"There is nothing more important in this world than your kids. Our goal became making this a better place for our children." Andrew McFadyen

WE ARE OFTEN TOLD THAT ONE PERSON REALLY CAN MAKE A DIFFERENCE in this busy world. Isaac McFadyen is living proof that not only can one tiny individual change a course of events but can even save lives, bring out the best in others and overturn government policy. However, at two and a half years old, young Isaac doesn't yet know he is that very person.

An inquisitive and happy child, Isaac captures the hearts of all who know him. He is a popular visitor at Winston Churchill Public School in Kingston, where his father, Andrew McFadyen, is a teacher. "He's our first-born son. He likes to play and colour and run around and is incredibly bright," says the proud dad, beaming. Isaac has even been featured on the front page of the *Globe and Mail* — not, alas, because of his infectious charm but because of his rare genetic disorder, called MPS VI, and his parents' race to find a cure.

Born at home on April 14, 2004, Isaac was a much anticipated, much loved little fellow. But before long, with his growth over the 97th percentile mark, his parents suspected he had some kind of overgrowth disorder. At the genetics department at the Hospital for Sick Children in Toronto, he was eventually found to have an extremely rare metabolic disease (occurring in only 1 out of 340,000 live births) called MPS VI, or Maroteaux-Lamy syndrome. Simply put, Isaac is missing an enzyme needed to break down carbohydrate compounds, which can build up in the body tissues and cause a myriad of health issues — stunted growth, breathing problems, poor mobility, liver enlargement, clouded corneas, changes in facial features and even eventual heart failure.

The darkest news for Ellen Buck-McFadyen, Isaac's mom, and for Andrew McFadyen was not only that Isaac would most likely stop growing by the age of four and have a compromised quality of life but that he might not live past his 20s. After the initial shock wore off, this proactive couple sprang into motion, learning everything they could about their son's progressive and debilitating disease. Their race to save Isaac began in earnest.

Mucopolysaccharidosis (MPS) is a family of seven closely related inherited diseases, and all forms are lysosomal-storage disorders where, basically, the lysosomes (nature's recycling bins for cells) don't work. When material builds up in the body's cells, the results are crippling. The disease is passed along genetically, but in this case, because neither parent had the disease, there was no way of knowing that each had one working and one non-working gene. It is rare to be a carrier, even rarer to partner with another carrier. Unknown to them at the time, for each pregnancy there was a one in four chance that the child would inherit both of the parents' non-working genes and have MPS VI. Isaac developed MPS VI, whereas his baby brother Gabriel did not.

There is no cure yet, but there are treatments. The McFadyens forced themselves to hold on to that, to the positive, to something greater. "When we initially got the diagnosis for Isaac," says Andrew, "we were told it was MPS 1, which affects the brain. We were told that by the age of two, he would start losing words, slowly shut down and be gone by seven. Our specialist told us he was absolutely sure he had this type, so I prayed every day.

"But then they phoned us four days later and said, 'We were wrong. It's MPS VI.' This is still a devastating disease, but regardless of what was going to happen physically, we would still not lose Isaac. So, for me, my prayers were answered. It wasn't a cure, but I still had my kid until we figured this out. I have faith — and hope."

Clinging to that hope, they were thrilled to discover that treatment for MPS VI exists in the form of enzyme replacement therapy (ERT), where the specific missing enzyme can be administered intravenously. This miracle drug, called Naglazyme, is produced by the American company BioMarin Pharmaceutical Inc. Andrew and Ellen's jubilation was complete when they found out that by starting treatment so early in his life, many of Isaac's symptoms could be reversed. But there was one hitch —

the cost of treatment for one year was over $300,000 for a child and nearly one million dollars a year for an adult.

Still undaunted, the McFadyens appealed to the drug company to help them out temporarily on a compassionate basis. The longer Isaac went without treatment, the worse his symptoms would become, until they were irreversible. Time was something they did not have. Isaac was showing symptoms — stiff shoulders and corneal clouding — and he had already undergone surgery to relieve spinal compression.

