https://www.thestar.com/news/gta/a-mystery-illness-stole-her-son-doctors-in-canada-couldnt-find-the-answer-but-she/article_9dfff7d0-63b3-11ef-b1a2-936fa34e1412.html

FOR SUBSCRIBERS | GTA

A mystery illness stole her son. Doctors in Canada couldn't find the answer, but she wouldn't give up

Mackenzie Wright joined a clinical trial that is bringing hope to Down syndrome families who have struggled with sudden, mysterious regressions.

Updated 30 mins ago | Jan. 5, 2025

Mackenzie Wright is pictured at the Wrights' family cottage in Haliburton, Ont., this summer. That's where five years earlier his parents realized something was wrong and tried to seek help.

Arlyn McAdorey for the Toronto Star

By Amy Dempsey Raven Senior Writer

Kerry Wright found her son slumped in a chair by the lake, staring into the distance, his eyes unfocused and drool running down his chin.

It was a cool morning in August 2019 at the family cottage in Haliburton. Mackenzie, 21, normally greeted his mother with a warm smile and a clever observation, but now his face looked blank. "It was like he was not in there," Kerry said. She called his name, but he didn't answer — didn't even make eye contact.

“Something is wrong with Mackenzie,” Kerry, a nurse, said to her husband, Gordon Wright.

Mackenzie, the third of Kerry and Gordon’s four children, was an aspiring cook who dreamed of being the world’s first Master Chef with Down syndrome. He had graduated from high school in the spring and now worked in a commercial kitchen, making fried chicken sandwiches. He was captain of a colour guard team in Kitchener and a greeter at the church where his father was a minister. A talented public speaker, he spoke in schools and churches about having Down syndrome, which he called “a good disability that gives me a big heart.”

Kerry and Gordon got Mackenzie into the car and drove to the nearest hospital. Kerry sat in the backseat with Mackenzie and went into “nurse mode” — outwardly calm, inwardly running through worst-case scenarios. “I thought, my child is going to die, and we’re going to find out later what he died of,” she said.

They would visit three emergency departments that day, ending up at Sunnybrook hospital in Toronto. Doctors ran tests: blood work, a CT scan, an EKG, an EEG. Mackenzie lay motionless in an ER bed, drooling and muttering. When he tried to answer questions, his words came out slurred.

The tests came back normal. Mackenzie wasn’t having a stroke or a seizure. He didn’t have a brain tumour or an aneurysm. And yet, he was barely functioning. Doctors couldn’t figure out what was wrong.

After one night in the ER, hospital staff discharged Mackenzie, determining he didn’t need acute care. They booked him for an MRI the next month, and recommended the family follow up with their primary care provider.

Kerry and Gordon left the hospital with Mackenzie, baffled. Something was clearly wrong with their son. It felt like they were the only ones who could see it.

At home, Mackenzie struggled to chew food and brush his teeth. He couldn’t follow a conversation or write a text message. He needed help to shower. He stopped doing the things that once brought him joy: colour guard, cooking, boating at the cottage. He had a panic attack at church and refused to go back.

Everything Mackenzie loved, and everything his family loved about him, seemed to fade.

“It was like this body walking around that looked like my son, but nothing about him was Mackenzie,” Kerry said.

It would be four years before the family learned what was wrong, and the answer wouldn’t come from the doctors whose advice they sought, one of whom misdiagnosed him with Alzheimer’s disease. It would be Mackenzie’s own mother who would figure it out, and getting there would break her faith in the health-care system, and require going outside the country.

Gordon, left, Mackenzie and Kerry Wright at the family cottage near Haliburton. Kerry, a nurse, retired early when she needed to stay home with Mackenzie.

Arlyn McAdorey for the Toronto Star

Getting used to the 'new normal'

In the months after Mackenzie became sick, Kerry and Gordon sought answers wherever they could. They took him to see psychiatrists and neurologists. He had an MRI and a sleep test. He was prescribed anti-seizure medication and sertraline for anxiety. None of it helped.

Doctors told Kerry and Gordon that people with Down syndrome can sometimes experience declines in functioning, and said they needed to adjust to Mackenzie's "new normal."

As a nurse, and as a mother, Kerry couldn't accept that explanation.

"This wasn't a decline," she said. "This was a complete crash."

