

Delivering hope

Lauren has a rare genetic disease. On Friday, she welcomed a new sister whose cord blood could cure her. But it isn't that simple.



Lauren Bromet, 2, right, and sister Katherine, 4, meet their newborn sister Madeline on the day of her birth as mother Rebecca looks on at West Suburban Medical Center in Oak Park. (Tribune photo by Scott Strazzante / February 12, 2010)

By Deborah L. Shelton, Chicago Tribune

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Mike and Rebecca Bromet thought their 2-month-old daughter's porcelain complexion was a harmless family trait.

But their pediatrician suspected Lauren's pale skin was a sign of trouble.

A splatter of the girl's blood, accidentally spilled during a test, grabbed her father's attention. Instead of a normal deep red, he saw a tiny puddle of pink. Lauren eventually was diagnosed with a rare, life-threatening blood disorder called Diamond Blackfan anemia, a condition that doesn't allow her body to produce red blood cells without

assistance.

The diagnosis propelled the Bromets on a journey they never expected to take, down a road no parent wants to travel.

"We have to cure Lauren," Rebecca Bromet remembers thinking.

On Friday, the hope of a cure arrived when the Oak Park couple welcomed another baby daughter. Blood from the infant's umbilical cord was saved, potentially providing a lifesaving stem cell transplant for her sister.

The couple know the baby won't have Lauren's disease because they underwent a procedure called pre-implantation genetic diagnosis. Pioneered in Chicago, the process allowed doctors to implant a healthy embryo who is a tissue match for Lauren.

The technology to create so-called savior siblings has been around for about two decades, leading to a few dozen donations, but the decision to use it remains difficult.

Despite their considerable financial and emotional investment, the Bromets are torn about pursuing the stem cell transplant, which carries serious risks for Lauren, now 2.

And the clock is ticking. Lauren, a chatty toddler, is doing well on medication now, but no one can predict how long that will last, and stem cell transplants have the highest success rate in younger children.

Rebecca said she has agonized over her daughter's uncertain future. How can a mother look into a child's innocent eyes and feel she hasn't done everything possible she can to help her?

On the other hand, the couple don't want to put Lauren at risk of unnecessary complications, or even death.

While the Bromets are grateful for the technology providing them with options, they are mindful that science cannot answer all of their questions.

A tough choice

In Lauren's first year of life, she had seven blood transfusions. When she was about 6 months old, she was prescribed a daily dose of prednisone, a corticosteroid delivered in a grape-flavored liquid squirted into her mouth.

The steroid stimulates her bone marrow to produce red blood cells. If a monthly blood draw shows she has too few or is producing them too slowly, her medication is adjusted. If that doesn't work, she must get a transfusion.

When Lauren is grouchy, her parents wonder if she's severely anemic and needs a blood

transfusion or if she's just behaving like a typical 2-year-old.

"We're always asking ourselves, is she pink enough?" Mike Bromet said. "She's always pale so it's always a debate."

Up to 80 percent of patients initially respond positively to prednisone, and some live into their 30s or 40s. But the side effects of long-term use can include stunted growth, elevated blood sugar and high blood pressure. It increases the risk of osteoporosis and certain cancers. And sometimes, it stops working.

"You can't predict at the beginning which patients are going to respond one way or other," said one of Lauren's doctors, Dr. Rishi Lulla, a fellow in hematology, oncology and stem cell transplantation at Children's Memorial Hospital.

Stem cell transplantation can provide a permanent cure for the anemia, but the transplants carry a 10 percent mortality risk, and enduring one can be a brutal ordeal.

A transplant also wouldn't help with complications of the disorder, which can include congenital abnormalities of the heart, kidney and bone. But so far, Lauren appears to have been spared those problems and her treatment has gone well.

Still, there have been scares. Once she was rushed to a hospital for a transfusion after arriving in California for a holiday visit.

And there may be consequences to delaying a transplant. The Bromets said they were told outcomes were best in children 5 and younger.

Parents often agonize over making these choices, Lulla said.

"The Bromets are not the first parents of children we take care of who have pursued an option like this," Lulla said, referring to preimplantation genetic diagnosis. "It's a complicated, emotional decision and it's different for every family. ... We support the family whatever the choice is."

Sometimes, stem cells are taken from the bone marrow of an older donor, either through a surgical procedure or by using a drug to force marrow cells into the bloodstream, where a special machine extracts them. But tests showed Lauren's sister, Katherine, 4, wasn't a match.

The other option is stem cells from a public cord blood bank or from the umbilical cord of a newborn sibling.