Andrew says: "We called the drug company in our three-week haze just after we found out. We were ready to bankrupt ourselves, and my father-in-law was ready to cash in his $300,000 retirement fund. We could pay for one year just to get started. We told them that our whole family was going into debt, and could they please give this to us at cost?" But the drug company was unable to help.

Their next step was to appeal to the Ontario government to help fund Isaac's treatment, but they hit a roadblock at Queen's Park too. Drugs like Naglazyme are known as "orphan drugs" — drugs often abandoned or neglected during development because so few people need them (only three children in Canada are affected by this disease) — and so they have limited potential for profit. Some countries, like Great Britain, provide funding for those who can't afford such medicines and have created policies to protect people with rare diseases. In the United States, private insurance pays for treatment. Canada is only in preliminary discussions about its National Policy on Orphan and Catastrophic Drugs, and the Ontario government said it could not provide funding for Isaac.

The couple were on their own. Andrew says: "We did all the advocating and fighting to get this funded. We phoned every day to the province. We stayed up late working on this and went down to the Ontario legislature."

Getting desperate, Andrew, who is eligible for British citizenship, even considered relocating his family to England, where the government would help Isaac just as they were already helping 12 other children with the same disease. But one radio show, one phone call and one compassionate politician changed everything.

"One day I was driving home," Andrew says, "and heard Health Minister George Smitherman say on the radio that they had a new drug plan that would guarantee access for Ontarians to drugs that they normally couldn't afford. Elizabeth Witmer, Deputy Leader of the Official Opposition and Critic for Health and Long-Term Care, was on right after saying, 'This is not true.' So I stopped the car, called her number, wrote a letter and sat down with her the next week. She told me she would help me — not for political gain, but because she is a mother herself."

Witmer, MPP for Kitchener-Waterloo, is also a teacher by profession and an advocate for children. She has spent a number of years working on behalf of people with Fabry's Disease, another rare illness, and helped them obtain funding.

"I was touched by the letter from Andrew," she said, "and by the fact that Isaac was two and that the disease was progressing rapidly. We had an obligation to do what we could to help the family. As a mother, how must you feel knowing that there is treatment that could help your child, treatment that had been approved for use in Canada, and yet somehow you couldn't access it?"

True to her word, Witmer repeatedly asked the government for provincial bridge funding for the ERT for Isaac until the National Policy on Orphan Disease and Catastrophic Drugs was in place. "You just want to make sure that Isaac has the same chance in life that all other children have, and if you can help make that happen, you do everything you possibly can," she says.

The life-changing call came one day while the McFadyens were shopping. They broke down in tears. The Ontario government had agreed to fund Isaac's ERT. Andrew still gives all the

credit to Elizabeth Witmer. "Everything that took place was because of her and the media, but she even helped with the media," he says. "We are so indebted to her. We probably sped up having our son get treatment by years, and he wouldn't be here if it weren't for her."

The Canadian orphan-drug policy is at present undergoing a policy and costing analysis, but in the meantime, Witmer still follows the family's progress and hopes to visit Isaac at Sick Kids during one of his treatments. "I was overjoyed when they received funding, because this family worked so hard on behalf of their son. They did everything they possibly could. The credit goes to them. I was moved and touched."

So less than a year after diagnosis, at two and half years old, Isaac began his intravenous treatments through a permanent catheter in his chest. Ellen does the weekly three-hour drive from their home in Campbellford to Toronto with her mother, Paula Buck. As Ellen says, "This brings you closer to family, and you appreciate your extended family. There are four generations of us all within a block. We rely on them so much."

Little Isaac is a trooper when he is given the double-bag drip over four and a half hours at Sick Kids every week. This is truly a groundbreaking event, because he is the first child in Canada to get this treatment. And after a half-dozen weekly treatments, so far, so good.