Health providers didn't seem to be treating her son's sudden illness with the urgency she believes they'd have if a 20-something man without Down syndrome had the same symptoms.

Kerry and Gordon carried on, living with this stranger who was their son. Kerry retired early from nursing because Mackenzie could no longer be left alone.

Mackenzie had loved family events, but now he preferred solitude. He found being around his toddler niece and nephew overwhelming. Crowds made him panic.

Alone in his room, Mackenzie would mumble, having angry conversations with imaginary people. He made strange movements and contorted his face into twisted expressions, or extending his arm out, like he was reaching for something that wasn't there. He watched Disney's "Pinocchio" on repeat, which seemed to comfort him.

Kerry said Mackenzie's neurologist told them, "Something else is going on, but I don't know what, and we'll just have to keep watching and waiting.'"

Mackenzie Wright's family believes health providers weren't treating her son's sudden illness with the urgency they might have if a 20-something man without Down syndrome had the same symptoms.

Arlyn McAdorey for the Toronto Star

'Not something that needs to be investigated'

Three years after Kerry found Mackenzie on the dock, Kerry got an email from a local health organization promoting a webinar about an illness she'd never heard of: Down Syndrome Regression Disorder, or DSRD.

The Wrights were at their cottage that day in August 2022. Kerry drove to the public library to stream the webinar.

DSRD, she learned, was a rare and debilitating condition that causes a rapid loss in functioning, behavioural changes and psychiatric symptoms in people with Down syndrome. It was just about everything that was wrong with Mackenzie.

The webinar gave a checklist of eight symptoms.

Altered mental status or behavioural dysregulation? Yes.

Cognitive decline? Definitely.

Developmental regression? Language deficits? Catatonia? All yes.

Having three of the eight symptoms was a suspected case of DSRD. Six symptoms met the threshold for a diagnosis. Kerry took notes, marking Mackenzie's symptoms off on a pad of paper: he had eight out of eight.

"I think we found it," Kerry said to Gordon when she got home. "I think this is what's wrong with him."

Kerry noted the name of a pediatric neurologist at Children's Hospital Los Angeles — Dr. Jonathan Santoro — who was studying DSRD.

Earlier that year, Santoro had published a paper that had given a name and diagnostic criteria to an illness long described but never formally identified. He believed DSRD was an autoimmune disorder.

That night, Kerry sent him an email, describing what they had been through with Mackenzie.

They met over Zoom that week and Santoro told them what he had learned about DSRD while treating 200 patients in his clinic since 2020.

“I have seen this before, hundreds of times,” Santoro said. “We’re treating it here, on an experimental basis, and we’re having incredible results.”

For years, Kerry and Gordon had been encouraged to accept Mackenzie’s condition as their “new normal.” But now Santoro was validating what they knew all along about their son. “What you are seeing and describing is an illness,” Santoro said. “It’s not normal.”

Suddenly there was a path forward. Kerry and Gordon broke down in tears during the call. “And we’re not criers,” Kerry said. “Gordon’s British, and I’m a nurse.”

Santoro gave them a list of tests to seek and offered to work with their health providers toward a diagnosis. He said he would be running a clinical trial in 2023 and Mackenzie could have a spot if diagnosed.

The doctor told them he couldn’t make any promises about outcomes, but said he would do everything he could to help them.

A major roadblock

To be accepted into the clinical trial, Mackenzie needed a formal diagnosis, which would require additional testing to rule out other causes for his symptoms: extensive blood work and, crucially, a lumbar puncture to determine whether he had markers of brain inflammation.

Kerry made an appointment with Mackenzie’s neurologist and prepared a folder documenting what they had learned. She printed out Santoro’s research, information about the clinical trial, the checklist of diagnostic criteria and Santoro’s list of recommended tests.

The appointment, in December 2022, did not go well. Kerry and Gordon say the neurologist, who through the hospital declined an interview request for this story, barely looked at the research.

“She opened the binder and said, ‘This is not a real diagnosis,’ ” Kerry said.

Kerry, who took detailed notes after the appointment, said the neurologist told them the testing would be “a cost to the health-care system that she couldn’t justify.”

The neurologist would not order the lumbar puncture and advised them against going to Los Angeles, Kerry said. She said the treatment was experimental, and not worth pursuing.