The Bromets had been planning to have a third child anyway. But the only way to ensure that the baby could help her older sister was to turn to science.

'One beautiful baby'

The Reproductive Genetics Institute, located on Chicago's North Side, pioneered the technology that is helping the Bromets under its late founder and director, Dr. Yury Verlinsky, two decades ago.

Since then the institute has fostered 59 pregnancies involving healthy, tissue-matched babies, said the institute's laboratory director, Lana Rechitsky.

"We have five ongoing pregnancies and 45 babies were born," she said. "As far as we know, 25 babies had successful transplants." In the other cases, the procedure has yet to be performed, she said.

Another two to three dozen children worldwide have become sibling donors as a result of preimplantation genetic diagnosis performed elsewhere, Rechitsky said.

In the Bromets' case, the institute first needed to make sure the baby didn't have Diamond Blackfan anemia, which can be inherited. Testing showed neither parent was a carrier; a spontaneous genetic mutation caused Lauren's illness.

Rebecca went through three rounds of in-vitro fertilization. Most of the embryos were not viable. Just when they started to give up hope, the last round produced two healthy embryos, a boy and a girl.

A single cell from each was screened for Diamond Blackfan anemia, tissue type and major chromosomal abnormalities. Both embryos were cleared for implantation.

"My heart jumped out of my chest," Rebecca said. "It was such a blessing."

Two weeks later, an ultrasound showed "one beautiful baby growing," she said.

Over the years, ethical questions have been raised about embryo selection. Some critics worry it could lead to the creation of designer babies, selected for gender or other traits unrelated to genetic disease. And they fear that children screened as embryos might later feel unloved or exploited.

Rebecca Bromet said she would never undergo such a grueling and expensive process to pick a child's gender or eye color.

The couple, both lawyers, spent more than \$50,000 given to them by family members on the procedure.

"It is physically and emotionally difficult to go through this," Rebecca said. "I couldn't imagine going through this except to ensure a healthy tissue-matched sibling for a sick child."

She said the couple find the term "savior sibling" objectionable.

"This child means so much more to us than her bone marrow," she said. "That term suggests that that is her only value to us and that is absolutely not true."

A risky solution

Lisa Nash understands what the Bromets are going through. She and her husband were the first couple to use preimplantation genetic diagnosis for the purpose of ensuring a perfect stem cell donor for an ailing sibling. That baby, Adam, is now 9. His sister, Molly, is 15.

Molly was critically ill with Fanconi anemia, a lethal genetic blood disease, when she received Adam's umbilical cord stem cells in 2000. The transplant saved her life.

Nash, of Denver, said parents pursuing this course ride an emotional roller coaster.

"You have the emotions of watching your child who was born sick and knowing what could ultimately happen to them," she said. "You have the emotions of having gone through this procedure, and you are going to have a healthy child, which is amazing in itself."

The Bromets are hoping for the best with Lauren's condition but also believe in planning for worse.

"Sitting here today, my goal is that Lauren will continue to respond to medication and she won't ever have to go through a stem cell transplant," Rebecca said three weeks before the baby was due.

But if Lauren needs repeated blood transfusions or begins to suffer side effects from the steroids, they plan to go forward.

Lauren would undergo chemotherapy to empty her bone marrow and suppress her immune system. Then the donor cells would be injected intravenously into her bloodstream, creating healthy marrow. Patients are usually in isolation for about 30 days afterward, and full recovery typically takes three to four months if all goes well, Lulla said.

The Bromets hope that advances in science will make the transplants less risky in the future, which would make it worthwhile to wait.

Meanwhile, they are educating themselves about Lauren's disorder. Rebecca joined the board of directors of the Diamond Blackfan Anemia Foundation (www.dbafoundation.org). The Bromets have attended the organization's annual Camp Sunshine outing in Maine and met other affected families.

On Rebecca's final prenatal visit, she had one pressing question for obstetrician Dr. Lisa

Chorzempa.

"Mike asked me to ask if you know ways to get the maximum amount of cord blood," she said. As patients receiving the stem cells gets older, more cells are needed. "We want to make sure we have enough that we can use it at any point in the future."

During her pregnancy, Rebecca carried a cord blood collection kit with her when she was away from Oak Park in case she ended up delivering unexpectedly at some place other than West Suburban Medical Center, where her cesarean section was scheduled.

On the big day, everything went as planned. Madeline Cohen Bromet was born at 9:27 Friday morning, and her umbilical cord blood was collected.

"She's a great baby," said her ecstatic father. "She is just beautiful."

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