

## FAMILY ALBUM

### A weekly profile of a family--its history, joys and trials; On the Trail of a Killer, They Discovered Hope

By Mimi Avins

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Of the many ties that bind families together, misfortune is certainly among the strongest. Although one terrible circumstance irrevocably changed the lives of Milton Wexler and his daughters, Alice and Nancy, their shared tragedy brought them closer and set them on a course that has affected thousands of families around the world.

Leonore Sabin Wexler was 53 in 1968 when she was diagnosed with Huntington's disease. Her father and three brothers had already died of the incurable, degenerative disorder, sometimes known as Huntington's chorea, that would end her life 10 years later. She had believed the neurological illness affected only men. Her husband, Milton, a prominent clinical psychologist and psychoanalyst, quickly learned the truth: His daughters, then in their mid-20s and already on their way to impressive academic careers, faced a 50-50 chance of having inherited Huntington's.



For the next 32 years, Milton devoted his considerable energy, intelligence and charisma to trying to save his family from Huntington's. His efforts paved the way to a breakthrough when it was discovered that the Venezuelan descendants of a woman who lived 180 years ago battle the same fate as his children.

Studying the Venezuelan village where nearly everyone had the disease helped scientists funded by the Wexlers make significant progress in ways that have already impacted other hereditary diseases, such as Alzheimer's and Parkinson's. Nancy hopes a cure will be found in her father's lifetime. Milton is 91 now and legally blind, yet he still treats patients several hours a day.

"I want him to live very, very long," his daughter said. "But you see what kind of time frame I'm operating in."

Charity ranks so high in the American value system that nearly every malady in the dictionary seems to spawn some kind of group engaged in fund-raising, education, research or patient care. Nevertheless, in 1968 Milton started the Hereditary Disease Foundation, an organization dedicated to furthering research on Huntington's.

"I became an activist because I was terribly selfish," he said. "I was scared to death that one of my daughters would get it too."

The foundation, as conceived by Milton, was consequently different from organizations that seemed to have similar goals. He had long been a popular, if unorthodox, Westside therapist who drew many writers and artists to his practice. As he treated them and became a proponent of group therapy, he developed an interest in the creative process and the power of individuals to motivate one another.

Milton knew a number of science superstars from Caltech, UCLA and USC, and it wasn't unusual for a Nobel prizewinner to attend a foundation seminar. But initially, Milton thought the best way to find a cure would be to bring the brightest young scientists in the country together--curious assistant professors and postdoctoral students--and get them involved by providing an atmosphere that encouraged creativity and communication. Workshops would be kept small, he decided, and unlike other medical meetings, there would be no lectures, no papers delivered, no slides.

Allan J. Tobin, director of the UCLA Brain Research Institute, said, "The Wexlers got people to exchange ideas in such a way that we came away with more inspiration than we'd started with. Often in science, whatever you do, you're told that you're doing it wrong. The rules are to be rigorous and think things through and focus, focus, focus. Suddenly, we were asked to brainstorm and free associate together and we were told, 'We want to hear your wildest ideas, and don't be afraid to make a mistake.' It was liberating and compelling to be part of this very unusual experiment in scientific intervention."

It was also effective. In 1969, there were 32 reports of medical research with Huntington's disease in the title. In 1998, 239 appeared.

Perhaps the Wexlers got some of the good luck they were due, because genetics had become the new hot topic in medical research beginning in the mid-1950s, when the structure of DNA was discovered. A century ago, the reigning disease theory blamed all ills on the presence of bacteria.

"This is the high genomic period," UCLA's Tobin said.

Milton didn't rely on scientists' fascination with genetics for the success of his workshops. Over the years, he had assembled an eclectic group of glamorous, wealthy and accomplished friends and patients who volunteered to help the foundation in any way they could. Sometimes, that meant they'd give parties for the visiting researchers, who would return home and drop names like Cary Grant, Jack Lemmon, Carol Burnett, Frank Gehry, Julie Andrews, Blake Edwards, Norton Simon and Jennifer Jones Simon.

Researchers don't usually rub shoulders with celebrities in their laboratories, and, hunched over their microscopes and computers, they can lose touch with the outside world as well. Nancy deliberately brought people with Huntington's to the workshops. The scientists could ask them questions, but more important, they could see the reality of the disease they dealt with as an abstraction.

The disease currently affects 30,000 Americans, with 150,000 more at risk. Today, Alice is 57 and Nancy 54. The average age of onset for Huntington's is 40, and since neither sister has it yet, their risk is substantially less than when they were first told they might have inherited it.

The symptoms first surface when a person begins to jerk and stumble. Leonore Wexler's experience was typical: She was crossing a street when a policeman stopped her, asking why she'd been drinking so early in the morning. However, cognitive decline and emotional disturbances that go unrecognized frequently precede the involuntary movements that are Huntington's signature.

Depression, irritability, obsessive-compulsive thoughts, memory lapses and loss of attention span often occur. One in four victims of Huntington's attempts suicide (including Leonore). It is often misdiagnosed as alcoholism or schizophrenia, is progressive and always fatal. Ultimately, it becomes a wasting disease.