The neurologist said she believed Mackenzie had early-onset Alzheimer’s disease.

This diagnosis made no sense to Kerry. While people with Down syndrome are at greater risk for early-onset dementia, most are diagnosed in their 50s. His sudden decline didn’t strike Kerry as consistent with Alzheimer’s either.

Mackenzie's illness is "not something that needs to be investigated," Kerry remembers the neurologist saying that day.

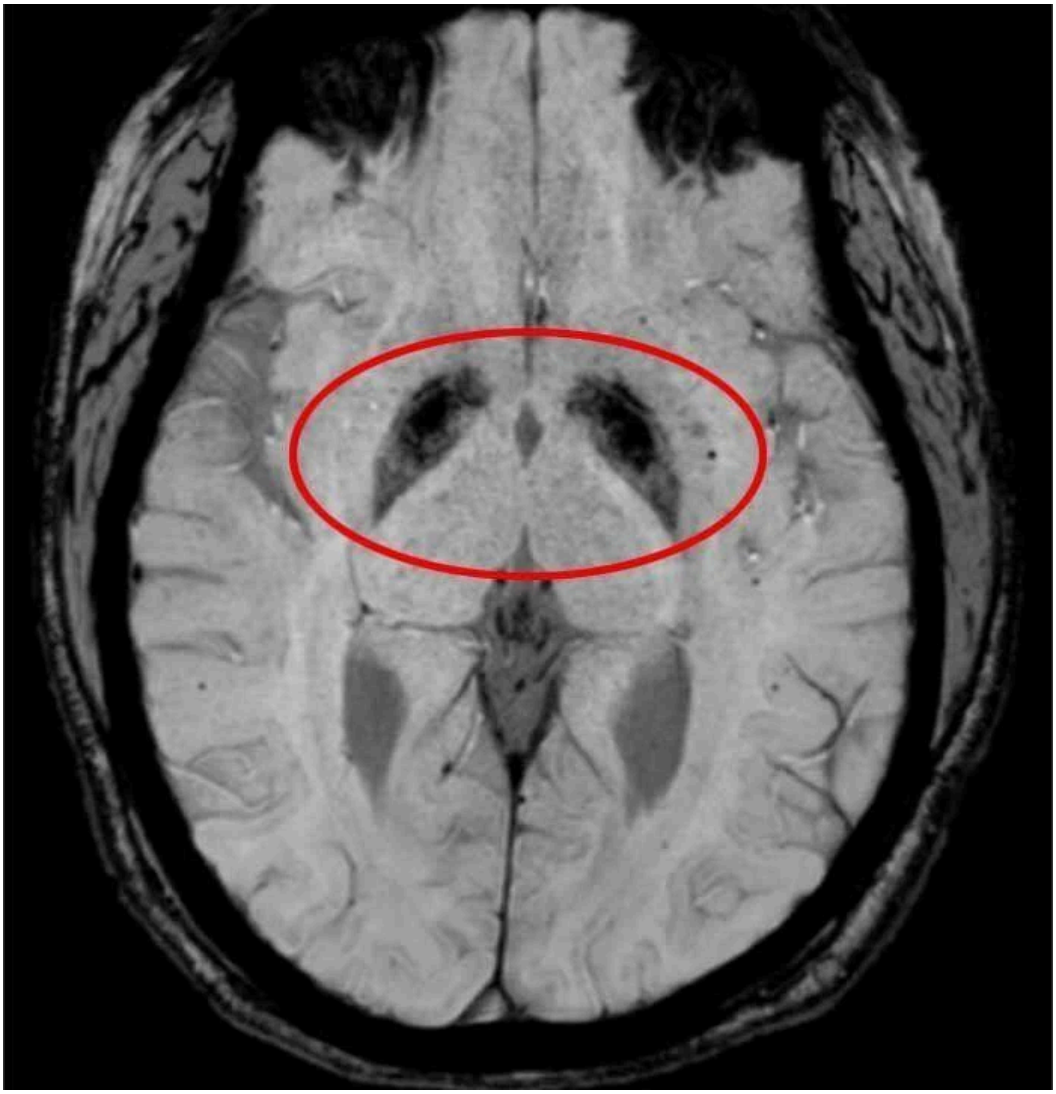
The experience "was really deflating," Gordon said.

