

## Improved Diagnosis Leads to an Easier Treatment for Monogenic Diabetes



Lilly (center) with father, Mike (left), and mother, Laurie (right)

Sixteen-year-old Lilly remembers the pressure of being a young child on insulin therapy for what was thought to be type 1 diabetes—the monitoring of her blood sugar (glucose), the pain of needle sticks, the lack of independence and freedom. “It was very stressful,” Lilly says, “and it was really hard.”

But now, instead of shots and constant monitoring, Lilly only needs to take several pills twice a day.

This new treatment is possible because Lilly actually has a rare—and often misdiagnosed—

form of diabetes known as monogenic diabetes, and some types of monogenic diabetes can be treated with a class of drugs called sulfonylureas. This medication helps her pancreas release the

insulin it makes, allowing her to live without the need for insulin injections.

Lilly’s mother, Laurie, describes Lilly’s transition from insulin to sulfonylurea as a miracle. “We prayed for a long time after Lilly was diagnosed that there would be a cure,...but we in our wildest dreams didn’t think that it would happen so quickly, and certainly not that it would come in the form of a pill!”

### Growing Up with Diabetes

Lilly was diagnosed with type 1 diabetes when she was 1 month old. Type 1 diabetes is an autoimmune disease in which the body launches a mistaken attack that destroys the insulin-producing beta cells in the pancreas. As a result, people with this disease must carefully monitor their blood sugar levels and must receive insulin either by injection or through an insulin pump. Lilly’s pancreas was not releasing insulin, though her case was atypical because tests indicated that her immune system wasn’t

attacking her beta cells. Additionally, though type 1 diabetes is most often

diagnosed in young people, it is not often found in month-old babies. However, as Laurie says, the doctors diagnosed Lilly with type 1 diabetes because “there was nothing else to call it.”

**“You can never let your guard down when you have a child with diabetes, let alone a baby with diabetes,” Laurie says.**

# PATIENT PROFILE

Lilly's parents provided the rigorous monitoring and treatment Lilly needed. Laurie would prick baby Lilly's heels—sometimes 10 to 15 times a day—to check her blood sugar levels and then give her food if her blood sugar levels were too low or give her insulin if her blood sugar levels were too high. “It made me very sad, as a mother, to have to withhold food from my baby when she was hungry because her blood sugar was [too]

high,” Laurie says.

Likewise, if Lilly's blood sugar was too low, Laurie would have to feed her, even

if Lilly wasn't hungry. Laurie kept tubes of cake frosting around for such times, because it was a ready source of sugar she could rub on Lilly's gums to help bring her out of her “lows.”

Maintaining Lilly's health those first few years meant constant vigilance. Laurie says that diabetes was like having an extra child in the family, in addition to Lilly and her brother, Nathan, and sister, Charlotte. “You can never let your guard down when you have a child with diabetes, let alone a baby with diabetes,” Laurie says.

When Lilly was 4 years old, she was put on an insulin pump after she had two seizures in 3 months due to low blood sugar. The pump made insulin administration easier by providing insulin through a tube that stays inserted under the skin. The pump helped stabilize Lilly's blood sugar

levels and also freed her from having to endure individual insulin shots throughout the day.

However, changing the pump's infusion set still required being stuck with a long needle, which Lilly hated. “When my mom was trying to stick the needle in me, I would run away from her,” Lilly remembers. “And it was very frustrating, obviously, for my mom, because that was

something I needed.” The pump made life easier, but Lilly was still too young to monitor her blood sugar on her own.

***Living with diabetes as a young child can be confusing. When Lilly was put on the insulin pump, she says, “A lot of my friends would ask, ‘Oh, why do you have to wear that?’ And I really didn't know.”***

She needed an adult to calculate how much insulin she required and operate the pump.

Living with diabetes as a young child can be confusing, Lilly says. She didn't always understand why she couldn't do the same things that her siblings did, such as go on sleepovers, or why her mother had to come along and monitor how much she ate at birthday parties. And sometimes other children didn't understand, either. When Lilly was put on the insulin pump, she says, “A lot of my friends would ask, ‘Oh, why do you have to wear that?’ And I really didn't know.”

## **A New Diagnosis and Hope for Easier Treatment**

After Lilly's diagnosis, her parents became involved with the type 1 diabetes advocacy organization, JDRF. In June 2006, her father, Mike,

# PATIENT PROFILE

attended a meeting sponsored by JDRF where a speaker mentioned new research on a rare form of diabetes called “monogenic” diabetes. Mike was immediately intrigued, as the description of monogenic diabetes fit Lilly perfectly.

Monogenic forms of diabetes result from changes in a single gene (as opposed to other forms of diabetes, which result from the activity of multiple genes). Monogenic diabetes accounts for about 1 to 5 percent of all cases of diabetes in young people. A subset of monogenic diabetes is called neonatal diabetes, which is diagnosed before 1 year of age and which is often misdiagnosed as type 1 diabetes. In most cases of monogenic diabetes, the person has an altered form of a gene involved in insulin production, and that change reduces the amount of insulin the person makes or secretes into the bloodstream. Most excitingly, as Mike heard at the meeting, a common and inexpensive class of oral medication used to treat type 2 diabetes, called sulfonylureas, had shown promise as a treatment in specific types of monogenic diabetes. These medications help the body’s beta cells release insulin. A “transition” therapy had been tested that involved slowly replacing insulin treatment with sulfonylurea pills.

Laurie was skeptical, but hopeful. After years of constant testing and insulin administration, the idea that Lilly could instead just take some pills seemed preposterous. Nonetheless, Mike and Laurie decided to have Lilly’s DNA tested. The test confirmed that Lilly had monogenic diabetes and that she was a candidate for the transition to sulfonylurea therapy. But this therapy had

not been widely used in the United States, and there were no guarantees that sulfonylurea would be able to replace Lilly’s insulin treatment. Finally, the transition attempt might also cause Lilly’s blood sugar levels to fluctuate wildly, a frightening proposition for a family that had spent so much time working to keep Lilly’s blood sugar in a healthy range.

