Huntington disease

Huntington disease is a progressive brain disorder that causes uncontrolled movements, emotional problems, and loss of thinking ability (cognition).

Adult-onset Huntington disease, the most common form of this disorder, usually appears in a person's thirties or forties. Early signs and symptoms can include irritability, depression, small involuntary movements, poor coordination, and trouble learning new information or making decisions. Many people with Huntington disease develop involuntary jerking or twitching movements known as chorea. As the disease progresses, these movements become more pronounced. Affected individuals may have trouble walking, speaking, and swallowing. People with this disorder also experience changes in personality and a decline in thinking and reasoning abilities. Individuals with the adult-onset form of Huntington disease usually live about 15 to 20 years after signs and symptoms begin.

A less common form of Huntington disease known as the juvenile form begins in childhood or adolescence. It also involves movement problems and mental and emotional changes. Additional signs of the juvenile form include slow movements, clumsiness, frequent falling, rigidity, slurred speech, and drooling. School performance declines as thinking and reasoning abilities become impaired. Seizures occur in 30 percent to 50 percent of children with this condition. Juvenile Huntington disease tends to progress more quickly than the adult-onset form; affected individuals usually live 10 to 15 years after signs and symptoms appear.

Frequency

Huntington disease affects an estimated 3 to 7 per 100,000 people of European ancestry. The disorder appears to be less common in some other populations, including people of Japanese, Chinese, and African descent.

Causes

Mutations in the *HTT* gene cause Huntington disease. The *HTT* gene provides instructions for making a protein called huntingtin. Although the function of this protein is unknown, it appears to play an important role in nerve cells (neurons) in the brain.

The *HTT* mutation that causes Huntington disease involves a DNA segment known as a CAG trinucleotide repeat. This segment is made up of a series of three DNA building blocks (cytosine, adenine, and guanine) that appear multiple times in a row. Normally, the CAG segment is repeated 10 to 35 times within the gene. In people with Huntington disease, the CAG segment is repeated 36 to more than 120 times. People with 36 to 39 CAG repeats may or may not develop the signs and symptoms of Huntington disease, while people with 40 or more repeats almost always develop the disorder.

An increase in the size of the CAG segment leads to the production of an abnormally long version of the huntingtin protein. The elongated protein is cut into smaller, toxic fragments that bind together and accumulate in neurons, disrupting the normal functions of these cells. The dysfunction and eventual death of neurons in certain areas of the brain underlie the signs and symptoms of Huntington disease.

Inheritance Pattern

This condition is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder. An affected person usually inherits the altered gene from one affected parent. In rare cases, an individual with Huntington disease does not have a parent with the disorder.

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).

Other Names for This Condition

- Huntington chorea
- Huntington chronic progressive hereditary chorea
- Huntington's chorea
- Huntington's disease

Diagnosis & Management

Genetic Testing Information

- What is genetic testing?
  /primer/testing/genetictesting
- Genetic Testing Registry: Huntington's chorea
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0020179/
- Genetic Testing Registry: Juvenile onset Huntington's disease
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0751208/

Research Studies from ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22huntington+disease%22

Other Diagnosis and Management Resources

- GeneReview: Huntington Disease
  https://www.ncbi.nlm.nih.gov/books/NBK1305
- Huntington's Disease Society of America: HD Care
  http://hdsa.org/living-with-hd/
- MedlinePlus Encyclopedia: Huntington Disease
  https://medlineplus.gov/ency/article/000770.htm
- University of Washington Medical Center: Testing for Huntington Disease: Making an Informed Choice
  http://depts.washington.edu/neurolog/images/neurogenetics/hungtinton.pdf

Additional Information & Resources

Health Information from MedlinePlus

- Encyclopedia: Huntington Disease
  https://medlineplus.gov/ency/article/000770.htm
- Health Topic: Huntington's Disease
  https://medlineplus.gov/huntingtonsdisease.html

Genetic and Rare Diseases Information Center

- Huntington disease
  https://rarediseases.info.nih.gov/diseases/6677/huntington-disease
- Juvenile Huntington disease
  https://rarediseases.info.nih.gov/diseases/10510/juvenile-huntington-disease

Additional NIH Resources

- GeneEd
  https://geneed.nlm.nih.gov/topic_subtopic.php?tid=142&sid=169
- National Human Genome Research Institute: Learning About Huntington's Disease
  https://www.genome.gov/10001215/
- National Institute of Neurological Disorders and Stroke: Huntington's Disease Information Page
  https://www.ninds.nih.gov/Disorders/All-Disorders/Huntingtons-Disease-Information-Page
- National Institute of Neurological Disorders and Stroke: Huntington's Disease: Hope Through Research
  https://www.ninds.nih.gov/Disorders/Patient-Caregiver-Education/Hope-Through-Research/Huntingtons-Disease-Hope-Through

Educational Resources

- Centre for Genetics Education
  http://www.genetics.edu.au/publications-and-resources/facts-sheets/fact-sheet-55-huntington-disease
- Genetic Science Learning Center, University of Utah
  https://learn.genetics.utah.edu/content/disorders/singlegene/
- HOPES: Huntington's Outreach Project for Education, at Stanford
  https://web.stanford.edu/group/hopes/cgi-bin/hopes_test/
- Johns Hopkins Medicine
  https://www.hopkinsmedicine.org/psychiatry/specialty_areas/huntingtons_disease/patient_family_resources/education_whatis.html
- MalaCards: huntington disease
  https://www.malacards.org/card/huntington_disease
- Merck Manual Consumer Version
  https://www.merckmanuals.com/home/brain-spinal-cord-and-nerve-disorders/movement-disorders/huntington-disease
- National Health Service (UK)
  https://www.nhs.uk/Video/Pages/Huntingtonsdisease.aspx
- Orphanet: Huntington disease
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=399
- Your Genes Your Health from Cold Spring Harbor Laboratory
  http://www.ygyh.org/hd/whatisit.htm
- Your Genome from Wellcome Genome Campus
  https://www.yourgenome.org/facts/what-is-huntingtons-disease

Patient Support and Advocacy Resources

- Family Caregiver Alliance
  https://www.caregiver.org/health-issues/huntingtons
- HDBuzz
  https://en.hdbuzz.net/
- Hereditary Disease Foundation
  http://www.hdfoundation.org/
- Huntington Society of Canada
  https://www.huntingtonsociety.ca/
- Huntington's Disease Society of America
  https://hdsa.org/

- National Organization for Rare Disorders (NORD)
  https://rarediseases.org/rare-diseases/huntingtons-disease/
- Resource list from the University of Kansas Medical Center
  http://www.kumc.edu/gec/support/huntingt.html

Clinical Information from GeneReviews

- Huntington Disease
  https://www.ncbi.nlm.nih.gov/books/NBK1305

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28Huntington+Disease%5BMAJR%5D%29+AND+%28Huntington+disease%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- HUNTINGTON DISEASE
  http://omim.org/entry/143100

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