Kerry asked the neurologist for a second opinion — a referral to another specialist. The doctor referred them to a neuroimmunologist in London, but that clinic declined to see Mackenzie. Another specialist at a children's hospital couldn't see him because he was too old.

Mackenzie's primary care provider, a nurse practitioner, couldn't order the test. They needed a specialist, and they were running up against the clinical trial enrolment deadline.

Mackenzie could have the lumbar puncture in California, but the Wrights would have to pay. The test would cost between $10,000 and $40,000 (Canadian), depending on whether Mackenzie had to stay overnight in hospital. It was money they did not have.

Kerry and Gordon decided that they would remortgage their house, if it came to that. They were going to L.A.



A photograph of Mackenzie Wright's brain scan showing mineralization in the basal ganglia region, which suggests interferon dysregulation, one of the possible mechanisms of Down Syndrome Regression Disorder. These calcifications are found in 30 per cent of DSRD patients.

Like ‘waking up from a dream’

During Dr. Jonathan Santoro’s residency in neuroimmunology, which is the study of how the immune and nervous systems interact, a young patient died at the hospital where he was training after a sudden illness. After her death, doctors discovered she had a rare stroke disorder called Moyamoya disease.

“I became obsessed with this case,” Santoro recalled. He kept asking himself, “How did we miss several strokes in this little girl?”

They missed the signs, Santoro came to believe, because the patient’s symptoms had been chalked up to her Down syndrome.

Santoro, a pediatric neurologist and immunologist, said that while doctors with his training and background typically treat patients with multiple sclerosis, this experience set him on a different path.

In 2020, Santoro, now director of neuroimmunology at Children’s Hospital Los Angeles, began seeing patients with Down syndrome who had suddenly regressed come into his clinic.

These patients had a similar profile. They had experienced years of psychiatric symptoms without any improvement. Many had been diagnosed with late-onset autism or early-onset Alzheimer’s, and were not receiving treatment. Some had been prescribed antipsychotics by doctors who believed they had schizophrenia or bipolar disorder, but months or years later they were in the same condition.

Each time Santoro met one of these patients, he thought, “If this person didn’t have Down syndrome, we’d be rushing them to the hospital. We’d be giving them a million-dollar workup.”

Santoro’s team decided to do a full workup, including detailed brain imaging, extensive blood work and a lumbar puncture.

The tests showed abnormalities suggesting the patients had inflammation in their brains, similar to what doctors see with multiple sclerosis or autoimmune encephalitis.

Santoro began treating them with a form of immunotherapy called intravenous immunoglobulin, or IVIg, which helps the body fight infection by boosting the immune system.

The first regressed patient Santoro treated had been catatonic and drooling when they met. “And just a couple weeks after he got his first infusion, he’s running down the hallway and giving me a hug.”

In some cases, Santoro said, it was like patients were “waking up from a dream.” Santoro and colleagues followed 82 patients who had spent nine months to a year on IVIg and found that nearly 50 per cent remained well after stopping treatment; the others resumed immunotherapy and all improved again.

Santoro came to believe that the regression symptoms he was seeing in Down syndrome patients were the result of an autoimmune condition. It surprised him to learn that no one had previously probed any link to brain inflammation. It is widely known that people with Down syndrome are more susceptible to autoimmune disorders, such as celiac disease, thyroid conditions and type 1 diabetes. “But no one had ever said, ‘maybe the brain’s involved as well,’” Santoro said.

People with Down syndrome had been experiencing regression-like symptoms for decades, but there was no formal definition.

In 2022, Santoro and his team put out a paper, giving the illness a name and diagnostic criteria. They published it open access, to make it easily searchable.

As word spread that there was a doctor treating people, families began to come from all over the country. One mom told Santoro about a Facebook group, started by a physician whose own daughter had regressed.

Dr. Eileen Quinn, a developmental pediatrician at the University of Toledo in Ohio, started the group in 2016. At the time, her daughter, Sara, had been in regression for five years, and Quinn had been pushing the medical community to recognize these catastrophic declines in functioning as requiring deeper investigation.

Like Mackenzie, Sara's decline had been sudden and devastating. "It was like she died, and I didn't even have time to mourn her because I had this stranger in my midst who needed a lot of care," Quinn said.

