

A Brief History of Huntington's Disease

Timeline of Events			Notable People
16th Century	Late 1950s	1978	Paracelsus
17th Century	1966	1979	Thomas Sydenham
1630s	1966	Late 1970s	George Huntington
1692	1968	1980	Woody Guthrie
1840s	1972	1981	The Wexler Family
1872	1973	1983	Lake Maracaibo, Venezuela
1900-1917	1974	1993	
1950s	1976	2000	
1955	1977		

Timeline of Events

More Information

16th Century

[Paracelsus](#), a Renaissance alchemist, coins the term "chorea" to describe the dance-like, uncoordinated movements that are now known to be symptomatic of HD.

17th Century

English physician [Thomas Sydenham](#) attempts to classify different types of chorea and describe their causes.

1630s

English colonists in Massachusetts, Connecticut, and New York (especially Long Island) use names such as "that disorder" and "Saint Vitus' dance" to describe HD.

1692

The Salem Witch Trials occur in Salem, Massachusetts. Many of the "witches" are now believed to have had HD. Their choreic movements and odd behavior, likely caused by HD, were seen as possession by the devil.

1840s

For the first time, HD is described in the medical literature as "chronic hereditary chorea." Physicians in the United States, England, and Norway write about people with involuntary movements and mental disturbances that were inherited from a similarly affected parent. Three separate accounts are recorded, all by young physicians.

1872

[George Huntington](#) writes a landmark paper entitled "On Chorea." Using personal accounts of his father's patients, Huntington provided a classic description of HD's symptoms and emphasizes HD's hereditary nature.

1900-1917

Significant interest in HD, especially its genetic component, occurs due to George Huntington's paper, "On Chorea" (1872).

The American eugenicist Charles B. Davenport writes *Heredity in Relation to Eugenics* (1911), in which he uses genetic diseases, including HD, to argue in favor of compulsory sterilization and immigration restriction for those afflicted with HD. Davenport founds the Cold Spring Harbor Biological Laboratory and Eugenics Record Office in 1910 to track families with inherited disorders, and he produces what is, at the time, the largest study of families with HD.

Researchers first note that the brains of HD patients are destroyed as the disease progresses. They identify the [caudate nucleus](#) as the central target of brain cell death.

1950s

An upsurge in publications on HD research occurs with the growing interest in human genetics and the 1953 discovery of DNA's structure by Watson and Crick.

1955

Americo Negrette publishes a book describing communities in Lake Maracaibo, Venezuela, with unusually high numbers of individuals affected by HD.

Late 1950s

Arvid Carlsson and Oleh Hornykiewicz, two European scientists, make the breakthrough discovery that [dopamine](#) pathways between [neurons](#) are destroyed in [Parkinson's disease](#) patients. Since the symptoms of Parkinson's disease are almost the exact opposite of those of HD, the scientists hypothesize that decreasing HD patients' dopamine levels might be a key step in treating the disease.

1966

The first Department of Neurobiology is established at Harvard University.

Ntinos Myriantopoulous writes a review article decrying the lack of knowledge of HD.

1967

Famous poet and songwriter [Woody Guthrie](#) dies of HD. Guthrie's wife, Marjorie, creates the Committee to Combat Huntington's Disease (CCHD), now called the Huntington's Disease Society of America ([HDSA](#)), to provide public health outreach on HD.

- 1968** The International Society for Neuroscience is founded.
- 1972** The International Centennial Symposium on Huntington's Disease is held on the hundredth anniversary of George Huntington's historic publication (See [1872](#)). The Symposium aims to gather all HD researchers and assess the current state of knowledge, generating new optimism for HD research.
- Thomas L. Perry finds diminished levels of [GABA](#) in the brains of HD patients.
- 1973** John Meeks and Natalie Stein suggest that the [HD allele](#) causes premature aging.
- 1974** Milton Wexler establishes the Foundation for Research in Hereditary Disease, which will later become the Hereditary Disease Foundation.
- 1976** Joseph T. Coyle develops the first rat model of HD by using kainic acid.
- 1977** The Congressional Commission for the Control of Huntington's Disease and Its Consequences is held to develop a comprehensive report on HD in the United States.
- 1978** The Second International Centennial Symposium on Huntington's Disease is held to review progress since the 1972 Symposium. The sheer volume of research that is accomplished over the six years indicates a heightened interest in HD.
- 1979** Mike Connelly establishes the National HD Research Roster at the Indiana University School of Medicine.
- Nancy and Tom Chase go to Venezuela for an exploratory visit to the Lake Maricaibo area, a hot spot for HD (see [1955](#)).
- Late 1970s** Researchers find evidence that HD affects cells all over the body, not just in the brain.
- 1980** NINDS funds the first two "Centers Without Walls" in Boston (Harvard/MGH) and Baltimore (Johns Hopkins).

- 1981** [Nancy Wexler](#) begins her fieldwork in the Venezuelan communities around Lake Maracaibo, a hot spot for HD.
- 1983** Scientists discover a gene marker linked to HD on the short arm of chromosome 4, which indicates that the Huntington gene is also located on chromosome 4. Predictive linkage testing is introduced to assess the likelihood of contracting HD.
- 1993** The location of the Huntington gene is discovered at the 4p16.3 gene site on chromosome 4. The gene is found to contain a [C-A-G codon](#) of variable length. An abnormal number of CAG repeats is a highly reliable way to diagnose and predict HD.
- 2000** The Huntington's Disease Advocacy Center ([HDAC](#)) is created to provide information and support for people with HD and their families.

