The Power of a Name

I first met Taylor and her mom, Anna, at an early morning physical therapy session. Through my research on PURA syndrome before our meeting, I found very little except a couple of case studies describing neonatal hypotonia and a mouse model with similar genetic mutations. I was unsure what symptoms Taylor might have, or even what questions to ask.

Sitting in the waiting room, I looked up to see Anna expertly pushing 3-year old Taylor's wheelchair and a stroller down the hallway at the same time. After making our introductions, we met Taylor's physical therapist. Since it had been some time since their last session, Anna updated the therapist on Taylor's progress. The therapist took off Taylor's leg braces and stood her up, and Taylor slowly started walking towards her mother. Taylor was practicing walking up and down stairs so Anna and I went to discuss how life has changed for their family since the diagnosis. Our conversations have helped me appreciate how overwhelming and frustrating living with rare genetic disorders can be for families who have involuntarily become pioneers of medicine.

When Taylor was born, she seemed like a normal baby except for being very sleepy, falling asleep four or five times during feedings. Anna was a first time mother so she assumed that was normal, until Taylor's four-month check-up when she showed severe head lag in a pull-to-sit test. The nurse practitioner recommended that Taylor start in the Help Me Grow program and they would reassess later. Anna was uneasy waiting for further testing and pushed for a referral to a neurologist. Taylor initially received a diagnosis of benign congenital hypotonia. Their neurologist also referred them to genetics, and from there the genetic counselor, Matt, took them through every test he could. Every time he ordered a new test, Anna would research and often found the possibilities terrifying. She broke down when they discussed Spinal Muscular Atrophy testing, and Matt explained that he wasn't testing Taylor for what he thought she had, but

to prove what she didn't have. After two years and ruling out almost every other disease, the neurologist changed the diagnosis to Cerebral Palsy. This confused Anna, as there were no signs of brain damage in a MRI or any trauma during birth. In an important lesson about the healthcare system, the neurologist explained that although the diagnosis does not explain what changed in Taylor's brain to cause her symptoms, it would help insurance to cover Taylor's therapy.

At two and a half years old, Taylor finally received whole exome sequencing within weeks of its approval as a diagnostic test, and the genetic counselor believed this would be their answer. Unfortunately the results came back inconclusive, and their family was left to continue trying to help Taylor reach as many developmental milestones as she could. Anna couldn't help but feel isolated, as no one could tell her even what was wrong, let alone what would happen.

Five months later, Matt called to inform Anna that a new study had identified a disease-causing genetic mutation in Taylor's PURA gene, a gene involved in the control of DNA replication and transcription. There were ten other children known to have a mutation in this gene. They finally had an answer. Within hours of receiving a diagnosis, Anna had already connected with another mother of a child with PURA syndrome on Facebook, and two more before the end of the day. And so their "PURA tribe" was born.

After having settled into the diagnosis after the last few months, life has returned to as close to normal as possible for the family. Taylor has regular visits with genetics, neurology, urology, GI, physical therapy, and speech therapy. One of the concerns with having a rare genetic disorder is that no one knows conclusively which organ systems are involved. Since some of the other children with PURA syndrome have heart problems, Anna was working to get a referral for Taylor to see cardiology. No one knew if Taylor's kidney problems were related or another spontaneous event. They have to be ready at all times for a new problem to arise, while continuing therapy to keep her developing. Anna has

also been dealing with transitioning Taylor to school, and learning to handle an older child with disabilities. Soon, Taylor will not be easily picked up, and will require new transportation options.

When I asked Anna what was most beneficial about having a diagnosis, her first response was the sheer fact of having it. It seems like the same relief you have when you are frantically searching for a lost item and then find it. It was something they had known was there the whole time, something that had profoundly changed their lives, but couldn't name. They could finally stop searching. And while waiting months for a diagnosis was painful for them, Anna told me about other PURA families who had waited years without knowing.

Another advantage of having a diagnosis is the financial benefits. Anna explained that when Taylor turned three, if she was only diagnosed with hypotonia, insurance might not cover all of the therapy she needed because most children with hypotonia grow out of it and don't need rigorous treatment. But every specialist Anna met with agreed that Taylor would not grow out of her delay, and needed early, intensive physical therapy to develop as normally as possible. When they received the Cerebral Palsy diagnosis, she said it brought the relief of having a diagnosis that would cover all of the therapy and specialists they needed. Her physician had not given an actual diagnosis that named the true problem, but one that allowed the system to work for Taylor. This is why I believe there should be some consideration put into creating an ICD-9 code for "unknown genetic syndrome". This might be defined by having unexplained problems in two seemingly unrelated organ systems, or having a geneticist and another specialist agree that there is a syndrome present. It is in everyone's best interest, including insurance companies, to provide early treatment for children with chronic conditions. The earlier the treatment, the better the child will do long term. In Taylor's case, early physical therapy may be able to prevent her from being wheelchair-bound in the future, which not only affects quality of life but also creates more healthcare costs.

The PURA tribe is growing stronger; in fact, the day that I went to physical therapy with Anna and Taylor was the same day their website went live. On their Facebook page, proud parents post pictures of their kids sitting up for the first time after struggling in Physical Therapy for months, or a child learning to use an assisted speech device, all with comments of love and support from around the world. They plan to gather in the next month so that all the families can meet. Anna wrote describing the deep connection she feels with these parents and children, “We learned so much about our own children by looking at them reflected back in the faces and experiences of the other children.” She told me that a physician who is interested in PURA syndrome will be attending as well, and performing movement studies on the kids. This is a great way to strengthen relationships between physicians, patients, and families, while also furthering research in rare genetic disorders. It is very difficult to do studies on rare disorders because of the very limited number of patients, but by convening with them we will be able to further our goals of understanding their disorder. It will also help us understand the families’ other struggles, and I believe it will help further the passion we have to improve their medical treatment. Families would also appreciate their physician’s desire to understand their struggles on a basic human level, and this would strengthen the patient-physician relationship.

