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Hoping for a rare find

A Wellesley family works to fund, promote research on son's disease

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In many ways, Ben and Noah Siedman have a typical brotherly relationship. They play football, ride scooters, fight over the television, and chase each other with water balloons. The two Wellesley boys share a bedroom, with one side dominated by Ben's passion – farm animals – and the other reflecting Noah's interests in science and space. Noah, 8, gets frustrated sometimes when his 6-year-old brother can't keep up with him, but in true younger sibling fashion, Ben looks up to his big brother.

The boys' games and antics may be typical, but their lives are not. At an early age, Ben was diagnosed with Sanfilippo syndrome, a rare and fatal genetic disorder. Unless a cure is found, Noah will not watch his younger brother grow up.

Sanfilippo syndrome falls into a category of diseases called lysosomal storage disorders, said Dr. Mark Korson, Ben's physician at the Floating Hospital for Children at Tufts New England Medical Center.

Korson, who specializes in pediatric metabolic diseases, explained that children afflicted with Sanfilippo are missing an enzyme that is needed to break down a complex body sugar. As this sugar molecule accumulates in the cells, tissues, and brain, it causes progressive damage, leading to a loss of language and cognitive skills, the ability to walk, and, ultimately, death. In cases of Sanfilippo syndrome, Korson said, "the brain is the most affected organ."

Children with this disease have an average life expectancy of 10 to 15 years, although there are exceptions, depending on the severity of the disease, according to Dr. Robert Yu, director of the Institute of Molecular Medicine and Genetics at the Medical College of Georgia.

Ben's family has had to undergo an unwanted education about the illness. Noah offers this analogy to explain his brother's disease:

"Let's say you have a garbage truck in your body to take stuff out," he said. "Benjamin doesn't have that. So it all builds up. And then it takes over – mostly in his brain and legs."

Ben's and Noah's parents have been talking to them gradually about Ben's situation. Ben knows he is special, said his father, Stuart, 39. They have been counseled to wait until Noah asks questions and answer them honestly.

"Ben doesn't exhibit a lot of things that will come," said his father.

He has experienced some symptoms, though. His flexibility, strength, and range of motion have decreased noticeably in the past nine months, leaving him unable to sit cross-legged or stand up from a sitting or lying position.

Emotionally and behaviorally, he is having an increasingly difficult time staying focused and

sitting still. He is quicker to break down than he used to be, and he is getting more frustrated with his inability to do what he sees other children doing. And he has always been hit harder by common illnesses, such as colds or flu, than normally developing children, said his father.

Cognitively, he is still on the upswing, said Stuart, although he is well behind most children his age. His language continues to develop and his ability to construct complex sentences and recognize letters is still improving.

Because he was diagnosed early, he was taught sign language to help him converse. Although he did not start speaking until he was nearly 4, "once we broke down that barrier, it all came out in a rush," Stuart said.

Right now, Ben is a polite, active child with an engaging smile, who is eager to lose his first tooth. He is integrated into a regular kindergarten class at Bates Elementary School. He rides a bike, goes to classmates' birthday parties, and rides horses as part of a special needs program. He also plays with his younger sister, Isabelle, 3.

Ben's mother, Jennifer, 36, said that he is doing remarkably well for a child with Sanfilippo syndrome.

"There could be another 6-year-old who is wheelchair-bound, who never learned to speak,

and who is further progressed. There's a range of how this progresses."

At some point, Ben will plateau and then begin to lose skills.

"When he'll get there, we don't know," said Stuart. "It'll all go downhill from there. There's going to be a point when even if a cure is found, it'll be too late."

"I don't know when I'm going to lose that smile," he said tearfully. "That's going to be the hardest time."

"It was very hard when he turned 6 years old," said Jennifer. "He's 6, and that could be half his life."

Ben was diagnosed with Sanfilippo when he was 15 months old. The Siedmans had taken him to Children's Hospital after a high fever had sparked a seizure.

"I'm positive that without that chain of events, we wouldn't have known it until he was 2 or 3," said Stuart.

"It was a surreal moment," said Jennifer, "when you're standing in the room with your baby and the CAT-scan-room lady is behind the glass, and all of a sudden, there's only one lady, and then there's a phone call and there's two, then there's another phone and there are four people in the room. And then the books are coming off the shelf."

Sanfilippo was identified in 1963, and when Ben was diagnosed, little had been written about the disease. Stuart said that when doctors were pulling books off shelves, "They were showing us a paragraph, not a chapter."



GLOBE STAFF PHOTO/DAVID KAMERMAN
Stuart and Jennifer Siedman with their children (from left) Noah, 8, Ben, 6, and Isabelle, 3. Ben has been diagnosed with Sanfilippo syndrome, a rare and fatal genetic disorder.

It is still a relatively unknown disease that often goes undiagnosed until age 5 or 6, said Korson, when children exhibit obvious speech and language problems.

"Doctors are not very well trained about metabolic disorders," he said. "It's hard to diagnose what you've never seen or heard about."

A Sanfilippo child might develop normally for a few years, Korson said, but then may develop upper respiratory problems, recurrent ear infections, and delayed speech. It's not until the accumulation of sugar causes symptoms such as hyperactivity, irritability and restlessness, sleep disorders, stiffening joints, and further delayed development that the pieces get put together.

The disease affects about 1 in 25,000 births, according to the National MPS (Mucopolysaccharides) Society. Both parents must be carriers of the gene, something the Siedmans were not aware of when they married 13 years ago.

