

## Huntington's disease

Huntington's disease is a progressive brain disorder caused by a single defective gene on chromosome 4 – one of the 23 human chromosomes that carry a person's entire genetic code. This defect is “dominant,” meaning that anyone who inherits it from a parent with Huntington's will eventually develop the disease.

The defective gene codes the blueprint for a protein called huntingtin. This protein's normal function isn't yet known, but scientists have identified its defective form as the cause of Huntington's disease.

The disease is named for George Huntington, the physician who first described it in the late 1800s.

### Prevalence

About 30,000 Americans — one in every 10,000 — have Huntington's. An additional 150,000 to 200,000 are known to be at risk because they have a parent with the disease.

### Symptoms

The hallmark symptom of Huntington's disease is uncontrolled movement of the arms, legs, head, face and upper body. Huntington's also causes a decline in thinking and reasoning skills, including memory, concentration, judgment and ability to plan and organize.

In addition, Huntington's disease brain changes lead to changes in mood, especially depression, anxiety and uncharacteristic anger and irritability. Obsessive-compulsive behavior is also common, causing a person to repeat the same question or activity over and over.

### Diagnosis

A diagnostic test can confirm if the defective gene for huntingtin protein is the cause of symptoms in people with suspected Huntington's disease. This test can also detect the defective gene in people who don't yet have symptoms but are at risk of developing Huntington's because a parent has the disease.

### Causes and risk factors

The defective gene, identified in 1993, causes virtually all cases of Huntington's disease. This gene codes a protein that scientists named “huntingtin” after linking it to

the disease. The huntingtin protein gene, like all human genes, carries its biological blueprints in repetitions of simple chemical codes. This particular gene defect involves extra repeats of one specific chemical code in one small section of chromosome 4. The normal huntingtin gene includes 17 to 20 repetitions of this code among its total of more than 3,100 codes. The defect that causes Huntington's disease includes 40 or more repeats. Genetic tests for Huntington's disease measure the number of repeats present in an individual huntingtin protein gene.

Scientists don't yet understand the normal function of huntingtin protein or how a few dozen extra repeats in its genetic blueprint lead to the devastating symptoms of Huntington's disease. Researchers are eager to solve these mysteries, not only to find better understand Huntington's, but also because the answers may offer important insights into a wide range of other brain disorders, including Alzheimer's, Parkinson's disease and amyotrophic lateral sclerosis (ALS).

### Outcomes

Huntington's is a progressive disease, meaning symptoms and brain changes gradually get worse. Symptoms usually develop between ages 30 and 50, but they can appear as early as age 2 or as late as age 80. People with Huntington's survive an average of 15 to 25 years.

### Treatment

There is currently no cure for Huntington's disease and no way to slow or stop the brain changes it causes. Current treatments focus on managing symptoms. In 2011, a group of more than 50 international experts recommended the following treatments as first-line strategies for three of the disorder's most troubling symptoms:

- **Chorea (involuntary movements):** Some experts believe beginning treatment with an atypical antipsychotic drug, such as olanzapine, is best. Others start with another type of drug recently approved by the U.S. Food and Drug Administration (FDA) specifically for Huntington's, called tetrabenazine.
- **Irritability:** For severe anger and threatening behavior, experts agree that an atypical antipsychotic drug is the preferred approach. For less severe, nonthreatening irritability, experts recommend first trying a selective serotonin reuptake inhibitor (SSRI), a type of antidepressant.
- **Obsessive-compulsive thoughts and actions:** Experts also recommend SSRIs as the standard treatment for these symptoms.

Other symptoms of Huntington's, such as anxiety, depression and insomnia, should also be treated. Due to the complexity of the disease, effective treatment of symptoms may be a lengthy process, and may include several approaches with different drugs and doses.

## Research

The effort to combat Huntington's involves several lines of inquiry, each providing important information about the disease:

- **Basic neurobiology.** Investigators in the field of neurobiology, which examines the anatomy, physiology and biochemistry of the nervous system, continue to study the huntingtin gene to learn how it causes the disease.
- **Clinical research.** Neurologists, psychologists, psychiatrists and other investigators are improving our understanding of the symptoms and progression of the disease in patients while attempting to develop new therapeutics.
- **Imaging.** Scientific investigations using positron emission tomography (PET) scans and other technologies are enabling scientists to see what the defective gene does to various structures in the brain and how it affects the body's chemistry and metabolism.
- **Animal models.** Laboratory animals, such as mice, are being bred with the hope of duplicating the clinical features of Huntington's disease to help scientists learn more about the symptoms and progression of the disease.
- **Fetal tissue research.** Investigators are implanting fetal tissue in rodents and nonhuman primates with the hope that success in this area will lead to understanding, restoring or replacing functions typically lost by neuronal degeneration in individuals with Huntington's.

These areas of research are slowly converging and, in the process, are yielding important clues about the gene's relentless destruction of mind and body.

### Additional resources

Huntington's Disease Society of America

[hdsa.org](http://hdsa.org)

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