Thankfully the PURA community was able to find each other. However, Anna wished that their specialists could share information of families with similar conditions who are interested in connecting so that they could also find support. Unlike more common illnesses like breast cancer, it’s not possible for most hospitals to host in-person support groups with other patients, but these are a vital way that many people prevent feeling isolated. This is why I think we should create a national database for families with rare disorders that physicians could refer them to. If interested, families could register online and find others with similar conditions. The medical community could better empower patients by more fully leveraging the power of the Internet. Patient confidentiality is paramount, so participation in the database would be on an opt-in basis to maintain privacy when desired. The database would provide a much-needed

sense of community so that families knew they weren't alone, which provided tremendous comfort to Anna and her family.

A national database would also be beneficial for physicians, as they could become connected to other healthcare providers treating patients with the same disease. I imagine that many physicians feel rather helpless when confronted with an illness they know nothing about. After spending years of your life learning to heal someone, it would be incredibly painful to not know how to properly care for them. If physicians of these rare and unique patients could easily find each other, they could share advice or consult each other. There is power in the size and depth of knowledge in our medical community, and we need to utilize each other to give the best care possible to people with neglected diseases.

As Anna said, “The good side of a diagnosis was knowing what’s wrong. The bad side of a diagnosis was knowing what’s wrong.” There was no longer any possibility that Taylor’s hypotonia would resolve itself. By comparing her daughter to the other children with PURA syndrome, Anna knew Taylor would probably never live as an independent adult. And it created new things for her to worry about; while Taylor has never had a seizure, it is common in other children with PURA syndrome. Anna described her fear that Taylor would develop seizures and lose the ability to walk or other skills that she has fought so hard for. Becoming involved with the PURA syndrome community has included becoming involved with research, which has taken a toll on Anna. “When you imagine the first time you see your daughter’s photo printed, you think it will be in a dance recital program or maybe on the side of a Fisher-Price box. But I definitely wasn’t planning on it being in a medical journal.” While Anna confirmed my belief that families often find it rewarding to be involved in research, she shared that it challenges the way she views her child. She read papers where Taylor is renamed Subject 8 and had a black line across her eyes in unsmiling pictures, taking away the bright personality of her vivacious young daughter.

As we were leaving physical therapy, Anna ran into another mother in the hallway, Brianne. She gave her a big hug and started talking to her and Brianne's daughter, who has a different genetic disorder. This made me think about the bond that Anna shares not only with other parents of children with PURA syndrome, but with children with many rare genetic disorders. Many of them have suffered through long periods of uncertainty and face the prospects of raising a child with a disease that few people have even heard of, let alone understand. Joining forces with other support groups would add to the sense of community and would increase their bargaining power. Anna described how parents of children with Cerebral Palsy fought for insurance coverage and access to resources by working as a unit. To increase their influence and draw further notice, rare disorders need to band together. There is power in numbers, which, by their very natures, rare genetic disorders are lacking. But just because there aren't as many people affected doesn't make it any less devastating to a family. If anything, it is more difficult, because an already terrifying experience can become that much more isolating. Rare genetic disorders deserve our attention, and creating more inclusive support groups will make it easier to rally additional people.

To give other families the relief of having a diagnosis, and to eventually treat currently neglected genetic conditions, we need to insure that medical students are informed about genetic disorders. I believe the best way to do this is to fundamentally change how we teach genetics. It is consistently taught as a separate subject, completely isolated from physiology; in reality, genetics dictate the anatomy and function of our entire body. While most students will not become geneticists, they will undoubtedly have patients who are affected by mutations, either through cancer, a de novo mutation, or a hereditary syndrome. If genetics were taught as an integrated portion of the curriculum, more students would see the relevance of genetics, become more involved in studying it and be more aware as caregivers. Discovering more about genes, what they do, and how to fix them, will benefit every specialty. Medical schools should also present more material on the current state of research in genetics and other evolving

fields. Medical students want to know what the big questions in the field are, and what is currently being done to try and answer them. We are inquisitive people with a deeply rooted drive to push the boundaries of science; I believe that by presenting these questions to us, we will begin to think of solutions and in doing so will become involved in genetic research.

In the eyes of many parents of children with rare disorders, I have seen a fierce passion and protective aura, not unlike that of a soldier. They have been through many battles – with insurance, healthcare providers, and their own fears. They have fought bravely for their child's right to an explanation and proper therapy. They know that their child could easily get lost in the immensity of the healthcare system, but they do not allow that to happen. They guarantee that the physicians, the insurance companies, and the policy makers alike will pay attention to their child's needs. But sometimes, even the fiercest warrior needs a tribe behind them; they need someone who ensures they stand back up when they fall and protects their cause when they are vulnerable. That is what a diagnosis gives – it is the difference between one person and an army, and they are fighting for attention and resources from a medical system that is often pulled in many directions. As physicians and scientists fighting for an answer, we are providing them that army, and in doing so becoming a part of it. And I can imagine no greater cause to fight for than a child's right to proper medical treatment.