Doctor offers unique perspective as father of a child with rare genetic disease

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Thanks to his new wheelchair, Levi Hoot is now mobile and can explore his surroundings. Levi is diagnosed with type 1 spinal muscular atrophy and inspired his father, Nathan Hoot, MD, to write a piece in Pediatrics about his perspective as a physician and father of a child with a rare disease. Credit: Nathan Hoot,

From a professional standpoint, Nathan Hoot, MD, Ph.D., understands the value of medical research that leads to new, groundbreaking drugs in the treatment of rare diseases. And as an emergency medicine physician, he's familiar with adjusting ventilators and managing patients' airways. But the magnitude of these matters also weigh on Hoot personally—as the father of a son with type 1 spinal muscular atrophy (SMA), a rare genetic disease that affects the part of the nervous system controlling voluntary muscle movement.

"It's a purely movement disorder. People with this disease cannot move. His brain is completely normal and he has the same thoughts, intelligence, and desires as other kids. There are different degrees of severity and type 1 SMA is the most severe," Hoot said.

In an incredibly moving article published in the October issue of *Pediatrics*, a medical journal published by the American Academy of Pediatrics, Hoot offered a glimpse into his life as a medical professional and father of a child diagnosed with a rare disease. Hoot is an associate professor of emergency medicine at McGovern Medical School at The University of Texas Health Science Center at Houston (UTHealth).

After Hoot and his wife Leah realized that Levi had low muscle tone and was much fussier than most babies, he was diagnosed with SMA. That diagnosis blurred the lines between the roles of physician and father—Hoot could no longer take off his white coat and stop thinking like a physician when he arrived home from work.

"We thought he was fine when he was born, but it was in his first week of life that I had this sort of sixth sense that something was off. I

couldn't put my finger on it," Hoot said. Levi was just 3 1/2 months old when he was diagnosed.

After Hoot found results of clinical research on a medication called nusinersen for SMA, he and Leah made the decision to treat Levi with the medication. His son, who had already lost some function including the ability to swallow, began receiving therapy when he was 4 months old. Nusinersen, an injection administered into the fluid surrounding the spinal cord, was approved by the Food and Drug Administration in 2016 as the first drug to treat children and adults with SMA. It is considered an orphan drug, a drug developed to treat a rare and usually serious medical condition. Few orphan drugs were available until Congress passed the Orphan Drug Act of 1983 to encourage the development of orphan drugs.

"It was just a few weeks before his diagnosis in 2016 that the FDA approved this drug. Before that, there was nothing available. It's more or less a universally fatal condition, or at least it was," Hoot said. "It's a progressive disease—we know it continues to get worse with a continued loss of movement abilities, and that's why the timing was critical."

Before treatment, Levi's condition was rapidly deteriorating. After beginning the injections, he showed no visible improvement or worsening for a long period of time. Then, Levi hit a significant milestone: he gained the ability to lift his head.

Looking at this from the perspective of a physician, this milestone moved his son two points upward on the Hammersmith Infant Neurological Examination, a measurement tool for motor development milestones in children with SMA. But through the lens of a father, this meant Hoot's son could now look up into the faces of his mom and dad whenever he wanted. Coupled with newly developed abilities to reach for toys and pick them up, he was able to choose the toys he wanted to

play with—giving him a sense of autonomy that wasn't there before.

Nusinersen is incredibly expensive: the list price is $750,000 for the first year of treatment, then $375,000 annually beyond that, making it one of the most expensive orphan drugs available. Hoot said that there's no way to place a value on their son's life and the milestones he has reached due to the use of this treatment. But, it's expensive nonetheless and he considers the high cost a consequence of the nation's for-profit system of pharmaceutical development.

"This system divides the benefits of marketing approval between patients and financial stakeholders," Hoot said. "Without financial incentives spurring development, nusinersen would not likely exist, and as parents we are grateful that it does. The price of nusinersen is difficult to accept, however."