Another mom from the DSRD Facebook group introduced Santoro to Dr. Joaquin Espinosa, a Down syndrome researcher at the University of Colorado, who also believed the illness was an autoimmune condition. Espinosa had recently begun using a medication that targets interferon receptors to treat people with Down syndrome for skin conditions such as psoriasis and alopecia, and had been stunned to find the treatment brought his regressed patients back to normal.

Their "serendipitous" introduction would lead to the first randomized control clinical trial of treatments, which Santoro and Espinosa teamed up on in 2023.

The trial came together quickly. The study received funding from the U.S. National Institutes of Health and met its enrolment goals within six months, far ahead of schedule, Santoro said, which "reflected the need for it."

Word about the trial spread through the Facebook group, which now has more than 2,400 members globally.

Some participants, like Mackenzie Wright, could not get the tests or treatment back home, "so we had to bring them in for it."

The Wrights are one of 100 Canadian families in the group whose children either have a confirmed case of DSRD or have symptoms but aren't diagnosed. The Star spoke with four Ontario families — from Kitchener, the GTA and Thunder Bay — who all described similar barriers to accessing testing and treatment for their children.

Mackenzie Wright went to California in the fall of 2023 to participate in a Down Syndrome Regression Disorder clinical trial run by Dr. Jonathan Santoro, a pediatric neurologist at Children's Hospital Los Angeles.

Supplied

Santoro said it's his impression, based on the many hundreds of families he has met, that patients from Canada and the U.K. have the hardest time getting diagnosed and treated.

In August 2023, Kerry, Gordon and Mackenzie flew to California. At the hospital, Santoro greeted Mackenzie warmly and took him for a walk down the hall. Kerry and Gordon noticed that Santoro spoke to their son directly, rather than communicating through them.

In L.A., Mackenzie had all the medical testing he couldn't get in Ontario, including a lumbar puncture, for which Kerry and Gordon paid $14,000. Gordon's church community helped raise money for the trip.

Mackenzie was a "textbook case" of DSRD, Santoro concluded.

Reviewing Mackenzie's MRI results from 2019, Santoro found that while doctors in Ontario had concluded the imaging was normal, there were in fact markers in the brain's basal ganglia region that suggested Mackenzie had interferon dysregulation, one of the possible mechanisms of DSRD. Santoro said these calcifications are found in 30 per cent of DSRD patients that his team has examined.

Mackenzie was enrolled in the study. The first phase ran on a delayed treatment model, meaning there were no placebo patients, only a group that was studied for 12 weeks before and after receiving treatment.

The Wrights returned to L.A. in November 2023 for Mackenzie to start treatment.

The clinical trial is testing three interventions: immunoglobulin therapy, or IVIg, which Santoro had been treating his patients with on an experimental basis, with good results; tofacitinib, a JAK inhibitor that turns down the brain's overactive interferon signaling system; and lorazepam, used to treat catatonia in DSRD patients.

Mackenzie was randomized into the tofacitinib group.

Santoro was careful to manage expectations. Mackenzie had been unwell for four years. In his experience, patients had a better chance of improving if they were treated early.

Kim Murphy has been trying for years to get a diagnosis and treatment for her daughter, Chloe Murphy, 21, who has Down syndrome and regressed in 2022.

Hilary Gauld

Not the only ones

While Mackenzie was receiving treatment in L.A., Kim Murphy was trying to figure out what was wrong with her 21-year-old daughter, Chloe. Born with Down syndrome, Chloe had been a bright and bubbly teen who played floor hockey, volunteered at a soup kitchen and was a considered a leader at her Kitchener high school. (Coincidentally, the Murphys live near the Wrights, but they hadn't met at this point.)

In 2022, Chloe's behaviour and personality changed dramatically. Chloe had been responsible and independent, cooking her own eggs for breakfast and packing her bag for school, but suddenly she couldn't do anything on her own. She refused hugs and retreated from her family. She became antagonistic with friends and teachers.

Alone in her bedroom, Chloe would nod and laugh like she was talking to a group of people. She made involuntary movements with her limbs. She spoke rarely and in a whisper.

Once, Kim and her husband found Chloe staring at the ceiling, unable to move her eyes back down. They took her to the hospital, and ER doctors there referred her to a psychiatrist who prescribed medication that didn't help and turned her into "a zombie," Kim said.

