

Rare gene disorder common in FLDS

Genetic disorder: About 20 cases have been discovered in 15 years
in two polygamous towns

By Brooke Adams
The Salt Lake Tribune

For more than 15 years, an Arizona physician has quietly cataloged a growing number of cases of a rare genetic disorder in a polygamous community on the Utah-Arizona border that causes severe mental retardation.

Called fumarase deficiency, the disorder occurs so infrequently that fewer than 50 cases have been documented worldwide. Yet pediatric neurologist Theodore Tarby counts somewhere between a dozen and 20 children suffering from the metabolic disease in the twin towns of Hildale, Utah, and Colorado City, Ariz.

"I would say we have about half of the world's population [of the disorder]," Tarby said in a telephone interview from Phoenix.

Genetic diseases are not uncommon in closed societies, experts say, pointing to rare disorders that are found among the Amish, Mennonites and Bedouins.

The twin towns are home to some 8,000 members of the Fundamentalist Church of Jesus Christ of Latter Day Saints, a polygamist sect that has called the Arizona Strip home since 1935.

Most residents trace their family lines back to four original founders - John Y. Barlow, Leroy Johnson and Richard and Fred Jessop - and intermarriages can contribute to the genetic risk.

"The whole town is related to each other one way or another through marriage," said Ben Bistline, an ex-FLDS member and author of *The Polygamists: A History of Colorado City, Arizona*.

Tarby said he first saw a child with the problem about 15 years ago, when an FLDS couple came to a Phoenix clinic with a son suffering from a degenerative condition. He took a urine sample, sent it to a lab in Colorado for analysis and received the startling diagnosis.

Tarby later determined that another child in the family had the same problem - though her parents had thought it was cerebral palsy. Since then, the number of children in the community with fumarase deficiency has grown.

In the disorder, an enzyme necessary to generate energy from food is missing. As a result, cells - particularly brain cells - don't get enough fuel to grow, multiply and function properly. The disorder causes varying degrees of disability, including severe mental retardation, muscle control problems and debilitating epileptic seizures.

Some of the children Tarby has seen look completely normal as infants; others have facial deformities.

"Usually the kids can appear completely normal at birth but then they show delays in development as they grow older," said Nicola Longo, a professor of pediatrics at the University of Utah.

Some children with the severest form of the disorder do not live long. Like many genetic disorders, fumarase deficiency makes children with it more susceptible to common childhood infections, he said.

"Infections that wouldn't normally kill children can be deadly for these children," said Longo, who also is director of metabolic services in the Department of Pediatrics.

Tarby said that in the years he has treated children with the disorder, just one has died. The oldest is now 20 years old.

Longo said the disease can't be detected by existing newborn screenings, though amniocentesis would pick up problems in a developing fetus. That is an option the FLDS are unlikely to pursue.

There is no screening test that might identify gene carriers, either, though researchers could isolate the particular genetic changes found in a patient and then look for the same DNA markers in blood relatives to find carriers,

There may be other identifying clues, however. Longo said the most current research on the disorder has found that people with the recessive gene are prone to certain benign skin tumors and, in women, benign fibrous uterine tumors.

"Carrying the gene is nothing unusual," Longo said. "We all carry at least 20 bad genes. The problem is when you have children with someone carrying the same bad gene."

Even then, odds of giving birth to a child with the disorder is a genetic crapshoot - not, these experts say, due strictly to intermarriage.

"That's a bad concept," said D. Holmes Morton, a physician who has spent more than 20 years working with Old Order Amish in Strasburg, Penn.

Morton's work in the community has led to identification of two genetic disorders: an inherited form of sudden infant death syndrome and a rare form of microcephaly.

He also was instrumental in discovery of a genetic disorder among Mennonites known as maple syrup urine disease, a metabolic disorder.

Morton attributes 10 percent of the genetic disorders seen in the Amish to intermarriages and 90 percent to random genetic drift.

He said small, rapidly expanding populations like these - and the FLDS - cause bad genes to become amplified. Predicting how many children are likely to be affected is a matter of simple math - and chance.

When two carriers of the recessive gene marry, there is a one in four chance of their children having a genetic mutation.

"The problem is when you toss the coin, you never know which way it will come out," Longo said. "It is just a matter of chances."

Some communities, such as the Orthodox Ashkenazi Jews, test for the gene that causes Tay-Sachs disease and share those findings with matchmakers, who then avoid pairing carriers.

"If they arrange marriages, there is an opportunity there," Morton said.

But Tarby has little reason to believe science will influence mating habits of the FLDS, where church leaders decide who marries whom.

Tarby met with about 150 members of the FLDS community in November to explain the disorder and how it could be prevented.

He quickly dispelled a rumor that it was being caused by something in the town's water, saying it was simply procreation. Otherwise, he said, the audience had intelligent, concerned questions.

He told them things that would "stop production of these kids," such as prenatal testing, but that is "only worthwhile if you are going to interrupt pregnancies" and genetic testing would only work if "they would change their mating habits."

"They consider these children to be their responsibility from God and their duty is to produce as many children as possible," he said. "There isn't any reason in their view to slow down the having of children."