Testing curbs some genetic diseases

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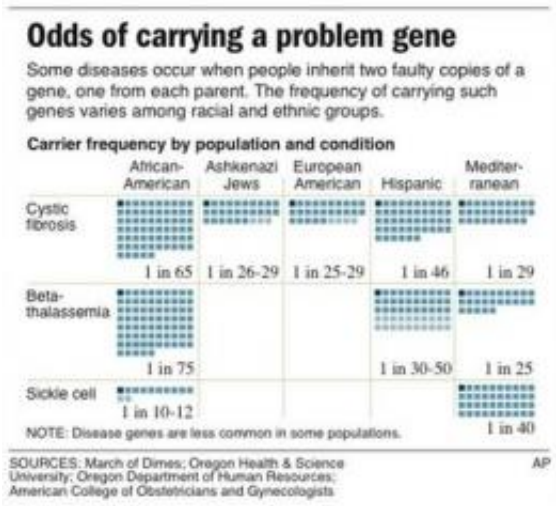

Graphic shows odds of carrying a problem gene by racial and ethnic groups

(AP) -- Some of mankind's most devastating inherited diseases appear to be declining, and a few have nearly disappeared, because more people are using genetic testing to decide whether to have children.

Births of babies with cystic fibrosis, Tay-Sachs and other less familiar disorders seem to have dropped since testing came into wider use, The Associated Press found from interviews with numerous geneticists and other experts and a review of the limited research available.

Many of these diseases are little known and few statistics are kept. But their effects - ranging from blood disorders to muscle decline - can be disabling and often fatal during childhood.

Now, more women are being tested as part of routine prenatal care, and many end pregnancies when diseases are found. One study in California found that prenatal screening reduced by half the number of babies born with the severest form of cystic fibrosis because many parents chose abortion.

More couples with no family history of inherited diseases are getting tested before starting families to see if they carry mutations that put a baby at risk. And a growing number are screening embryos and using only those without problem genes.

The cost of testing is falling, and the number of companies offering it is rising. A 2008 federal law banning gene-based discrimination by insurers and employers has eased fears.

Genetic testing pushes hot-button issues: abortion, embryo destruction and worries about eugenics - selective breeding to rid a population of unwanted traits. Yet it is touching a growing number of people:

- In suburban Cleveland, Beth and Thad Meese were stunned to learn during her second pregnancy that they carry genes that can cause cystic fibrosis. Tests show the baby won't have the disease, but they have decided against having a third child or to screen embryos if they do. "I feel like we got lucky" and should not tempt fate again, she said.

- In Boston, Harvard psychologist and author Steven Pinker and his wife, novelist Rebecca Goldstein, learned last year that they carry genes that cause a serious neurological disease, familial dysautonomia. Too old to have children, they shared the news with younger relatives, who are being tested to see if they, too, have the gene. "There's a tendency psychologically to think these are very rare and what are the chances that two people could both have rare genes," Pinker said. "Not only can it happen, but it happened to me."

- In the Canadian city of Vancouver, Jeff and Megan Carroll screened embryos to have two children free of the Huntington's disease gene Jeff has. "I felt very strongly that I didn't want to pass on this," he said. Huntington's "is done killing people in my family when I am gone."

Although genetic testing can raise moral dilemmas, at least one conservative religious group - Orthodox Jews - has found ethically acceptable ways to use it to lessen diseases that have plagued its populations.

"I am a Holocaust survivor. I was born in the middle of the second World War. I hope that I am not a suspect for practicing eugenics. We are trying to have healthy children," said Rabbi Josef Ekstein of New York, who founded a group that tests couples and discourages matches when both carry problem genes.

Some diseases - sickle cell, cystic fibrosis, Tay-Sachs, thalassemia, spinal muscle atrophy - occur when people inherit two bad genes, one from each parent. The genes can pass quietly for generations until two carriers mate; then children have a one-in-four chance of getting the disease.

(Down syndrome is the best known disorder for which prenatal testing has long been available, but it's caused by an extra chromosome during abnormal cell division - not genes inherited from the parents.)

Statistics for inherited diseases are hard to come by - birth certificates often don't list them, and they sometimes aren't diagnosed for months or years after birth. Yet, there's little doubt that testing has put a dent in many.

"We're definitely seeing decreased rates of certain genetic disorders as a result of carrier screening," said Dr. Wendy Chung, clinical genetics

chief at Columbia University. In five years, she has seen only one case of Tay-Sachs, a neurological disease that used to be more common in Ashkenazi, or Eastern European Jews. Children with the disease lack a key enzyme; they lose mental and physical abilities and usually die by age 4.

In the last decade, only about a dozen new cases of Tay-Sachs occurred each year in the United States, said Dr. Michael Kuback, a professor at the University of California at San Diego who tracks the disease.

Ekstein, the rabbi, lost four children to it before founding Dor Yeshorim, a Brooklyn-based group that recruits Jews to be tested. Using confidential PIN numbers, they call a hotline to see if a prospective mate would be a risky match. The group has 300,000 members and tests for nine diseases, including cystic fibrosis.