Kim, who had gotten a list of Santoro's recommended tests from the DSRD Facebook group, asked her daughter's family doctor for an MRI and a neurology referral. The doctor said they would need the MRI results before a neurologist would see Chloe, Kim said.

They waited five months for an MRI and were told it would be another nine months to see a neurologist. They've decided not to wait.

In February, they plan to travel to L.A. for an appointment with Santoro at Children's Hospital Los Angeles, where Chloe will receive further testing, including a lumbar puncture, which they can't get in Ontario without a neurologist's referral.

If Chloe is eligible, Kim and her husband will enrol her in the second phase of the clinical trial. The tests, flights and accommodations will cost them about $40,000. It's a lot of money, but they want their daughter back.

Kim is feeling hopeful about L.A. — she had coffee with Kerry Wright, and learned about Mackenzie's experience — but the challenges she has faced in Canada have left her bitter and incensed.

"It's not free health care if you can't access it.".

Mackenzie Wright with his parents Gordon and Kerry. His family has been amazed at his progress since he joined the clinical trial in L.A.

Hilary Gauld

'Stuck' in the back of his own head

Two weeks into the trial of tofacitinib, Mackenzie started to become himself again.

He wrote more clearly in his notebook. He spoke in longer sentences. He was able to follow conversations and answer questions. He became less angry and emotional.

The Wrights returned home in early December, feeling hopeful but wondering if the change was real.

By Christmas, Mackenzie was having a Mario Kart tournament with his siblings and their partners, something he hadn't done in four years. Kerry couldn't believe it. The year before, Mackenzie had a panic attack on Christmas Day and couldn't open his gifts. Now Kerry sat on the couch watching him laugh and play video games with his brothers and sister.

Mackenzie's brother-in-law, Tristan, who had joined the family only after Mackenzie became ill, said it felt like meeting him for the first time.

When the family returned to L.A. for Mackenzie's assessment in January, he was 75 per cent back to his baseline.

Santoro and his colleagues are now halfway through the clinical trial. Preliminary results suggest the treatments are safe, with no serious side effects reported, and effective, with patients in all three medication groups seeing improvement. The two immunotherapies "are doing really well," Santoro said.

While trial participants have seen varying degrees of improvement, Mackenzie has been transformed.

"He's definitely been our most responsive patient, and probably one of our most impacted at the beginning of the study," Santoro said.

By his one-year check-up in November, he was back to his baseline — fully himself again.

Once recovered, Mackenzie was able to describe the feeling of being in regression. He said it was like he was stuck in the back of his own head. He felt rattled and unsafe. He believed his words "had no value." It sometimes felt like "nuclear explosions" were going off in his brain, and he was often "confused about what to do."

"It felt like missing out on something important," he said.

Mackenzie now feels like he's once again part of what's going on around him, rather than "a houseguest" in his own life.

He has returned to many previous activities and started new ones. He boxes at a gym. He helps clean tables at his brother's coffee shop. He joined a choir that performed last month at the Christmas market in Kitchener.

He continues to take tofacitinib. The medication isn't covered by OHIP or private insurance because it's not approved to treat DSRD in Canada; it's considered an off-label use. DSRD isn't even a recognized diagnosis yet, Kerry points out.

Once Mackenzie's trial participation ended in February, the Wrights had to pay for the medication — $400 a month for a bottle of pills that made their son himself again. But in August, the pharmacy team at St. Michael's Hospital in Toronto, where Mackenzie sees a new neurologist, applied for compassionate funding from Pfizer. They were approved.

One day at the cottage this summer Mackenzie looked over at Kerry during supper and “grinned with his full face” in that joyful and deeply loving way he had before his regression. “He’s back,” she knew then. “We have him back.”

Amy Dempsey Raven is senior writer for the Star, based in Ottawa. Follow her on X: **@amydempsey**.

Related Stories

A boy on a futon in an office. Teens in budget hotels. How Ontario is failing kids who are ‘too complex’ for care

Sharp increase in Ontario kids in child protection being housed in hotels, offices and Airbnbs with nowhere to go

Hospital staff suggested ‘surrendering’ a child. Another was taken by nurses to CAS in a taxi. What happens when the system can’t cope