfortunately, many of these drugs have side-effects. Depending upon the individual’s reaction to the drug, the negatives may outweigh the positives. Furthermore, the success of one drug may aggravate other symptoms. For example, taking a medication to decrease chorea may in turn cause increased difficulty with voluntary movements2. Cysteamine is a radioprotective drug that decreases the amount of Somatostatin in the animal brain, but does not affect other neuropeptides. It is currently being researched to see if it will have a positive effect on symptoms of HD; however, a recent study looking at five patients with HD after treatment with cysteamine for two weeks showed no valuable changes5.

Physical therapy would be beneficial for patients with HD to provide a plan of care directed at symptom management, training in functional activities and use of assistive devices, and home modifications2. In the early stages of the disease, patients decline in functional capability due to weakness and decreased coordination. This leads to a sedentary lifestyle which quickly creates a situation of declining health. PT can create a fitness plan to improve physical functioning and decrease depression11. In the middle stages of the disease, patients continue to lose functional strength and balance is significantly affected. A PT can provide balance training and task-specific core stability exercises to reduce risk of falls11. A therapist can also teach strategies to prepare for challenges in balance that use neurons in the healthy frontal lobe for stability regulation instead of depending upon postural responses from the damaged basal ganglia11. Aerobic activities geared toward increased endurance should be in areas of interest of the patient for increased adherence and should be short in duration to prevent over fatigue11. These patients will also benefit from energy conservation techniques. Due to the potential cognitive effects of the disease, the therapist should begin training of these strategies early in the progression to decrease the effects of dementia and cognitive decline on adherence and understanding. Family members should also be educated on home exercise programs and strategies for increased functional ease11. In the late stages of HD, the therapist should focus on positioning for decreased risk of skin irritation and protecting the patient with padding in their surroundings as needed to prevent injury during an involuntary movement. Contraction management is also an important consideration if the patient experiences disuse of muscles surrounding a joint11. Assistance from other disciplines such as occupational therapy, speech therapy, dietician, geneticist, and a psychologist would also be helpful to complete the multidisciplinary team2.

*Outcome Measures*

1. Berg Balance Scale12
2. Single Limb Stance1
3. Functional Reach test
4. Huntington’s Disease Health-related Quality of Life Questionnaire (HDQoL)16
5. Sickness Impact Profile14
6. Gait velocity17
7. Stride length17
8. Cadence17
9. Functional Independence Measure12
10. Timed Up and Go Test12
11. 10-M Walk Test12
12. Unified Huntington’s Disease Rating Scale (UHDRS)12

References

1. Weiner WJ, Goetz CG. Neurology for the Non-Neurologist. 2nd edition. Philadelphia, PA:Lippincott Company; 1989: 141-144.
2. Aubeeluck A, Wilson E. Huntington’s Disease. Part 1: Essential Background and Management. British Journal of Nursing. 2008;17(3):146-151.
3. Conneally PM. Huntington Disease: Genetics and Epidemiology. American Journal of Human Genetics. 1984;36:506-526.
4. Harper PS. The Epidemiology of Hunington’s Disease. Human Genetics. 1992;89:365-376.
5. Martin JB, Gusella JF. Huntington’s Disease: Pathogenesis and Management. New England Journal of Medicine. 1986;315:1267-1276.
6. Hogg JE, Massey EW, Schoenberg BS. Mortality from Huntington’s Disease in the United States. Advanced Neurology. 1079;23:13-25.
7. Barbeau A. Update on the Biochemistry of Huntington’s Chorea. Advanced Neurology. 1979;23:449-461.
8. Cross A, Rossor M. Dopamine D-1 and D-2 Receptors in Huntington’s Disease. European Journal of Pharmacology. 1983;88:223-229.
9. Topper R, Schwarz M, Lange HW, Hefter H, Noth J. Neurophysiological Abnormalities in the Westphal Variant of Huntington’s Disease. Movement Disorders. 1998;13(6):920-928.
10. Reed TE, Chandler JH. Huntington’s Chorea in Michigan. Demography and Genetics. American Journal of Human Genetics. 1958;10:201-225.
11. Imbriglio S. Physical and Occupational Therapy Huntington’s Disease: Family Guide Series. Huntington’s Disease Society of America. Published 2010. Accessed March 26, 2014 at http://www.hdsa.org/images/content/1/1/11697.pdf
12. Busse ME, Khalil H, Quinn L, Rosser AE. Physical Therapy Intervention for People with Huntington’s Disease. Journal of the American Physical Therapy Association. 2008;88(7):820-831.
13. Ho AK, Gilbert AS, Mason SL, Goodman AO Barker RA. Health-Related Quality of Life in Huntington’s Disease: Which Factors Matter Most? Movement Disorders. 2009;24(4):574-578.
14. Helder D, Kaptein AA, van Kempen GM, van Houwelingen JC, Roos RA. Impact of Huntington’s Disease on Quality of Life. Journal of Movement Disorders. 2001;2:325-330.
15. Financial Implications of Promoting Excellence in End-of-Life Care. Missoula, Mont.: Promoting Excellence in End-of-Life Care, a national program of The Robert Wood Johnson Foundation, 2002.
16. Hocaoglu MB, Gaffan EA, Ho AK. The Huntington’s disease health-related quality of life questionnaire: a disease-speciﬁc measure of health-related quality of life. Clin Genet 2012: 81: 117–122.
17. Rao AK, Quinn L, Marder KS. Reliability of Spatiotemporal Gait Outcome Measures in Huntington’s Disease. Movement Disorders. 2005;20(8):1033-1037.
18. American Physical Therapy Association. Interactive Guide to Physical Therapy Practice. APTA. 2003. Accessed 3/27/14 at <http://guidetoptpractice.apta.org/content/current>.