

Researchers have dedicated their careers to helping lupus patients

Autoimmune disease affects one in 1,000 Canadians and primarily strikes women of child-bearing age

David Israelson

Christina Girgenti was 21 years old when she got the diagnosis that would change her life. She had been experiencing painfully inflamed joints and extreme fatigue, and blood tests revealed the cause: lupus. It was a disease she knew little about.

"When I was diagnosed, I had no idea of the severity of the illness," says Christina, now 35. "It was very painful. It was debilitating. I was very limited in what I could do."

Lupus is an autoimmune disease that affects one in 1,000 Canadians and primarily strikes women of child-bearing age. Because lupus can attack any tissue in the body, the symptoms can vary from case to case, and may include headaches, painful joints, skin rashes, mouth ulcers, fatigue, fever and many others. In addition, the inflammation caused by lupus can attack organs such as the brain, the lungs and the heart. In Christina's case, her lupus flare-ups affected her kidneys.

"Over time, the inflammation caused my kidneys to slowly get worse, until I lost kidney function," she says. "I was on dialysis for a year."

Because of the severity of her symptoms, Christina didn't know whether she would ever be able to pursue a career or have children.

Now, 14 years after being diagnosed with lupus, Christina is symptom-free, with a flourishing career as a registered nurse, a husband and a two-and-a-half-year-old son, Charlie. She attributes her current health to a 2012 kidney transplant and the ongoing, diligent care of Dr. Murray Urowitz and his team at the Lupus Clinic at Toronto Western Hospital.

"I truly believe that if I hadn't met Dr. Urowitz, I wouldn't be here today," says Christina.

Dr. Urowitz is a researcher at the Krembil Research Institute, a rheumatolo-

gist and clinical director of the Centre for Prognosis Studies in the Rheumatic Diseases at UHN. He has dedicated his career to helping lupus patients like Christina lead happier, healthier lives, while also working to unravel the mysteries of a very complex disease.

"In lupus, something goes wrong with the immune system, so that rather than being protective and warding off outside invaders, the immune system actually [attacks] the body itself," he explains.

"But the questions are: 'Why do some people get kidney inflammation, while some people get inflammation in the brain or the lungs?' And, 'Are there subsets [of lupus] that are going to respond to treatment differently than others?'"

At the heart of Dr. Urowitz's quest to answer these kinds of questions is a treasure trove of data. For more than 30 years, he has been developing a lupus databank of patient information, from physicians' assessments to lab tests to patient-reported outcomes. Currently, the computerized database contains information about 1,900 patients and 48,000-plus visits, making it one of the richest and most expansive lupus data collections in the world.

As Dr. Urowitz puts it, he's a scientist with a data lab. Instead of test tubes and chemists, there are computers, programmers and biostatisticians. "The basis of the research is to use the data lab to try and understand this disease better, by dissecting it and breaking it down," he says.

Over the years, insight gleaned from the lupus databank has led to important discoveries that have had an impact on the diagnosis, prognosis and treatment of the disease. Dr. Urowitz and his team have been able to map the course of their patients' disease, allowing them to group together, or phenotype, patients into clinical subsets. Lupus has traditionally been identified as a "relapsing-remitting"



Dr. Zahi Touma, below left, and Dr. Murray Urowitz, are focused on helping patients with lupus. Christina Girgenti, shown right with her son Charlie, was diagnosed with lupus 14 years ago and is now symptom-free.



illness – in other words, it comes and goes. But the team found that some patients are "monophasic," meaning they somehow kick the illness for good.

"Some patients have flare-ups for one to three years, then it goes away, and for the

next 20 years, nothing. They've reset their immune system," says Dr. Urowitz.

"With those patients, we're hoping they're going to give us a clue: 'How did you do that?' If we could figure out how they did it, we would try to do it for others," he says.

Dr. Urowitz works with basic scientists and geneticists to see whether they can identify specific biomarkers or genes that are present in a particular lupus subset. It's this kind of discovery that could lead to doctors being able to predict the course of a patient's illness.

"Wouldn't it be nice if we could tell a person up front, 'You are going to be in the monophasic subset of lupus. I'm treating you for two years and then you're out of here.' Once you've broken lupus down into its components, you can then examine each component. And if we find a [bio] marker for the component, we can tell the patient up front what their disease is going to be like in the future."

Another example of the power of data is with lupus patients who hope to have children, as Christina did. In the past, women with lupus were told not to get pregnant because pregnancy could worsen their disease or result in a higher-than-normal risk of miscarriage or premature birth. But Dr. Urowitz and his colleagues found that only

women with active lupus have a higher risk of flare-ups or pregnancy loss.

"Now we tell our patients with lupus and who want to be pregnant, 'All you have to do is work with us to get your disease inactive for a year or two and then you can go for it,'" says Dr. Urowitz. "We learned that by going back to the data and asking, 'Who had the complications and who didn't?' changed [our] practice. And now I have about 300 godchildren."

One of Dr. Urowitz's current passions is identifying lupus comorbidities – complications that are not from the disease itself, but are a consequence of the disease or its treatment. One such example is premature atherosclerosis, where young women whose lupus is now controlled develop heart attacks and strokes at a younger age than ordinarily expected. This has alerted physicians to screen patients earlier for evidence of atherosclerosis and to initiate appropriate therapy. It has also stimulated research into the role of inflammation in the development of atherosclerosis in the general population. Dr. Urowitz and his team have also been able to identify osteoporosis (decreased bone strength) and osteonecrosis (bone death) as important comorbidities in patients with lupus, likely due to long-term corticosteroid treatment.

Another comorbidity they are work-

ing on decoding is cognitive impairment in lupus patients. That investigation was prompted when Dr. Urowitz noticed more and more patients telling him they were having difficulty finding words or remembering names.

"When you hear that once or twice, you don't pay much attention. [But] when you start hearing it over and over again, you start paying attention," he says.

Through initial testing, Dr. Urowitz and his team determined that people with lupus do have more cognitive abnormalities than normal, age-matched people.

Now, Dr. Zahi Touma, a rheumatologist, clinician-scientist at Krembil and another researcher at Toronto Western Hospital's Lupus Clinic, is working on developing a standardized test that could be used to assess cognitive decline in lupus patients. By monitoring patients with a standardized test, says Dr. Touma, researchers could identify which patients are experiencing cognitive decline, and ultimately determine why it's happening.

"Cognitive impairment could be related to the inflammation within the brain. But it could also be related to blood clotting, which we often see in lupus patients. And there are thoughts, as well, that maybe it's a combination of the lupus and the corticosteroids [used to treat the inflammation]," says Dr. Touma. "The better we can measure it, the better we can understand it. And maybe, down the road, we will be able to develop a preventive measure or a treatment or cure for this."

Dr. Urowitz says patient input is essential to his research, and he considers his patients a valuable part of his team. "When I describe my team, I say, 'There's the principal investigator, a full-time programmer, a full-time biostatistician and a team of physicians, including Drs. Dafna Gladman and Jorge Sanchez-Guerrero and many fellows from here and around the world,'" he says.

"But right in the centre is the patient. If she's not there, all of this is gone. So it's a very special relationship."

Though her lupus is in remission, Christina still gets a checkup with Dr. Urowitz every three months. And she says she's always happy to take part in the studies at the clinic.

"I had two family members who died from lupus many years ago, and back then they didn't know as much as they do now," she says. "If it's going to help them gain more knowledge and discover new things about lupus, I am more than willing to do it." ■