IBD R&D

Inflammatory bowel disease is on the rise in children, but the research of a Cedars-Sinai physician is leading the way to a new future of personalized treatment.

By Katie Sweeney

It should have been a carefree, fun-filled summer for 11-year-old Claire Goldsmith. But beginning in June 2007, she found herself with little of her normal boundless energy, frequently falling asleep in the middle of the day—even while sitting up at the dining room table. Just as mysteriously, she hadn't grown for months, seemingly stuck at just over 5 feet tall.

Concerned, Claire's parents took her to her pediatrician, who referred them to Marla Dubinsky, MD, director of the Pediatric Inflammatory Bowel Disease Program at Cedars-Sinai Medical Center and one of the world's leading researchers studying pediatric IBD. Dr. Dubinsky performed a battery of tests that confirmed her suspicions: Claire had Crohn's disease.

The diagnosis was all too familiar to Claire's father, Bruce Goldsmith, who has battled Crohn's for 35 years. "There are things you hope your kids inherit, but Crohn's isn't one of them," he says. "It's a pretty awful illness."

Crohn's, a chronic autoimmune disorder that causes inflammation of the digestive tract, is one of two common forms of inflammatory bowel disease (IBD). Crohn's can affect any part of the digestive tract, while the other main form, ulcerative colitis, is limited to the large intestine. IBD affects approximately two million children and adults in the United States, and both forms cause debilitating symptoms such as stomach pain, diarrhea, low energy, intestinal bleeding, and weight loss. The disease has no cure.

While IBD typically strikes people in their 20s or 30s, the fastest growing group of newly diagnosed patients are children under 18. That's especially worrisome because children with IBD often have more severe disease, and without effective treatment, IBD can interfere with their normal growth and development.

"How we treat IBD in childhood has a major impact on that child's long-term prognosis and quality of life far into adulthood," says Dr. Dubinsky, who is associate professor of pediatrics and the Abe and Claire Levine Chair in Pediatric IBD at Cedars-Sinai.

Dr. Dubinsky has made it her mission to find better ways to treat IBD with a new, personalized medicine approach—using genetic and molecular data to tailor treatments to individual patients. That's critical, as some IBD drugs work wonders on some patients but have no effect on others. What's more, many treatments can be associated with significant but rare risks, including serious infections and even cancer.

Traditionally, patients were treated using a "pyramid" approach, starting with drugs that offer the fewest side effects—but often have the lowest efficacy. If those failed the patients, they were gradually treated with more potent therapies.

Dr. Dubinsky's goal: to use genetic- and immune-marker blood tests that identify high-risk patients—and the specific therapy most likely to work for them—right away.

"We waste too much time at the bottom of the pyramid in high-risk patients, especially children," she explains. "Meanwhile, their disease rapidly progresses, leading to serious complications that we could have prevented with early, effective treatment."

In 2008, she and her team published the first study predicting which children with Crohn's will quickly develop major complications. The study found that children with certain markers of "immune reactivity" in their blood were 11 times more likely to need intestinal surgery within two years of diagnosis.

Last year, she broke new ground again, completing the first-ever


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genome-wide association study predicting patients' responses to an IBD therapy. Genome-wide association studies involve scanning markers across many people's genomes (complete sets of DNA) to find genetic variations associated with a particular disease or treatment response.

Dr. Dubinsky's study discovered specific genetic markers in children who didn't respond to Remicade®, a "top-of-the-pyramid" treatment first approved for children in 2006. Remicade, a genetically engineered antibody that blocks inflammation caused by a protein, is taken intravenously every eight weeks. The drug has been a major breakthrough in IBD treatment, but it carries risks and doesn't work for everyone.

Claire originally took a combination of immunosuppressant drugs and antibiotics, but her symptoms didn't go away completely. In April 2008, she switched to regular Remicade infusions. While this was prior to Dr. Dubinsky's research findings, Claire had another genetic model: her dad, who has been successfully treated with Remicade for five years.

The day after her first treatment, she woke up feeling better. Soon, she was in complete remission. Now 13, she stands 5 feet 8 inches tall and is a healthy and spirited eighth grader who is on her school swim team.

She recently started a peer support group at Cedars-Sinai for other kids and teens with IBD. "When you are a kid, this disease is the scariest thing that's ever happened in your life," she says. "And it's not easy to talk about it. You don't want people to think of you as defined by an illness instead of who you are."

The idea behind the informal group is to match newly diagnosed young patients with another young "pal" who already has been treated successfully.

"For me, it helped so much that my dad knew exactly what I was going through," explains Claire, who dreams of being an English teacher or a psychologist. "I thought it would be really great if I could be that role model for other kids, to tell them that there's hope and that they're going to be OK."

Remicade's long-term efficacy is unknown, and it can sometimes stop working in patients. But Bruce is optimistic that his daughter's path with IBD will be smooth.

"The therapies today are so much better than they were 35 years ago," he notes. "Maybe there will even be a cure in Claire's lifetime. The key is research and the work that Dr. Dubinsky does. That's what gives me hope."

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—Claire Goldsmith, 13