

## All in the family—a genetic legacy

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One morning in May of 1968, Leonore Wexler was on her way to jury duty at a Los Angeles courthouse when she was pulled over by the LAPD. The officer, having noticed Leonore's erratic weaving, shouted, Hey lady, aren't you ashamed of being drunk so early in the morning? Leonore had not been drinking that fateful morning, and her wild driving was the result of something much more terrible than the officer could have guessed—she had begun to show symptoms of Huntington disease.

At that time, the disease was called Huntington's chorea due to the constant involuntary twitches and jerks it causes. A person with Huntington disease appears to be controlled by some unseen choreographer with a repertoire of rather badly planned dance steps. When George Huntington first described the disease in 1872, he made note of not only the physical symptoms that are the hallmarks of the disease, but also of the mental deterioration and the emotional suffering it caused in multiple generations of his patients.

It took us over a hundred years after Huntington's classic description to find the gene which causes the disease. According to Friedrich Nietzsche, In the mountains the shortest way is from peak to peak; but for that you need long legs. In fact, it was Leonore's daughter, Nancy, whose legs proved long enough to bridge the gap in our understanding of the genetics of Huntington disease. Nancy did not just sit by and watch her mother and other family members slowly die from Huntington disease. Instead, she went to the *pueblos de agua*, houses built on top of the water of Lake Maracaibo, Venezuela, to gather the information that would lead to the discovery of the gene that causes Huntington.

In the 1980's Nancy and her coworkers drew an enormous family tree of the Lake Maracaibo natives and took samples of their blood. The natives have such a large incidence of Huntington disease that in almost every house in this village there lives someone affected. Fortunately, not everyone in the family of an individual with Huntington disease is also destined to develop symptoms. Unfortunately, everyone in the family is impacted from their experience of seeing their relatives degenerate mentally and physically. By laboriously comparing the chromosomes of individuals with the disease to those without it, the gene was eventually mapped to chromosome 4 by a technique called linkage. However, it wasn't until the 90's that a DNA-based test was developed which can predict without fail who will become affected and who will not.

The family legacy of Huntington disease is perhaps more striking than any other hereditary condition, in part because its terrible symptoms do not develop until late adulthood, long after children have been born to those affected. Some of these children are destined to inherit the disease and potentially pass it onto their children as well.

The genes which cause many other disorders have also been discovered, and in many cases, testing for these disorders is currently available. For example, like the Lake Maracaibo natives, many ethnic groups have a higher incidence of certain genetic conditions. Caucasians are the group most likely to get cystic fibrosis, which affects the lungs and other organs. Jewish individuals are more likely to be carriers for Tay-Sachs, a condition that is fatal in infancy. Individuals of African ancestry are frequently carriers for sickle cell, a chronic blood disorder. All of these conditions can run in the family. Carrier screening and prenatal diagnostic testing are available for these and many other hereditary disorders.

Individuals who are concerned about their chances of having or carrying a genetic condition are encouraged to consult with a genetic counselor. Genetic counselors are health professionals trained to gather medical information, to provide accurate assessment of genetic risk, to educate people about their testing options and interpret the results of these tests. Once armed with an understanding of their own family's particular genetic situation, couples can make informed family planning decisions. Increasing our understanding in turn leads to healthier children, which is something that all families look forward to.

**GeneCare Medical Genetics Center, in Chapel Hill, offers genetic counseling and laboratory services, including prenatal screening and diagnostic testing. For more information, please call (919) 942-0021 or 1-800-277-4363. Or visit our web site at [www.genecare.com](http://www.genecare.com). The Wexler family's story describing their experience with Huntington disease is told in Alice Wexler's book, *Mapping Fate*.**