"In the Orthodox Ashkenazi community around the world, we virtually have wiped out the diseases we screen for," said the group's development director, Allan Binder.

One is familial dysautonomia. Since 2004, only a few children worldwide have been born with it each year, and it soon may cease to exist because of genetic screening, said Dr. Barron Lerner, a Columbia University medical historian. The disease causes faulty nerve development, floppy muscles, digestive and other problems, and kills many by young adulthood.

Fragile X syndrome, the leading cause of mental impairment in boys, may decline because carrier testing for parents and prenatal testing of fetuses is now available for it, said Barbara Biesecker, director of the genetic counseling program at the National Institutes of Health.

Lots of eyes are on cystic fibrosis, a disease that causes sticky mucus

buildup in the lungs, digestive problems and death in young adulthood. More than 10 million Americans - one in 25 to 29 whites, who are more at risk for it than blacks - carry a gene mutation for it. In 2001, the American College of Obstetricians and Gynecologists and other groups recommended that white pregnant women be offered testing for mutations. Tests on partners and fetuses often followed, and an unknown number of abortions.

The impact showed up two years later in Massachusetts, one of the few states testing newborns for the disease at the time. Births of babies with cystic fibrosis dropped, from 29 in 2000 to only 10 in 2003, ticking up to 15 in 2006, said Dr. Richard Parad, a Brigham and Women's Hospital physician who helped set up the screening program.

In California, Kaiser Permanente, a large health maintenance organization, offered prenatal screening. From 2006 through 2008, 87 couples with cystic fibrosis mutations agreed to have fetuses tested, and 23 were found to have the disease. Sixteen of the 17 fetuses projected to have the severest type of disease were aborted, as were four of the six fetuses projected to have less severe disease.

Comparisons to couples not given prenatal screening suggested that screening had cut births of babies with severe disease in half, researchers reported at a genetics conference in 2008. Studies in Canada, Italy, Australia and in Europe also found that cases dropped after screening began.

The Cystic Fibrosis Foundation's registry, which tracks voluntarily reported cases, shows a steady rise in recent years. But that is because more states have started testing all newborns, discovering cases that previously went unreported, some researchers believe. In December, Texas became the final state to add such testing; the first reliable national estimate of cases is expected in a couple of years.

Beth Meese, the Cleveland nurse who discovered from prenatal tests that she and her husband are carriers, wishes they had been screened before pregnancy. By the time they learned of their risk, they had seen an ultrasound and decided to have the baby no matter what its tests showed.

"We saw the baby, saw it moving," she said. "It makes that decision that much more difficult to make."

Gene testing hasn't led to declines in all diseases. Sickle cell, a blood disorder that causes anemia and pain and raises the risk of stroke, has not dropped. It mostly afflicts blacks; gene carriers are said to have sickle cell "trait," which sounds harmless.

"Now we're actually learning that it's not as benign as we thought it was," and that carriers have higher risks for certain medical problems, said Dr. Lanetta Jordan, a Florida physician and chief medical officer of the Sickle Cell Disease Association of America.

Newborn screening is finding more sickle cell carriers and cases, but this doesn't seem to affect parents' future family plans, Jordan said.

Gene testing also has had little impact on Huntington's disease, a progressive, fatal neurological disorder. Unlike many other inherited diseses, only one bad copy of a gene is needed to cause Hungtington's, and symptoms don't usually appear until middle age, after many have already had children.

Fewer than 15 percent of people in families with a history of it agree to be tested, said Kimberly Quaid, an Indiana University genetics researcher.

"They just prefer to live their life and hope for the best," she said.

Jeff Carroll, the Canadian who, with his wife, screened embryos because he carries the Huntington's gene, said it is "unconscionable" to procreate without taking steps to prevent passing on the disease. "Having my test result has immensely improved my life. I was able to make reproduction decisions that ended HD in my family," and to launch a career as a biologist researching the disease, he said.

The number of fertility treatments that include embryo screening has been on the rise in recent years, with nearly 5,200 screenings in 2006, according to the Society for Assisted Reproductive Technology. Carrier testing also is rising. A California company, Counsyl, sells a $349 saliva test for genes for more than 100 inherited disorders. Several thousand people used it over the last year, the company reports.

Eliminating disease is a noble goal but also "should give us pause," Lerner, the Columbia historian, wrote recently in the New England Journal of Medicine.

"If a society is so willing to screen aggressively to find these genes and then to potentially to have to abort the fetuses, what does that say about the value of the lives of those people living with the diseases?" he asked.

It's a touchy issue. The Cystic Fibrosis Foundation points out that the disease varies greatly in severity, and life expectancy with it is now 37 years.

Diseases like familial dysautonomia and Tay-Sachs, which kill before school age, are easier cases. If one of those vanishes, "thank God," said Rabbi Ekstein of the Jewish testing group. "It gives me a very good feeling that we are a part of such life-saving efforts."

More information: March of Dimes: www.marchofdimes.com/pnhec/4439.asp

National Human Genome Research Institute: www.genome.gov/19516567
American College of Medical Genetics: www.acmg.net