After Ben was diagnosed, the Siedmans joined forces with parents of a Sanfilippo child in Chicago to raise money for research on the disease. Stuart took advantage of a one-year paid social service leave offered by his employer, Xerox Corp., and spent the year working on behalf of the Children's Medical Research Fund.

In honor of Ben's fifth birthday, the Siedmans established their own association, the Sanfilippo Research Foundation, one of a handful of foundations across the country that raises funds individually but works collaboratively on funding research.

"We want to make sure that something that's viable doesn't go unfunded," said Stuart.

The Sanfilippo Research Foundation has held a variety of fund-raisers, said Stuart, the biggest one being an annual golfing event at the Sandy Burr Country Club in Wayland in mid-August.

"Birdies for Ben," first held on behalf of the Children's Medical Research Fund three years

ago, had a first-time goal of \$20,000, said Stuart. "We ended up raising over \$79,000. That activity really enabled us to say, 'We can do something,'" he said. Many local businesses have held fund-raisers, friends have run marathons, and strangers have sent money, all on behalf of the foundation, Stuart said.

"I'm still looking for that million-dollar donor, because I truly believe the research will reach the point where there will be a treatment or cure," he said, adding that \$100,000 funds about one researcher for a year. "I don't know how many diseases there are out there that have been cured by one person in one year."

In addition to his own research at the Medical College of Georgia, Yu listed the University of California, University of North Carolina, and Michigan State University as some of the academic institutions researching a cure. Locally, Transkaryotic Therapies Inc. in Cambridge, a biopharmaceutical company, is also conducting research on lysosomal storage disorders, according to president Richard Selden.

"The most important thing is to learn how to deliver the missing protein to the brain," said Selden, who lives in Wellesley. The brain is naturally protected by a biological shield called the blood-brain barrier, he said, and "solving the problem - getting past the blood-brain barrier - is very important" in curing diseases such as Sanfilippo.

"We're committed to finding a way to break down the barrier," Seldon said. "I just don't know how long. This is among the most important challenges in medicine today."

For his part, Noah does what he can to help his younger brother, including setting up lemonade stands to raise money. He has contributed proceeds of \$19 to the foundation, and he is hoping to move his stand to a site with more traffic.

"I still would like to help him more," Noah

Research still in early stages

Sanfilippo syndrome is a rare and fatal genetic disorder that affects about 1 in every 25,000 live births. It takes its name from Dr. Sylvester Sanfilippo, one of the doctors who first described the condition in 1963.

Sanfilippo, also known as MPS III, is a mucopolysaccharide disorder. It falls within a broader group of genetic disorders known as lysosomal storage disorders. Children with Sanfilippo lack an enzyme needed to break down natural compounds called mucopolysaccharides - long chains of sugar molecules used to build connective tissues in the body. Instead, the molecules are stored in cells in the body, causing progressive damage. This accumulation leads to loss of development and skills and ultimately results in death. The average life expectancy for a child with Sanfilippo syndrome is 10 to 15 years, according to Dr. Robert Yu, director of the Institute of Molecular Medicine and Genetics at the Medical College of Georgia.

Infants born with Sanfilippo typically appear normal at birth, but as cells become damaged, symptoms appear, including recurrent upper respiratory tract infections and ear infections, a coarse facial appearance, hyperactivity and irritability, and delayed development of cognitive and motor skills. As the disease progresses, the build-up of mucopolysaccharides causes further hyperactivity, sleep disorders, loss of speech, mental retardation, dementia, and, finally, death.

At present, there is no cure for Sanfilippo syndrome, but researchers are investigating gene therapy, cell therapy, and enzyme replacement, according to Yu. Gene therapy would deliver the missing gene to the central nervous system, but it carries serious risks, including brain tumors, Yu said, and cell therapy would deliver normal cells into to body. Enzyme replacement therapy has been successful in treating some other lysosomal storage disorders, Yu said, but it is more difficult with Sanfilippo syndrome because the disease affects the brain.

"The brain is protected from circulating blood components by the blood-brain barrier," he said. "Otherwise, you'd have a stroke. It prevents enzymes from getting into the central nervous system. People are trying to figure out how to open up this barrier, even temporarily, to allow enzymes to enter."

Research on Sanfilippo is four to five years old in the United States, Yu said, and he hopes that there will be a cure within 10 years. "That's too long for some patients. I know that," he said.



PHOTO/LOVELANE

Horseback riding therapy helps Benjamin Siedman combat the physical effects of Sanfilippo syndrome.

said. "We all would."

The second-grader recently wrote a letter to CBS after learning that "The Early Show" was sponsoring a "Week of Wishes." He asked for a horse for his younger brother so that he could ride and take care of it whenever he wanted.

"I could go with Ben and do things with him that he loves to do so much," he wrote, with help from his mother. "That would be special for me cause I think someday I will not have Ben to share things."

"Mostly, I want my brother to grow up but that is a very complicated wish so for now a horse would be just fine," he continued.

Noah's wish was not selected.

Perhaps the hardest part, said Jennifer, is the thought that Noah and Isabelle will grow up living with Ben's loss.

"I'm going to have the pain of losing a child, but I will have lived for 27 years without that pain," she said. "My son and daughter will essentially have that pain for their whole lives."

Always aware that the clock is ticking, the Siedmans try to balance their work with the foundation with their family activities.

"We know that time is precious, not only for Benjamin, but also for his siblings with Benjamin. We really want to make the most of it," said Stuart.

For more information, contact the Sanfilippo Research Foundation, P.O. Box 81268, Wellesley 02481, call 617-899-4158, or visit www.bensdream.org.

For more information on Sanfilippo syndrome, visit www.mppsociety.org.