Andrew is thrilled with the results. "I got to go to the first treatment, and on the way home, I thought he felt softer. [MPS children have very coarse skin and hair.] My wife didn't think it could work that fast. And then, because I rub his little feet every night before bed, I said, 'I know his skin is softer.' That night I could tell he was breathing softer too, and two days later I said, 'His stomach is definitely getting smaller.'"

And he was right! Isaac's stomach, once quite distended because of his enlarged organs, has now shrunk over an inch, and although his growth had shut down before treatment (MPS kids often don't grow over three to four feet), he has since grown more than an inch and is gaining weight quickly. But the couple remain ever vigilant, because ERT is not without risks. Children can have an adverse reaction to the synthetic enzyme: in the United States, one boy's heart stopped beating during his sixth treatment. Although he lived, it was a frightening reminder that this treatment is just a lifeboat, not a cure. Andrew says: "People ask if the treatment will be for the rest of his life. It is weekly

right now, for 10 or 15 years, and that is our time frame right now. That is fine. It's a small price to pay."

It's a testament to their spirit that despite having a severely ill child, having to raise funds and make exhausting trips into Toronto every week, Andrew still considers their family to be very fortunate.

"It usually takes four years to get a diagnosis, because there aren't many around who know much about it. We were lucky we were located geographically so that we could go to Sick Kids, we were lucky that we were already dealing with the genetics department, and we were lucky that our doctor could just walk across the hall and speak to Dr. Joe Clarke, who happens to be North America's leading expert on this disease. He met with us the day before he was supposed to leave the country on a trip. It's odd to say we are lucky, but we are."

Ellen echoes his thoughts: "The diagnosis was in October last year, and by this January, we decided to make something positive out of all this, and we lobbied the government. The funding announcement came in July, and Isaac started the enzyme in September. That was successful."

They soon set up The Isaac Foundation to raise funds for research and ultimately to find a cure for the disease. Peter Milliken, MP for Kingston and the Islands, helped them obtain charitable status. Ellen says: "It keeps us busy and helps us and in that first year, when it was so hard, kept our focus on something positive. It brought us closer together." That closeness and devotion were contagious, and the outpouring of support from friends and family and communities has been overwhelming.

Andrew is touched by it all. "The community in my school has been exceptional. Some Grade 5 girls raised $500 last year, and this year they canvassed on Halloween for The Isaac Foundation. Some local realtors have said they are even going to donate a portion of each house sale. Kingston has been just great. We're lucky."

The foundation is now ready to give out its first $40,000 research grant and has its eyes on a new development called "chemical chaperoning." Rather than replacing the missing enzymes synthetically as ERT treatment does now, this new process tries to get the existing enzymes (which are decreased in number or not functioning properly) to function more efficiently. This is an exciting breakthrough, and Andrew says this is where they hope to direct the funds.

"We take applications and try to help researchers cut through red tape. The time between application and getting the money can be up to 16 months, and our kids don't have that time. We want to get that money to researchers in 30 days."

Despite their optimism, it is a daunting task, because The Isaac Foundation is still run just by the two of them. Andrew is a full-time teacher, and Ellen, a public health nurse, takes care of two children as well as all Isaac's medical needs. They answer all e-mails, do the advocating, plan the charity events, speak to the media, run a web site and try to have a life. Ellen's mother, Paula (Nanny), says: "The two of them have done all this together and worked incredibly hard doing it. It is an inspiration. What they have accomplished is amazing."

But working as a team is nothing unusual for this couple. Andrew, proclaimed by his wife to be the more sentimental of the two, is adamant. "Even though it is rare to be a carrier [of a defective gene] and ultra rare to match up with another carrier, I know we are meant to be together. We were in the same Grade 5 class. She was the cute, smart girl, and I was the kid with grass stains on my knees and always in trouble. We reconnected in late high school and have been together ever since.

"We always said there must be some true reason why we kept finding each other. We honestly believe it was to have our family and find a cure for our son. The motto for The Isaac Foundation is 'Love, Laughter and Hope.' Our son gives us all three." ■

For more information about Isaac and MPS, please visit www.theisaacfoundation.com.