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An uncertain journey along the genetic trail

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At Risk for Huntington's Disease

HD is a genetically caused brain disorder that causes uncontrollable bodily movements and robs people's ability to walk, talk, eat, and think. The final result is a slow, ugly death. Children of parents with HD have a 50-50 chance of inheriting the disease. There is no cure or treatment.

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SATURDAY, SEPTEMBER 24, 2005

An uncertain journey along the genetic trail

This article about me is in the September 25, 2005 edition of *The Washington Post*. I will comment on it in my next entry.

washingtonpost.com

An Uncertain Journey Along the Genetic Trail

By Martha Nance
Sunday, September 25, 2005; B03

There is, unfortunately, a painful lag between scientific knowledge and its benefits. As an expert in Huntington's disease, a degenerative neurological condition, I am keenly aware of this. We know how people get this disease, and there's been an explosion of new information about it, but we still don't know enough to treat or cure it.

Huntington's is caused by a genetic abnormality, one that is easy to test for. And if you inherit it from one of your parents, you will, if you live long enough, eventually develop the symptoms, which can include dementia, depression, involuntary movements and lack of coordination.

This knowledge about one's fate is not unique to the 30,000 sufferers of Huntington's. As genes relating to Alzheimer's and Parkinson's disease and breast cancer and many other medical conditions are uncovered, there is an increasing ability to look into the crystal ball and see which of your parents' fates might be yours. It may seem somewhat distant when it is a disease unfamiliar to you, but it hits you between the eyes when it involves your family or friends.

That came home to me recently when I received a note from a college friend. I hadn't been in touch with him since we'd graduated. He read about me in a publication of the Huntington's Disease Society of America (HDSA) and he sent me his story. He did not know whether I would remember him or what I would think of his plight. His only hope was that I would recognize his ordeal and find some way to help. And I was distant enough not to compromise his desire to remain anonymous; the stigma associated with Huntington's can harm a person's career and relationships, not to mention the ability to get health insurance. He said he felt he was leading "a double life" between his outwardly serene routine and his inner struggle. He called his account "Looking Into the Genetic Mirror," which he was willing to let me quote at length.

"My future began to slip away the day after Christmas 1995, when I received the jolting news that my mother had tested positive for Huntington's disease (HD). Finally I understood her shaking limbs and increasingly angry, childlike manner," he wrote.

He had a good understanding of the medical implications for himself. "I had a 50-50 chance of inheriting HD," he continued. "If I did inherit it,

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there was no escape, as HD afflicts all carriers of the abnormal gene. Symptoms usually strike in a person's prime, between 30 and 50. There is no cure, nor effective treatment. I was 36, and I could pass HD on to the children my wife and I hoped for.

"I wanted to get tested immediately to find out whether or not I carried the abnormal gene, but local HDSA support group members warned that at-risk individuals had lost their jobs and could not buy health or life insurance. All our dreams went on hold. That night, as fear overwhelmed me, my wife held me tight.

"Each encounter with my mom became a view into a nightmarish genetic mirror. I watched her body jerk, head bob, and fingers fret. One night I found her wandering around our house confused and half naked. Within a year she lost most of her capacity to speak. She ate clumsily with her hands.

"With my wife pressing me to start a family, in mid-1999 I discovered my genetic fate through an anonymous testing program. The doctor's words echo: 'You have your mother's gene for HD.' Stunned, I fell into a fog of acceptance, denial, and defiance.

"The next look into the mirror was even more excruciating, because my wife became pregnant. For four months we waited to find out the genetic truth about the new life growing in her womb. Daily we debated whether she could care for two HD people while working. We pondered an abortion. But the anguish gave way to our most joyous moment: our 'miracle baby' -- now 5 -- was free of the HD gene.

"Yet the mirror looms. My mom, today 68 and wheelchair-bound, cannot hug her granddaughter. When I call my parents, she just listens and barely ekes out 'I love you.' Because of her incontinence, my parents can no longer make the trip to visit us. Imagining herself pregnant, one day my mother took her feces to my dad and said she had given birth. In August, he finally had to put her in a nursing home. Death draws near as she loses her ability to swallow.

"Now 45, I agonize as I approach her age of onset. We put off having a second child and save to pay off our mortgage faster, preparing for the day when I will become disabled. I panic when I think of losing the ability to pursue my greatest passions, reading and writing. Will I see my daughter fall in love and go to college?

"Suicide would spare my family an exhausting, financially ruinous burden. I would not suffer like the HD patients I recently saw at a nursing home, writhing uncontrollably, wearing diapers, belted in a special chair or confined to a padded room. But a suicide would devastate my daughter.

"We shelter her, telling her that Grandma 'has a boo-boo on her brain.' Yet we may soon need to explain how HD will affect me."

I have held that same mirror up to my patients many times, and I know what his future holds. What he needs from me is hope -- no, more than that, what he needs is progress. He needs a glimpse beyond the genetic mirror. He needs to know the rest of what I know, that treatments for neurodegeneration are on the horizon.

Experimental research in HD began with the 1993 discovery of the gene responsible for the disease. This monumental breakthrough allowed scientists to create "laboratory models" of HD, by inserting the abnormal, slightly enlarged, gene into the eye of the fruit fly, the roundworm, the mouse or cells in test tubes. They could then design experiments to understand how the production of the abnormally elongated Huntington protein encoded by that gene causes HD.

Using these laboratory models, researchers have now begun to identify steps in the process of nerve cell degeneration. An enzyme called caspase cleaves the abnormal HD protein, and the fragments overwhelm the cell's natural garbage disposal, called the proteasome. Many cell processes begin to go awry as the proteins accumulate. The mitochondria, little engines inside the cells, suffer damage along the way. Eventually the abnormal proteins collect in blobs inside the cell. Scientists aren't sure at this point whether the blobs themselves do additional harm or whether they merely reflect a cell no longer able to carry out its usual functions.

Scientists are now scouring libraries of chemicals for compounds that block the formation of these protein blobs, enhance the function of the mitochondria or the proteasome, or block the caspase enzyme. Early trials of promising compounds are beginning in animals and even in humans. Some researchers are studying ways to block the defective HD gene from ever producing the abnormal HD protein in the first place, using a new technology called "RNA interference." Like chemotherapy for cancer, or the AIDS cocktail, a combination of therapies may one day successfully treat Huntington's.

As my friend knows all too well, it is possible to know in advance who will develop HD. We might therefore have the opportunity to try treatments for HD even before any symptoms become obvious -- just as we can treat breast cancer more successfully when it is a pea-size spot on a mammogram than after it has spread throughout the body. And a treatment that works for HD may also benefit people with much more common disorders such as Parkinson's disease and Alzheimer's disease, which share similar sorts of nerve cell degeneration. Since we do not now have a way to know in advance who will develop Parkinson's or Alzheimer's disease, HD research will likely pave the way for advances in these disorders.

It's only been 12 years since we identified the gene that allowed us to begin experimental research on HD, yet early clinical trials of treatments for HD have already started.

I can't promise that this will help my friend, who closed his story with the following reflection: "When my mother lovingly conceived me, she unknowingly passed on a defect that is now our shared destiny."

Unlike his mother's generation, though, my friend does not struggle alone. He and others who are confronting their diseases are pioneers who can help end the stigma and suffering associated with all degenerative neurological diseases.

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Posted by Gene Veritas at 10:21 AM

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