Lilly, then 6 years old, also had reservations. When her parents explained what would be involved—a hospital stay, and then taking pills instead of needing her pump—she started crying. “I did *not* want to go to a hospital,” Lilly remembers. “I did *not* like them at that time, and I was not happy going.” Additionally, she had lived her whole life needing insulin and had grown very emotionally attached to her pump. “It was something I’d always had when I was younger...,” Lilly explains. “It was very important to me.”

Despite these reservations, the fact that Lilly’s health and quality of life could be greatly improved ultimately convinced Lilly and her family to take the risk and go ahead with the treatment. Lilly would be starting first grade that fall, and they hoped that she could start school no longer needing insulin.

## Trading One Therapy for Another

To begin the therapy transition, Lilly’s clinical team cut her insulin dose in half and gave her a small dose of the oral sulfonylurea medication. It was a balancing act to find the right dosage of the new medication while reducing her insulin use.

# PATIENT PROFILE

At first, the results were frightening: Lilly's blood sugars went, in Laurie's words, "sky high." Lilly was also scared, at first. Because she was a pioneering patient in this sort of procedure, there was a lot of attention focused on her, a lot of hospital staff coming and going, and a lot of tension all around. Lilly says that her friends were an incredible source of support while she was in the hospital. Their visits were a comfort and a welcome time of normalcy where Lilly could play with her friends.

"They helped me get through hard times," Lilly says.

***When a blood test showed that the treatment was working, Laurie says, "We all started crying and hugging, and it was just this incredible moment."***

On day 4 of the transition, Lilly reached a dramatic turning point. When she entered the hospital, a blood test had confirmed that her beta cells were not releasing insulin. By day 4, the medication had allowed her insulin dosages to be significantly reduced. Then, another test showed that her beta cells were now able to release insulin into her bloodstream. The new medication was working. When the doctor informed them of the good news, Laurie says, "We all started crying and hugging, and it was just this incredible moment. Even the doctor was blown away."

By the time Lilly left the hospital on day 5, she was still taking small doses of insulin, but her doctors were confident that the family could continue her treatment transition at home. On day 9—August 23, 2006—Lilly took off her insulin pump for the last time. Then, after taking her medication (but no insulin) for the night, Lilly celebrated with a big

bowl of ice cream while her parents looked on nervously. An hour later, her blood sugar levels were completely normal.

## A Life Without Insulin Therapy

When asked how it felt to no longer need insulin therapy, Lilly says, "It felt really good, because I got to be more independent at that time."

Finally, she could do many of the things that

other children her age could do, unconstrained by her diabetes. As of publication, the

sulfonylurea therapy has continued to keep Lilly's blood sugar levels in a normal range without the need for insulin for almost 10 years.

Unfortunately, not all people with diabetes can be helped by sulfonylureas. Lilly remembers hoping that her cousins and friends who have type 1 diabetes would be able to switch from insulin to pills. She was sad when her parents explained that the therapy wouldn't work for kids with type 1 diabetes, as they have a different form of diabetes than she has. Even for some people with monogenic diabetes, sulfonylurea treatment may work partially or not at all, depending on the genetic change that causes their disease and on their particular circumstances.

Lilly and her family have continued to share their story to raise public awareness about monogenic diabetes and the sulfonylurea therapy that can help some people with the disease. Most children

# PATIENT PROFILE

are not tested for monogenic diabetes, and many health providers are not aware that infants with diabetes may have monogenic diabetes rather than type 1 diabetes.

Lilly's family's advocacy led to the first neonatal diabetes registry in the United States. In 2009, Illinois passed "Lilly's Law," establishing a registry of Illinois children diagnosed with neonatal diabetes before their first birthday. This registry helps doctors connect children and their families with appropriate treatments and could also help scientists identify new genes that cause neonatal diabetes. Laurie and Mike have also produced a television documentary featuring their and other families' stories ("Journey to a Miracle: Freedom from Insulin"), which was released in early 2015.

Support for scientific research is critically important, Laurie says. "Research takes time. It takes decades. Research builds on research that builds on research." Thinking about the research that led to Lilly's diagnosis of monogenic diabetes from a DNA test, and her new treatment, Laurie explains, "This breakthrough seems sudden, but...it was decades in the making." Laurie is excited about the benefits that future research might bring.

## Looking to the Future, Reflecting on the Past

Now 16 years old, Lilly's future is bright. A high school sophomore, she enjoys history and vocal ensemble. She attends theater and acting programs and has enjoyed performing for years. She particularly loves singing and dancing, and she wants to pursue a career in musical theater.

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And what of Lilly's old insulin pump, that symbol of her first 6 years on insulin? They still have it...in a closet. They sometimes bring out the pump at interviews, using it as a visual reminder of how their lives have changed. In the past, there was the pump and all the supplies that went with it...and now, there is only Lilly's pills.

"I feel like I am very lucky," Lilly says. When she thinks about being on insulin, and of all the other children and families dealing with diabetes, she is very thankful. "I just feel really grateful to have this amazing thing happen to me."

*For more information on monogenic diabetes, please see [www.niddk.nih.gov/health-information/health-topics/Diabetes/monogenic-forms-diabetes-neonatal-diabetes-mellitus-maturity-onset-diabetes-young/Pages/index.aspx](http://www.niddk.nih.gov/health-information/health-topics/Diabetes/monogenic-forms-diabetes-neonatal-diabetes-mellitus-maturity-onset-diabetes-young/Pages/index.aspx)*