Targeting the Toughest Diseases

Episode 6 – Targeting Duchenne Muscular Dystrophy

John Killian: *It seems like both yesterday and forever ago, if that makes sense.*

That's how John Killian describes the day his son got a life-changing diagnosis.

John Killian: *I still remember, you know, the exact setting, the, the words that were said, it's one of those things in your life that you just don't forget.*

It was 17 years ago.

John Killian: *Sam was diagnosed when he was three years old.*

For John and his wife Stephanie, that's 17 years of not knowing what the future holds for their son. Seventeen birthdays… and every one of them spent hoping Sam will survive until his next.

The signs were there. But they were subtle. As a toddler, Sam just wasn't developing like their other kids:

John Killian: *He was sitting but not standing at the right times. And he's the fourth of our four kids. So, we were pretty in tune with what kids were doing at what age. And, but we also knew. Um, kids develop it at different speeds. And so, we weren't too, too worried.*

Even Sam's pediatrician didn't notice anything wrong at first. Then one day the family was playing at a park around the corner from their house, and Sam broke his leg.

John Killian: *That's how we ultimately got the diagnosis. He had a cast on his leg for six weeks and was having trouble, recovering from that. We went to a physical therapist to try and get him some help. And ultimately, she's the one who told my wife, 'Hey, I think that Sam might have muscular dystrophy.'*

Hi. I'm Jordan Gass-Pooré, a member of the University of Southern California's Center for Health Journalism.

This is *Targeting the Toughest Diseases*, a podcast from Bloomberg Media Studios and Vertex Pharmaceuticals.

In this series, we look at some of humanity's most challenging diseases, and how Vertex, a Boston-based biotech company is using innovative tools, methods and a unique philosophy to search for treatments and cures.

Today, we're looking at Duchenne muscular dystrophy or DMD. That's what Sam was diagnosed with. It's the most common muscular dystrophy in children, mostly affecting boys. Until recently, children with DMD were not expected to live beyond their teens.

John Killian: *Before Sam was diagnosed, there really was sort of an approach that there wasn't much you could do. And, you just sort of, took care of your kids and loved them.*

Sam is now 20 years old. Like most people that age, he's still trying to figure out what he wants to do with his life.

John Killian: *Sam went to college and he was super excited to be able to go to college.*

He'd really like to go into some kind of counseling. He said, "Hey, I think my life experiences would be good to be able to counsel people." And so, I thought that was a really good path for him to go down.

He ultimately would like to do that. Live on his own and have a job and a career. But I think he's still trying to figure out how that's going to work for him.

Duchenne muscular dystrophy affects one in every 5,000 newborns. The symptoms usually appear between the ages of three and five.

It's caused by mutations in a particular gene. That gene produces a protein called dystrophin. Dystrophin helps protect our muscle fibers from damage whenever they contract and relax.

But the DMD mutations means there's not enough dystrophin in the body. The result is progressive muscle weakness and deterioration.

Children born with DMD gradually lose their muscle mass and are eventually unable to walk. Over time, they often develop heart and breathing issues.

Dr. Mena Scavina: *I remember even at the age of 10, uh, sitting in the living room and there would, there was a Labor Day weekend telethon in which children with neuromuscular diseases were depicted.*

That's Dr. Mena Scavina.

Dr. Mena Scavina: *And I just remember thinking, I can't imagine not being able to dance or play sports or do the things that we were so active in.*

Those TV telethons influenced young Mena in a big way.

Dr. Mena Scavina: *So, at that time it was almost like a light went off and I thought, I think I'm going to do things to try to help these kids. I started having fundraisers in my backyard.*

Eventually Mena went to med school, and is now Director of the Neuromuscular Clinic at Nemours Children's Hospital in Delaware. She's also a clinical care team advisor at parent project muscular dystrophy.

Dr. Scavina has been working with families for 25 years. She's seen how DMD affects a number of different systems in addition to muscles.

Dr. Mena Scavina: *We're learning more and more that also the brain, which is affected in the sense of, we do see autism spectrum issues. We see some cognitive and learning issues. There can be things such as obsessive compulsive disorder. So, it really involves brain, heart, lungs, muscles.*

It's an incredibly complex disease, and there's a long history of studying it.

Dr. Mena Scavina: *It was a Dr. Duchenne actually, Dr. Guillaume Duchenne in France in the 1800s that began to describe a boy who had this condition and then started to amass a number of children and, and described it in more detail. And so he noticed that they were weak. They had enlargement of their calves, difficulty walking and progressed over time.*

The genetic link was identified 30 years ago.

Dr. Mena Scavina: *I was actually in medical school and remember sitting in a class when the news sort of broke and people thinking, oh wow. We now know the gene. And so within my lifetime that has been discovered. And then that led to a cascade of more discovery, understanding the protein in more detail and so it was really a breakthrough.*

With that breakthrough came medications and treatments to help alleviate some of the symptoms of the disease, including:

- **Steroids**
- **Physical therapy**
- **Surgery**
- **Ventilators for patients who need help breathing**
- **and Heart medication**

All of these developments have helped improve the quality of life for people living with DMD. They have also created the hope of longer lives.

Jon Rey-Hastie: *I'm 41 now. Which was completely unheard of.*

Jon Rey-Hastie is an extraordinary example of how modern medicine has extended the life of DMD patients. He uses a ventilator, which affects his speech.

