

## HEALTHY LIVING

## A deadly gene

Years of study unlock reasons behind infant's death

BY MARY ANN ROSER

Cox News Service

As soon as the Messers saw their newborn son, they knew something was wrong. The baby, who had hardly kicked in the womb, emerged with a beautiful face but with a tiny cry and a body too weak to move.

The delivery room doctor at Scott & White Hospital in Temple, Texas, told Ann Messer and her husband, then-state Rep. Bill Messer of Belton, that Andrew would not live to be a year old. He was diagnosed with congenital muscular dystrophy.

Andrew was 5 1/2 months when he died in 1985.

The couple then started noticing that other women in the family were losing children. Two of Ann Messer's cousins had sons die from what appeared to be the same disorder.

After 23 years, the Messers finally got some answers recently.

A team of scientists in the United States and Germany said it has discovered the gene that caused the rare disease — known as X-linked infant spinal muscular atrophy — that killed Andrew and three sons of Ann Messer's cousins. It was announced in a paper published in *The American Journal of Human Genetics*.

The X-linked form is the most severe type of spinal muscular atrophy, a disease in which the big nerves in the spinal cord die and can't send signals to the muscles, resulting in the "floppy" body the Messers saw in the delivery room. Without muscle tone, the condition worsens until the child can't chew food or breathe, said Lisa Baumbach-Reardon, the paper's senior author and an associate research professor in the department of pediatrics at the University of Miami's Miller School of Medicine.

The symptoms of the disease, which is in the family of muscular dystrophy, are similar to those of amyotrophic lateral sclerosis — also known as Lou Gehrig's disease — and in 75 percent of the cases, death occurs by age 2, Baumbach-Reardon said.

The odds are 50-50 that a woman who is a carrier will produce a son with the disease. The Messers' first-born son, Will, 28, doesn't have it.

Finding the gene means that scientists now know how the disease is transmitted (from mother to son only) and that tests can be done to determine whether a woman is a carrier and whether an embryo or fetus has the mutation. Although therapies have not been developed for turning off the gene that

causes the disease, technology exists for isolating embryos without the flawed gene so they can be implanted into the womb of a woman who is a carrier, ensuring a son free of the disease.

Finding the gene also means doctors can use a DNA test to diagnose a fetus or a boy who has the disease and perhaps one day develop treatments.

"We've been waiting so long for this breakthrough," said Ann Messer, 56, as she sat clutching a photograph of Andrew in her husband's Austin, Texas, office.

"It's a terrible tragedy," said Bill Messer, 56, now a Capitol lobbyist. "But a great good has come from it, not just for Ann's family but for all families."

Ann Messer and her cousins never believed the doctors who insisted that they had married men with the same flawed gene. The odds were simply too great. But that was the only explanation they had.

The gene discovery "confirmed what we thought 23 years ago," Messer said. "This is

## The gene discovery

Researchers searching for the cause of X-linked infant spinal muscular atrophy found a defect in the UBE1 gene on the X chromosome.

The gene carries flawed instructions for destroying proteins that the body needs to eliminate, which can clog the body like a garbage disposal system that's backed up. That means the body can't function normally.

The flaw is similar to what happens with Parkinson's disease, said Lisa Baumbach-Reardon, the senior author of the research paper and an associate research professor in the department of pediatrics at the University of Miami's Miller School of Medicine.

the proof."

Baumbach-Reardon said she doesn't know how many babies are born with the X-linked disease or how many women have miscarriages because of it, but she said she feels certain it is often undiagnosed or misdiagnosed.

The more common form of spinal muscular atrophy is believed to affect one in 6,000 births, she said. She identified 16 families worldwide with the X-linked variety, including the Messers and Ann Messer's cousins, who joined the study. She said it's possible that many of the 4 percent of the babies born with spinal muscular atrophy might actually have the X-linked form.

Because the defective gene is recessive and on the X chromosome, the disease can be passed on only to boys, who inherit the X chromosome from their mothers and a Y chromosome from their fathers. Girls, who have two X chromosomes, can carry the defective gene but won't develop the disease, Baumbach-Reardon said.

"It's fantastic to see this work come out," said Sharon Hesterlee, vice president for translational research at the Muscular Dystrophy Association, which helped finance the study. "It was a big needle-in-the-

**Lisa Baumbach-Reardon, a University of Miami geneticist who has been tracking the UBE1 gene that can cause infant spinal muscular atrophy, says Ann and Bill Messer's cooperation with her research was invaluable.**



PHOTO BY KELLY WEST / COX NEWS SERVICE

Researchers have discovered a rare, fatal gene that kills infant boys and is responsible for the death of four boys in the same Texas extended family. Ann Messer holds a photo of her son Andrew, who died of the disease, next to her husband, Bill, right, and brother, Phillip Whitworth.

haystack problem for Lisa."

Baumbach-Reardon said she spent 15 years seeking the gene, following the work of a Baylor College of Medicine researcher, the late Dr. Frank Greenberg, who suspected that the gene was passed by mothers to their sons but couldn't prove it without the gene.

Isolating the gene is a big step toward understanding how the disease process works, but it's like the end of a chapter, not the end of a book, said Vishy Iyer, associate professor of molecular genetics and microbiology at the University of Texas at Austin.

Years of work remain to develop therapies, if there are any, he said. It can take 10 years to develop a treatment after a gene is discovered, and finding money is always a challenge, Baumbach-Reardon said.

Some experimental drugs are in clinical trials for spinal muscular atrophy, Hesterlee said.

Having the Messers and Ann Messer's cousins in the study was a huge help, Baumbach-Reardon said. The families gave blood for study, and tissue and blood samples from some of their sons had been preserved for future research. All of that was needed to unravel a family mystery.

Ann Messer said her mother, Edna Whitworth of Austin, had a miscarriage and lost a 2-day-old son, probably because of the disease. But her mother also had

two healthy boys, including Ann's brother, Phillip Whitworth, an oil and gas lawyer in Austin.

Ann Messer's cousin Catherine Blevins of Houston was living in New Orleans in the 1980s when she gave birth to a "floppy baby" who died at 18 months. Everyone thought "it was one of those random things that happened," Ann Messer said.

Ann got pregnant, and two months after Andrew was born, Indiana cousin Connie Alexander, who now lives in Fort Worth, Texas, gave birth to a son who had the same "floppy" look as Andrew. He lived 11 months. The puzzle was starting to come together.

By then, Blevins had had another son, who looked just like the other sick babies. He lived to age 18 with the help of a feeding tube, a ventilator to help him breathe and constant care.

None of the boys had mental impairments, and Andrew, despite his health problems, was a sweet, happy child, Ann Messer said.

"He was very cherished for the 5 1/2 months we had him," she said.

Just knowing what caused the illness is important to families, and those with a family history can seek testing and get answers, the Messers said.

"There are a lot of blessings in all of this," Bill Messer said, "and it's a great one (we're getting) this week." ■



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