As a physician, he often treats patients suffering from diabetic ketoacidosis because they were forced to ration their insulin due to the cost of the medication. Though insulin was discovered as a treatment for diabetes nearly 100 years ago, it's still an expensive drug to this day. The list price for a vial of insulin roughly tripled between 2002 and 2013 and continues to increase by 15%-17% every year. When Hoot comes across patients who have rationed their medication because of finances, he wonders if Levi will have to do the same in the future.

Levi sits at the dining room table and paints, an act made possible thanks to an

FDA approved treatment for type 1 spinal muscular atrophy. The treatment journey inspired his father Nathan Hoot, MD, to write a piece in Pediatrics about his son. Credit: Nathan Hoot, MD/UTHealth

"It's a challenge. Access to care is difficult. We work in a system with scarce resources due to bottlenecks in finances and availability of medications," he said.

Hoot said he felt the urge to write the article for *Pediatrics* in part because of editorials he had read regarding the trial and the drug itself, and he wanted to provide personal input into the impact of having a treatment option, when none was available before.

"The FDA approved nusinersen before the Phase III trial was done and before its results were available, and that is unprecedented. We didn't know if the treatment would carry toxicity or risks, but we knew what would happen without treatment," Hoot said. "I felt like there were some bits of commentary around the drug that indicated some people didn't understand what a big deal this was for affected kids."

Hoot said Levi has changed his perspective as a physician and as a medical educator. "It's given me a great deal of perspective on what it means to have a chronic illness and what it means to be a caretaker of someone with a chronic illness. It's changed the questions I ask. Now I ask caregivers if they have the support they need," Hoot said. "It's changed my perspective on medical training, as many of my own residents have taken care of Levi. I need to be training them well enough to take care of my family. It's one of my goals as an educator."

Hoot's wife stopped working to provide care for their son, which was very time-intensive with feedings, respiratory care, and various

therapies. Hoot watched her transform from a cosmetologist with no medical training into a special-needs superhero mom. This experience helped him realize how important it is as a physician to listen to parents of patients with special needs, because even if they lack a medical background, they are usually experts in their child's condition.

Early in Levi's illness, Hoot said, his grandparents grieved after every visit with him, knowing that each visit might be the last. Even more heartbreaking was trying to explain to their older son, a preschool student at the time, that he might outlive his brother. Despite having a treatment available, many questions about the future remain unanswered.

"Do we save money for higher education when survival to kindergarten is not assured?" Hoot asked. "Most parents take for granted the expectation that their child will go to kindergarten, then grade school, and one day, college."

Hoot and his wife are incredibly grateful for all the unexpected joys this treatment has allowed his family, such as celebrating the little victories of what was once thought impossible—coloring, laughing, reciting the alphabet, and counting to 10.

Hoot said the care that Levi has received from both Children's Memorial Hermann Hospital and UTHealth has meant a lot to their family. He is especially grateful to the UT Physicians High Risk Children's Clinic, which serves infants and children with medical complexities.

Today, Levi is doing well and gradually acquiring new milestones. Recently, he received a wheelchair, which allows him to explore his surroundings on his own like a normal toddler would. Now his favorite hobby is chasing kittens around the house in his wheelchair.

"Shortly after getting his first wheelchair, there was a moment when he

scooted out of the room. It was quiet and then we wondered, 'Where's Levi?' Parents of healthy toddlers can relate to that, but this was a new experience for us since he could never move from the place we set him down. We found him in the other room, happily scribbling on the wall with a marker. I cringed but it was hard to get mad—he was simply being a toddler in ways he never had the opportunity before," Hoot said. "He completely changed as a person when he got his wheelchair—he could be independent and explore. Now it's 'I want go over there because I want to get that toy.' Before, he never had the independence to get things on his own."

"He was never expected to sit, yet in a sense, now he stands on the shoulders of the researchers who developed nusinersen," Hoot said.

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