abortion rate was 16 percent. This rate doubled, though, when the condition was likely to cause some form of mental dysfunction, such as cognitive impairment.

This emphasis on cognitive abilities also seems to hold when decisions are made about Down syndrome. That condition invariably involves, among other traits, mental disability. While the statistics are not wholly reliable, physicians in reproductive medicine estimate that when prenatal tests show that a fetus will develop Down syndrome, about 80 percent of women decide to terminate their pregnancies. Such decisions have become embroiled in abortion politics in recent years, as legislators in states such as Ohio have introduced bills that would ban abortions if Down Syndrome is the reason.

The issues connected with prenatal genetic testing, embryo testing, and abortion are complicated and contentious. Advocates on one side of the debate sometimes find themselves behaving at odds with it when their own circumstances force them to make a decision. When an issue becomes personal, abstract ideological commitments are frequently discarded.

CASE PRESENTATION

Huntington's Disease: Deadly Disorder, Personal Dilemmas

Huntington's disease (HD) is a particularly cruel and frightening genetic disorder. It has no effective treatment and is invariably fatal. Furthermore, each child of an affected parent has a 50 percent chance of developing the disease.

HD typically makes its appearance between the ages of thirty-five and forty-five in men and women who have shown no previous symptoms. The signs of its onset may be quite subtle—a certain clumsiness in performing small tasks, a slight slurring of speech, a few facial twitches. But the disease is progressive. Over time, the small changes develop into devastating physical and mental impairments. Walking becomes jerky and unsteady, the face contorts into wild grimaces, the hands repeatedly clench and relax, and the whole body writhes with involuntary muscle spasms. The patient becomes disoriented, volatile, and impulsive, and eventually loses the power of speech. Death may occur fifteen or twenty years after the onset of symptoms. Usually, it results from massive infection and malnutrition—as the disease progresses, the patient loses the ability to swallow normally.

In the United States, at any given time, some 30,000 people are living with an HD diagnosis, and as many as 150,000 more have the gene responsible for it. The incidence of the disease is only one in ten thousand, but for the child of someone with the disease, the chances of having it are one in two.

Gene Identified

The gene associated with Huntington's disease was identified in 1993 after ten years of intensive research carried out in six laboratories in the United States, England, and Wales. Following clues provided by genetic markers, scientists finally located the gene near the tip of chromosome 4. When the researchers sequenced the nucleotides making up the gene, they discovered a mutation known as a trinucleotide repeat. In healthy individuals, the nucleotides CAG are repeated eleven to thirty-four times, whereas in individuals with HD, the repetitions typically range from thirty-seven to eighty-six. Some evidence suggests that higher numbers of repetitions are associated with earlier onset.

When the HD gene was identified, it was expected that this would speed the development of effective treatments for the disease. This has not occurred, in part because the mechanism of the gene's action is still not fully understood. Furthermore, the HD gene

was expected to be found functioning only in the brain, but in fact radioactive tagging has shown that the gene operates in virtually every tissue of the body, including the colon, liver, pancreas, and testes. The protein that the gene codes for is believed to be involved in nerve cell development and function, so it has its most devastating impact on the brain.

Before the HD gene was identified or a marker for it discovered, the disease was known to be transmitted from generation to generation in the sort of hereditary pattern indicating that it is caused by a single gene. However, because the disease makes its appearance relatively late in life, an unsuspecting carrier may already have passed on the gene to a child before showing any sign of the disease. In the absence of a genetic test to detect the gene, the individual could not know whether he or she was a carrier.

In 1983, a major step toward the development of such a test was announced by James F. Gusella and his group at Massachusetts General Hospital. The team did not locate the gene itself, but discovered a "genetic marker" indicating its presence. They began by studying the DNA taken from members of a large American family with a history of Huntington's disease, then employed recombinant DNA techniques to attempt to locate DNA segments that might be associated with the HD gene.

The techniques involved using proteins known as restriction enzymes. A particular enzyme, when mixed with a single strand of DNA, cuts the strand at specific locations known as recognition sites. After the DNA strand has been cut up by restriction enzymes, short sections of radioactive, single-stranded DNA are added to serve as probes. The probes bind to particular segments of the DNA. Because the probes are radioactive, the segments to which they are attached can be identified. The various fragments of DNA produced by the restriction enzymes and identified by probes form a pattern that is typical of specific individuals. Thus, if the pattern of someone who does not have the disease is compared with the pattern of a family member who does, the fragments that include the faulty gene can be identified, even when the gene itself is unknown. The pattern serves as a marker for the presence of the gene, and Gusella's group found such a marker.

