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Tireless quest for a cure, Lorenzo-style

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When Jacob Trossman emerged from his mother's womb, his chest caved in as he drew his first breath. Doctors who resuscitated him were baffled. His anguished parents were told a diagnosis might never be made.

The boy with an infectious giggle and curly black hair was sent to some 20 specialists, where he received one test after another. Jacob could not eat, had poor muscle control and suffered from paralyzed vocal cords -- conditions the 3½-year-old boy lives with today.

As doctors searched for a diagnosis, the Toronto boy's parents began an exhaustive, parallel journey for a cure, reminiscent of the Oscar-nominated movie *Lorenzo's Oil*. In that 1992 film, a boy's disease is so rare that no one is working on a cure, so his parents vow to find one themselves.

"We looked through stacks of research papers, trying to figure out what he had," said Jacob's father, Andrew Trossman, adding that they searched scientific studies -- including one dating back to 1963 -- surfed the Internet and contacted doctors in three countries.

For the first 10 months of Jacob's life, a diagnosis eluded them.

Then one day, a test that was thrown in with a slew of others gave them the answer: he had Pelizaeus-Merzbacher disease (PMD). The rare central nervous system disorder is caused by the lack of myelin; a fatty covering that acts as an insulator on nerve fibres in the brain.

Often misdiagnosed as cerebral palsy, PMD causes the deterioration of co-ordination, motor skills and intellectual function. There was no real treatment, no cure. Jacob, one of an estimated 300 people in Canada with PMD, has a more severe form of the disease.

"In a way, it was worse to hear what he had," said his mother, Marcy White, a woman who smiles easily.

And in some ways, the answer was there all along.

Ms. White's grandmother bore two sons who died as babies: the first lived 36 hours and the second 22 months. When Ms. White thumbed through the boys' birth records, she noted

that they had breathing and reflux problems. Her mother's cousin, based in Israel, had two boys with the same symptoms.

"When I got the hospital records from my grandmother's two sons, it gave me goose bumps and shivers to read the files," she said.

Through blood tests done in Delaware, Ms. White learned she carries the PMD gene.

That means any boy she bears would carry a 50-per-cent chance of having the disease. Girls are overwhelmingly spared the disease, but they have a 50-per-cent chance of being a carrier. (Neither of her two daughters, Sierra and Jamie, both 11 months, have the disease. Nor are either of the girls carriers.)

The couple's quest for a cure meant boning up on Jacob's disease at the molecular level.

For Ms. White, it meant rifling through old textbooks from her McGill University days, where she earned a bachelor of science degree in anatomy. Mr. Trossman, a software engineer, went to a laboratory in Germany, where he met with a specialist in myelin disorders.

"It is not uncommon for Andrew and I to wake up in the middle of the night and start discussing some research we recently read and how it might apply to Jacob and PMD," said Ms. White, sitting on the couch in the finished basement of her Toronto home.

The couple's journey took them to Kenise Kilbride, aunt of Lorenzo Odone (on whom the film *Lorenzo's Oil* was based). Ms. Kilbride offered them advice and inspiration.

"I have enormous admiration for them," said Ms. Kilbride, a professor emeritus at Ryerson University in Toronto. ". . . Parents of a child can engage in scientific research in a number of ways and make a difference."

Certainly, that was the case with Ms. Kilbride's sister, Michaela Murphy, now deceased, and brother-in-law, Augusto Odone, who currently lives in Fairfax, Va., with Lorenzo, who is now 27.

They sought a cure for Lorenzo, who was diagnosed in 1984 at the age a 6 with adrenoleukodystophy (ALD), a rare disorder where the very long-chain fatty acids build up in tissues of the body. The buildup causes widespread loss of myelin in the brain, which, in turn, causes inflammation and destroys nerve cells.

Doctors recommended that Lorenzo ingest oleic acid, theorizing it might block the enzymes that synthesize very long chain fatty acids in the body. It helped, but not enough.

Lorenzo's parents were perusing arcane research papers, when an animal experiment using erucic acid caught their attention. Although the substance clogged the hearts of mice and rats, it didn't do that in people.

They tracked down a retired English chemist who was capable of synthesizing erucic acid. When Lorenzo ingested it, his saturated, very long-chain fatty acid levels tested normal.

Though their discovery made for the perfect Hollywood ending, many mainstream scientists were skeptical of the oil's effectiveness.

But last July, a long-term study, published in the Archives of Neurology, put doubts to rest. It found that Lorenzo's oil can prevent the severe form of the disease in a new generation of boys, if treated before symptoms appear.

The similarities between Lorenzo Odone and Jacob Trossman's case are striking: both have myelin disorders. (Though Lorenzo's problem was the destruction of myelin, Jacob's problem is that he was born with little, poor-quality myelin.) Parents of both children were preoccupied, some might say obsessed, with finding a treatment, knowing that if they didn't, maybe no one else would.

But that is where the similarities end.

While Lorenzo's parents were battling the medical establishment, Mr. Trossman, 38, and Ms. White, 37, are working with physicians.

Of particular interest is a drug called HP184, a sodium and potassium channel blocker that has been tested on spinal cord patients. When Jacob's parents brought the drug, made by Sanofi-aventis, to the attention of doctors, none had heard of it.

"They're very proactive, they were actually the ones who first told me about HP184, I didn't know about it until then," Jim Garbern, associate professor of neurology at Wayne State University School of Medicine, said in a telephone interview from Detroit.

But when Dr. Garbern, who specializes in PMD, heard about it, he immediately started to think of it as a potential treatment for PMD and more common diseases, such as multiple sclerosis.

Dr. Garbern said he is currently in talks with Sanofi-aventis to see if HP184 might help compensate for abnormalities in myelin.

"If animal studies are successful, the hope would be, we could know within a year," Dr. Garbern said. "And then we could probably pretty rapidly start testing it in human patients."

Jacob's parents want their son to be part of the research trial, provided the drug is safe. They would also like to obtain the drug, at some later time, under Health Canada's special access program.

Under that program, patients can, in some circumstances, get access to drugs before they have been licensed for approval.

"Although it is unusual to receive requests for products that are in earlier stages of development (pre-phase III) we will consider such requests if there is a good clinical rationale, data available to support the proposed use and no other regulatory option to provide access," Health Canada spokeswoman Jirina Vlk said.

Through a group called Jacob's Ladder, part of the Canadian Foundation for Control of Neurodegenerative Disease, they are trying to raise $100,000 (U.S.) -- the estimated cost to run the clinical trial on HP184. That amount will cover the testing on animals and help kick-start the study on patients afterward.

Today, Jacob attends Zareinu Educational Centre of Metropolitan Toronto, a Hebrew day school for children with special needs, located in Thornhill, north of Toronto.

There, he learns how to use a special switch, so he can communicate with others.

"If he doesn't get these tools, he's dependent on adults to read his mind," said Barbara Nash Fenton, his speech language pathologist at Zareinu. "I'm setting up an alerting device for him to say 'I need help.' "