No one understood why Leonore, once an outgoing, highly motivated woman, grew increasingly timid and melancholy during her marriage. In 1962, she and Milton divorced. He had given up a low-paying but intellectually gratifying position at the Menninger Clinic in Kansas a decade earlier and come to California to open a private practice because he knew he'd need to earn more money to support Leonore's three sick brothers. He also assumed financial responsibility for his ex-wife during the years that she moved from her Brentwood apartment to a succession of nursing homes and hospitals. He visited her every Sunday and often on weekdays until she died.

After their mother's diagnosis, Milton encouraged his daughters to go on with their plans: Alice had completed a Fulbright scholarship to study social change in Venezuela and went on to get a doctorate in history. Nancy spent her own Fulbright year at Anna Freud's Hampstead Clinic in London, then earned a doctorate in clinical psychology. Her doctoral dissertation was on "The Psychology of Being at Risk." She said, "I did a lot of in-depth interviews with people at risk, who were very poignant and forthcoming. When you're at risk for a disease like this, it really permeates every aspect of your life."

That's certainly been true for Nancy and Alice. Every job Nancy has taken has dovetailed in some way with her interest in and work with Huntington's. Since 1984, she has served as the foundation's president, a position for which she travels extensively yet receives no salary. She networks throughout the scientific community, inspiring and nudging researchers. In addition, she is a professor of neurology and psychiatry at Columbia University. She decided not to have children and has never married, although since 1984 she has been in a relationship with Herbert Pardes, vice president of Columbia Medical Center.

Alice, a teacher, historian and writer, is divorced and also chose not to have children because if she had inherited the gene from her mother, her children would have a 50-50 chance of getting the disease. If she did not have it, neither would her offspring: Huntington's never skips a generation. Alice is responsible for the foundation newsletter and sensitively told her family's story in "Mapping Fate: A Memoir of Family, Risk and Genetic Research" (University of California Press, 1996). Nancy says, "My sister is very courageous to write about a lot of things that are difficult to deal with and put it in a way that other families can recognize themselves and learn from it." Alice is currently working on another book about Huntington's.

The fact that Huntington's affects a relatively small number of Americans has hurt efforts to eradicate the disease in two ways. First, it made Huntington's research less attractive to pharmaceutical companies, who could expect a greater return for developing a drug for a more common sickness such as Alzheimer's, which afflicts 4 million Americans. Huntington's comparative rarity also made it difficult to study, because to find the gene, scientists needed a big family to study--the bigger, the better.

So in 1972, when a Venezuelan physician showed a film at a medical conference about a community on the shores of Lake Maracaibo that is riddled with Huntington's, Nancy organized and got funding for a research project there. She knew that several generations of many families with Huntington's could give scientists a chance to examine the DNA of those who had the disease and those who escaped it.

Since 1979, Nancy has gone to Venezuela at least once a year, and usually flies north carrying blood samples gathered there. Alice remembered her first impression of seeing so many Huntington's sufferers in one place. "It was very moving to see all these people who looked just like Mom," she said. "They staggered around, just like she did." On several of her trips, Alice charted family histories and eventually traced the disease to one woman, whose extended family now numbers 9,000.

In 1983, a molecular geneticist at MIT, working on blood drawn in Venezuela with a grant from the foundation, located human chromosomes that contained the Huntington's disease gene. A decade later, the gene itself was identified.

That was not only a major scientific achievement, it also meant that Nancy and Alice could take a test to find out if they had the defective gene. Nancy said, "When we were trying to develop a test, we assumed we'd both take it. Then once the test existed, we were thinking about it differently. Our family talked an enormous amount about the consequences. Even if you live at risk all of your life, and you've thought about it and cried about it, there's a certain amount of denial that helps you get through the day. Being tested can take that away."

Milton's position was clear: "If either of them came out positive," he said, "I felt that all our lives would be over. I don't think there's a single answer for everybody, especially for people who are considering having children, but I was against my daughters taking it."

Whether or not to be tested was only one of the dangling conversations the Wexlers had about Huntington's. The question of family secrets was another. Who knew what, when, and why wasn't everyone told? Did fear about the stigma of the disease keep Leonore silent? Even their conflicts brought them closer.

"It's a little like a family business," Alice said. "We argue about it, we always talk about it--about the foundation, how it runs, the administration and politics of it. I've written two books about Huntington's, and I find it intellectually exciting. I can't really remove myself from it, but sometimes working on it is a way of distancing yourself and making it bearable."

One of the things learned from Huntington's research is there are at least eight other diseases that similarly result from a particular defect in the cell proteins. Finding the gene makes the hope of a cure much closer.

The Wexlers all admit that the search for a cure has opened many doors. Being haunted by the threat of the disease made them decide to live their lives and not put things off. Being exposed to families struggling with it put everything in perspective.

"When we first found out about HD in our family, one of the worst aspects for me was the feeling that there was nothing I could do--it was beyond my control," Nancy said. "For me, the most important thing in my life has been that my father said one family can make a difference."

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To reach the Hereditary Disease Foundation, call (212) 928-2121, e-mail [cures@hdfoundation.org](mailto:cures@hdfoundation.org) or log on the Web site at <http://www.hdfoundation.org>.

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