The group faced the problem of finding a marker consistently inherited by those with Huntington's disease but not by those free of the disease. This meant identifying perhaps as many as eight hundred markers and determining whether one could serve as the marker for the HD gene. After twelve attempts, the team identified a good candidate marker, found in all members of the family they were studying. Those with the disease had the same form of the marker, while those free of the disease had some other form.

Gusella and other researchers were supported in their work by the Hereditary Disease Foundation. The organization was founded by Milton Wexler after his wife was diagnosed with Huntington's. Wexler hoped a treatment for the disease could be found that might benefit his daughters, Nancy and Alice, who stood a 50 percent chance of developing the disease. Nancy Wexler soon became an active participant in research activities aimed at discovering a genetic marker for HD.

In collaboration with the Hereditary Disease Foundation, plans were made to test Gusella's candidate marker in a large population. It was known that a large family with a high incidence of HD lived along the shores of Lake Maracaibo in Venezuela. Nancy Wexler led a team to this remote location to collect a family history and to obtain blood and skin samples for analysis. The Venezuelan family included some 100 people with the disease and 1,100 children with the risk of developing it. Analysis of the samples showed that those with the disease also carried the same form of the marker as their American counterparts. Subsequent work by Susan Naylor and others indicated that the marker was on chromosome 4.

Genetic Test Available

Once the location of the gene for Huntington's disease was known, a genetic test for its presence was quickly developed. The availability of the test, however, raises a number of serious ethical and social issues. A study conducted in Wales revealed that more than half of those whose parents or relatives were afflicted by Huntington's would *not* want to be tested for the HD gene. Considering that the disease cannot be effectively

treated and is invariably fatal, this is not a particularly surprising result.

Nancy Wexler told a reporter that she and her sister had assumed that once a test for the HD gene was available, they would both take it. However, when they met with their father to work out the details for a test based on the genetic marker, he asked, "What are we doing here? Are we sure we want to do this?" The sisters, Nancy recalled, "had a visceral understanding that either one of us could get bad news and that it would certainly destroy my father."

One argument for at-risk individuals getting tested for the HD gene is based on their obligations to others. Now that a test is widely available, is it fair to contemplate marriage or childrearing without finding out whether one is a carrier of the HD gene and informing others of the result? One may be willing to take the chance that one's offspring will have HD. But the tremendous burden the disease places on the entire family of those afflicted suggests that getting tested for the condition may be morally necessary for the sake of others. Should a potential carrier of the gene impose on his or her family the risk of having a child who will inherit the gene? Should such a risk be imposed on the child?

Prenatal Testing and Embryo Screening

The HD test now in use can also be employed in conjunction with amniocentesis to determine whether a developing fetus carries the relevant mutation. This fact raises problems for potential parents. A child born with the HD gene will inevitably develop the disease but may not do so for three, four, or even five or more decades. Does that delay make abortion less justifiable in the event of a positive test? But if prospective parents aren't prepared to seek an abortion, why administer the test in the first place? Finally, is the fact that the fetus can be expected to develop into an adult who will eventually succumb to the disease reason enough to make an abortion morally obligatory?

One alternative for prospective parents who have reason to fear that they carry the HD gene is to make use of the techniques of assisted reproduction. Once embryos have been produced by artificial insemination from the parents' donated ova and sperm, the embryos can be tested for the HD gene. Only embryos without the gene can then be transferred to the woman's uterus for implantation.

Personal Risks

The advent of a standard, inexpensive test for the HD gene raises various other personal and social issues. For example, insurance companies may refuse to provide life or long-term care insurance to individuals whose relatives have Huntington's disease, unless they prove that they are not carriers of the gene. (The Genetic Information Nondiscrimination Act and the Affordable Care Act do not forbid such specialized insurers from using genetic information in underwriting policies.) Adoption agencies have requested that infants up for adoption be tested to assure prospective parents that the children are not at risk for HD. As Nancy Wexler put the point, "In our culture, people assume that knowledge is always good. . . . But our experience with Huntington's has shown that some things may be better left unknown."

Informing someone that he or she carries the gene can also be devastating, both to the person and to the person's family. Evidence indicates that the suicide rate among those with HD is as much as ten times the rate in the general population. One study found that out of 4,527 patients who tested positive for the HD gene at major medical centers, 5 killed themselves, 21 attempted suicide, and 18 were hospitalized for psychiatric reasons. Thus, the mere act of conveying the information that someone will later develop HD can itself constitute a threat to life. Nancy Wexler has refused to disclose publicly whether she has been tested for the HD gene. "I don't want to influence anyone's decision," she says.

Envoi

In an ideal world, an effective means of preventing the onset of Huntington's disease or treating it effectively would be available. Then the moral, social, and personal issues associated with a genetic test for it would disappear without having to be resolved. Regrettably, that world still lies in the future.