Noteable People

More Information

**Philippus Aureolus
Theophrastus
Paracelsus
Bombastus von
Honenheim
(1493-1541)**

Paracelsus was a notable alchemist and reformer during the Renaissance period. He introduced the name *chorea sancti viti* (Latin for "St. Vitus' dance") to describe a peculiar disease characterized by writhing, sporadic movements. Most likely due to the mass hysteria and religious superstition of the time, this "dancing mania" had reached epidemic proportions in Europe. It is now thought that many of the sufferers may have experienced epileptic seizures or ergot poisoning. Near the end of Paracelsus's lifetime, the spread of the disease began to slow, the symptoms became milder, and Paracelsus termed this new form "chorea naturalis," or chorea due to natural causes.



**Thomas Sydenham
(1624-89)**

Thomas Sydenham was an English physician who is considered one of the most important revivers of Hippocrates' views. He stressed careful observation and bedside attendance, and he remarked keenly on many symptoms commonly associated with HD. He noted, for instance, "The hand cannot be steady for an instant. It passes from one position to another, however the patient may strive to the contrary." He believed that these movements were caused by "some humor falling on the nerves, and such irritation causes the spasm." Today, however, Sydenham chorea refers to chorea that is associated with rheumatic fever, even though Sydenham never explicitly made that link.



**George Huntington
(1850-1916)**

George Huntington, an American physician, was only twenty-two years old when he submitted his famous paper "On Chorea" (1872) to *The Medical and Surgical Reporter*. Much of the paper drew from the written observations of his father and grandfather, both physicians who had noticed the involuntary shaking of some patients. The paper gained Huntington instant notability because, in the words of Sir William Osler, "In the history of medicine there are few instances in which a disease has been more accurately more graphically, or more briefly described." Huntington was able to explicitly point to genetic inheritance as the mode of transmission, and he noticed that the first symptoms usually appear at an adult age and that they are usually accompanied by mental decline as well. It is due to these significant observations and conclusions that "Huntington's disease" is named after George Huntington's name.



**Woody Guthrie
(1912-67)**

Woody Guthrie was one of the most famous Americans with HD.

Born in Okemah, Oklahoma, Guthrie gained fame in the 1930s and 1940s as a folk singer and radio entertainer. He was known for putting political and social commentary in the lyrics of his music, and he often celebrated the plight of the American laborer. In his songs, Guthrie includes references to many of the 20th century's most historic events, including the Great Depression, the "Dust Bowl" migration, World War II, and the Cold War. His most famous songs include "This Land Is Your Land," "Grand Coulee Dam," and "I Ain't Got No Home."

Guthrie's mental state began to deteriorate in the early 1950s. His memory declined, and his behavior became unpredictable. He left his wife, Marjorie, and his home in New York to marry a woman twenty years his junior in California. However, due to his mental state, Guthrie was eventually forced to return to New York, where he was placed in one hospital after another. HD—the same disease that had killed his mother—claimed Woody Guthrie's life in 1967.



The Wexler Family

The Wexler family is inextricably tied to the history of Huntington's disease research. In 1968, Leonore Wexler was diagnosed with HD, which inspired her two daughters, Nancy and Alice, and her husband, Milton, to become involved in the search for a cure for HD.

Milton Wexler, a prominent psychologist, is responsible for bringing world renowned researchers together to focus on HD research. He founded the Hereditary Disease Foundation, which funds HD research and sponsors workshops for scientists to share ideas.

Nancy Wexler has played a pivotal role in the scientific research of HD. She pioneered the fieldwork in Lake Maracaibo, Venezuela that led to the discovery of the [Huntington gene](#) (see [Lake Maracaibo, Venezuela](#)) and has since helped other researchers map genes responsible for Alzheimer's disease, kidney cancer, manic depression, and other disorders. She served as the Hereditary Disease Foundation's president, and is currently a Professor of Neuropsychology at Columbia University.

Alice Wexler, a teacher, writer, and historian, chronicled her family's journey in the insightful book *Mapping Fate: A*



Huntington's disease in Lake Maracaibo, Venezuela

In the early 1950s, Dr. Amerigo Negrette first diagnosed Huntington's disease in Lake Maracaibo, Venezuela. Working as a rural physician, Negrette was perplexed by the fact that many townspeople often appeared drunk, staggering and weaving at all hours of the day. He learned from locals that these people were not drunk, but instead suffered from a disease referred to as *el mal de San Vito*, or the sickness of Saint Vitus. After visiting many people with the sickness, Negrette diagnosed the disease as HD. He discovered that HD ran deep in the community; people with the illness were interrelated and had common ancestry. In 1963, he published a book entitled *Corea de Huntington: Estudio de una Sola Familia a Traves de Varias Generaciones* describing HD in his community. The world learned of this tragic occurrence when Negrette's work was presented at the 1972 Centennial Symposium.

In 1981, Dr. Nancy Wexler led a team of scientists to study HD in Lake Maracaibo. Their original goal was to find an HD homozygote (an individual who has inherited two copies of the HD allele), but the team also ended up collecting blood samples from as many HD sufferers as they could find and test. These samples played a key role in the discovery of a genetic marker for HD in 1983 and led to the creation of a community pedigree, the largest of its kind in the world.



Nancy Wexler examines a section of the Venezuelan family's HD pedigree on a wall at NIH. The family tree now includes nearly 10,000 persons and is over 100 feet long.

-D. Chen, 6-21-02 / G. Schiel, 7-01-04