Jon Rey-Hastie: *I knew people with Duchenne at school and most of them died. I think the oldest one lived til age 30.*

When Jon was diagnosed as a toddler in England, he was never expected to live past his twenties.

Jon Rey-Hastie: *I remember, reading in a magazine that there was an adult who was 40 years old with Duchenne. And I think that really kind of opened my eyes. I think I might be 27, 28 at the time. I thought I was coming to the end, like maybe have a year or so left.*

Jon has tried just about every kind of medical help available.

Jon Rey-Hastie: *I mean, obviously there was the steroids, when I took them, it was very experimental. I only took them for about five years. They may have extended my ability to do things for maybe a year or so, but not enough to really transform my life.*

What has transformed his life is a ventilator – a machine that looks like a mouthpiece or a mask that goes over his nose and helps him breathe as his respiratory muscles have weakened. He also uses a system that simulates coughs which helps clear mucus out of his lungs.

Jon Rey-Hastie: *I wouldn't be here without the ventilation. And I think that's probably the single most important thing, because otherwise your lungs would deteriorate kinda in your late teens, early twenties. You would get a chest infection that you wouldn't be able to fight it off and that's how you would die.*

His ventilator along with his heart medication have allowed Jon to attend college, obtain his PhD and even make a documentary featuring adults with DMD doing inspiring things with their lives.

Spending time with others with the condition is a constant reminder that at 41 years of age, he is definitely the exception.

Jon Rey-Hastie: *To look at me and treat me as a typical case of Duchenne, I think would be wrong but that's cause there isn't really a typical case, you don't know how you are going to be affected by it. You don't know what's to come.*

Everything helping Jon and Sam live with DMD falls under the category of 'management of the symptoms.'

Dr. David Altshuler: *There's nothing really right now for these patients that gets at the underlying cause, but we understand the biology and have an approach that we think could be transformative.*

That's Dr. David Altshuler – the Chief Scientific Officer at Vertex Pharmaceuticals. As a company, Vertex focuses on diseases with huge unmet needs. In the case of DMD – Vertex is investigating a genetic treatment.

Dr. Altshuler: *Most companies seem to operate where they have a, what they call a platform. They'll pick a given approach. It might be small molecule pills, or it might be RNAI, or it might be protein therapeutics, gene therapy. What have you. And they then look for places to apply it.*

We have decided to be agnostic, to modality and use whatever tool is needed.
When patients have a serious disease and the underlying cause is known, it usually ends up that it needs a specific and bespoke solution.

So, we've turned it around and said, we're not in the business of having a hammer and looking for nails, we're in the business of looking for patients in need and gathering whatever tools are needed to make a difference for them. And what we've discovered is that actually we can make that work and it opens up the possibilities, so there are diseases that we can work on and potentially help people that we otherwise couldn't do.

Dr. Alison McVie-Wylie leads Vertex's research team targeting Duchenne Muscular dystrophy.

Dr. Alison McVie-Wylie: *Duchenne muscular dystrophy is caused by a mutation and a gene known as dystrophin or the DMD gene. And that gene is one of thousands of genes that we have in our cells.*

As part of research into this area, Vertex and other companies are using something called *CRISPR/Cas9*, highly sophisticated technology that uses gene editing. CRISPR technology is thought to work by removing, adding or altering DNA. And you can think of Cas9 like a microscopic pair of scissors. It allows researchers to cut the strands of DNA at a really specific spot.

Jordan Gass Pooré: *What type of DMD patients will these potential new treatments help?*

Dr. Alison McVie-Wylie: *Our initial programs were targeting a subset of patients. But our hope is that we'll be able with time to expand the program and treat as many DMD patients as possible. At the end of the day, gene therapy or gene editing, truly is personalized medicine, which is actually one of the most amazing things about it.*

Dr. McVie-Wylie knows the disease has a long history... But she's hopeful a potential treatment is on the horizon:

Dr. Alison McVie-Wylie: *I'm a geneticist by training and to be honest, when I was training like 20 years or so ago, I always thought, wouldn't it be fantastic if you could treat a genetic disease by actually correcting or repairing the mutations that patients have in their DNA and to think only 20 years later that we have the potential to do that. It's just phenomenal actually. It's incredible. So that's what excites me. That's why I'm here. That's why I'm here at Vertex to really work at company that has the commitment to kind of be on that cutting edge.*

Until a cure is developed, Jon Rey-Hastie, continues to serve as an example to others in the DMD community.

Jon Rey-Hastie*: It took me... it was quite a while before I really thought I actually had a future.*

A future, yes. But an uncertain one.

Jon has made an effort to get the most out of the days when he is feeling good:

He's gotten his PhD, established an advocacy group for people with muscular dystrophies, run by people with muscular dystrophies, and he's married.

Jon Rey-Hastie: *We like to do a lot of things together. We play computer games, we do a bit of gardening and just other hobbies, just like going out for meals, going out, socializing, being out with friends, and yeah, just enjoy spending time together really.*

They are even planning a vacation in Florida.

Jon Rey-Hastie: *I'm really looking forward to that. Just hope that we can get there with no issues beforehand.*

That's always the caveat – he makes plans, and he hopes for the best.

Jon Rey-Hastie: *It's hard work. Particularly being independent and advocating for yourself and it does get exhausting. But I do think the prospects for young people with Duchenne now is even greater than they were for me.*

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I'm Jordan Gass-Pooré, thanks for listening.