

THE CONUNDRUM OF GENETIC TESTING

Screenings offer knowledge, not necessarily wisdom, experts say. A study finds Gaucher disease counseling cut the number of abortions.

By Karen Kaplan, Los Angeles Times Staff Writer
September 19, 2007

Thirty-five years after genetic screening was first used to identify babies at risk of being born with debilitating diseases, a new study of a potentially serious but treatable illness among Ashkenazi Jews questions whether such testing has gone too far.

One-quarter of fetuses found to have Gaucher disease were aborted over an eight-year period, even though half of all children with the metabolic disorder will never experience any symptoms, such as pain, organ enlargement and anemia. The rest can lead normal lives with treatment.

The disparity underscores what some experts say is a flaw in genetic testing: It provides a bounty of knowledge that is not necessarily accompanied by wisdom.

The study, published today in the *Journal of the American Medical Assn.*, tracked nearly 29,000 Israelis who opted to be screened for mutations in their DNA that could lead to Gaucher disease in their children if they inherit faulty genes from both parents.

Similar screening tests are offered to other specific ethnic groups predisposed to disorders, such as albinism and congenital deafness.

Dr. William R. Wilcox, who treats Gaucher patients at the Medical Genetics Institute at Cedars-Sinai Medical Center in Los Angeles and was not involved in the study, said that given the ambiguity inherent in some genetic tests, they should not be given for diseases that are imminently treatable.

“Personally, that horrifies me,” he said. “Why is it there? Because we can do it. But just because we can doesn’t mean we should.”

Others say abandoning the genetic test would unfairly deny couples genetic information about their offspring.

“It’s an opportunity to gain information which some people might want,” said Karen Grinzaid, a genetic counselor at Emory University in Atlanta who coordinates care for Gaucher patients. “It’s their decision about what they want to do with that information.”

As gene-hunters find more DNA mutations associated with particular diseases, the number of people who will be left grappling with ambiguous results is likely to grow, experts said.

FROM THE DESK OF DAVID L. SCHUTZER

“This is just the tip of the iceberg,” Wilcox said. “There will be a time when we have the ability to screen for thousands of diseases in one blood spot. What are you going to terminate for?”

First successThe proliferation of screening tests was largely driven by the success of carrier screening for Tay–Sachs disease, another condition with high incidence among Ashkenazi Jews, or those of Eastern European descent.

Children with Tay–Sachs are unable to process a fatty substances, which builds up in the body and leads to blindness, deafness, paralysis and death by age 4. Since screening for Tay–Sachs carriers began in the early 1970s, the number of cases has dropped by 90%.

Other diseases that Ashkenazi Jews are frequently screened for include Canavan disease and Niemann–Pick disease, which lead to death in early childhood, and debilitating conditions like cystic fibrosis.

Dr. Ephrat Levy–Lahad, director of the Medical Genetics Unit at Shaare Zedek Medical Center in Jerusalem, and colleagues wondered how screening for a relatively mild condition like Gaucher affected couples’ family planning decisions.

Gaucher disease is the most common genetic disease among Ashkenazi Jews. Scientists estimate that 6% to 10% of Ashkenazi Jews are carriers of at least one mutation that can lead to the disorder. Roughly 60% of eligible couples in Israel take the screening test, Levy–Lahad said.

But among the eight to 14 Jewish genetic diseases commonly screened for, it is also the most controversial, Grinzaid said. Even knowing which mutations are in a fetus’ genes, she said, “we’re still not able to predict what’s going to be wrong with the child. It can be anywhere from something that presents in childhood, which is treatable, to something that can never present. . . What do you do with that?”

Among children who inherit two faulty genes, the most common result is Type 1 Gaucher. Half will become symptomatic at some point in their lives, when harmful amounts of glucocerebroside build up in the spleen, liver, lungs and bone marrow.

Patients can experience pain and suffer from fatigue, although the symptoms can be treated with biweekly infusions of the enzyme that their bodies fail to produce in sufficient quantities. The intravenous infusions take an hour or two at home and cost \$100,000 to \$400,000 a year.

The researchers surveyed all 10 centers in Israel that screen for Gaucher disease mutations. Between 1995 and 2003, the centers tested about 28,900 people and identified 83 couples where both partners had a mutation.

FROM THE DESK OF DAVID L. SCHUTZER

The researchers were able to interview 65 of the at-risk couples, who had a total of 90 pregnancies. In 68 of those pregnancies, parents opted for an amniocentesis or chorionic villus sampling to test for Gaucher in their fetuses.

Sixteen of those tests were positive for the disease. In four of the cases, couples opted to terminate their pregnancies.

The researchers surmise that lack of information about Gaucher may have played a role in some of those decisions. Among 13 couples who discussed Gaucher with an expert, one had an abortion. Three couples did not discuss the disease with an expert, and all of them had abortions, according to the study.

One couple, which learned that their particular mutations could lead to one of the most severe — and untreatable — forms of the disease, did not get pregnant. Those types can cause death in early childhood or severe neurological degeneration, and they are no more likely among Ashkenazi Jews than members of other ethnic groups.

In an editorial accompanying the study, Dr. Ernest Beutler said the Gaucher test does little to benefit carriers or their offspring. Instead, he said, it serves mainly to enrich hospitals, testing laboratories and pharmaceutical companies.

“Children are likely to be treated when they don’t really need treatment,” said Beutler, who chairs the department of molecular and experimental medicine at the Scripps Research Institute in La Jolla. “You get a child that’s 8 or 10 years old and has a slightly enlarged spleen and their hemoglobin is a little low. You can watch a child like that. But once the diagnosis is made, there’s pressure to treat. People tend to say, ‘Nothing’s too good for our child.’ “

Parents’ choice Just knowing that Gaucher is present can shape the lives of healthy children. “Maybe they won’t be allowed to play soccer with their friends,” Beutler said. “Maybe they’ll wind up being checked by a doctor every two months. It can really change their life and their self-image.”

Dr. Robin A. Ely, who raised three children with moderate levels of the disease, said she had counseled couples in the U.S. who were advised by their doctors to abort when genetic tests confirmed a Gaucher diagnosis.

“I tell them, ‘This is your choice, but I think it’s a mistake,’ “ said Ely, medical director of the National Gaucher Foundation based in Tucker, Ga. “It’s almost Nazi-like. It’s eugenics.”

But what may seem like a mistake to one family may be the right choice for another.

FROM THE DESK OF DAVID L. SCHUTZER

For instance, the high cost of enzyme replacement therapy may tilt some couples toward abortion, Levy–Lahad said. Insurance plans in the United States typically cover the treatment, but patients whose policies include a lifetime cap may run into trouble.

Cost was probably not a factor for couples in the study because the treatment is covered by Israel's national health insurance.

One of the couples interviewed by researchers said they were concerned about how they would pay for treatment if they left the country. However, they elected to carry their Gaucher baby to term.

karen.kaplan@latimes.com