Targeting the Toughest Diseases

Episode 2 – Targeting Sickle Cell Disease Script

Terri Booker: *And it's like if someone grabs your body and twist in the opposite direction with each hand, its like, you can feel the pressure in your bones and you can just feel every part of your body is hurting.*

20 years ago… during her sophomore year in college, Terri Booker was hit with the worst pain of her life:

Terri Booker: *My legs were burning, and then it just went up throughout my whole entire body to the point where I was unconscious, and I was put on life support. I wasn't able to breathe on my own. They told my mom I had kidney failure, I had lung failure.*

There was no clear path to treatment for her… just uncertainty.

Terri Booker: *They said, "You just pray because we don't know what's gonna happen to her."*

What happened was, she got better… for a while. But then the pain returned and she was back in the emergency room.

Her recurring visits to the ER seeking relief from the pain revealed a second problem – not a medical one… a societal one.

Terri is Black. And as an African American woman seeking pain meds she was treated horribly – she was presumed to be a drug addict, and her medical issues were ignored.

Terri Booker: *It is infuriating because when you go into the ER, you're expecting to receive help, you're expecting to be treated as a patient in need of something, not treated as someone who is wanting to get their next high.*

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

This is *Targeting the Toughest Diseases*, a podcast produced by 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 sickle cell disease, a blood disorder which can cause organ failure, stroke and even death.

It's a disease that affects roughly 100-thousand Americans, including Terri Booker:

Sickle cell disease is not something you catch. It is a genetic condition you're born with. Often babies are diagnosed before they are even born.

Terri was an exception. She didn't know she had it until she was 11.

Terri Booker: *They pricked my finger and, um, I remember them putting it under a microscope, and when they had it under a microscope, all these people were rushing over, and I remember this so vividly, and they were like, "Oh, come here. Come look,"*

Terri was in 5th grade and her mom had taken her to the doctors because she had been complaining of pain.

Terri Booker: *And I'm like, "Okay," and they said, "You see all these little funny shaped cells?" And I'm like, "Yeah?" They're like, "Yeah. That's sickle cell," And I said OK. And I'm like, "Well, what does that mean?"*

'What it meant' **- was that, while sickle cell disease *does have a cure* for *a very limited* number of patients – Terri wasn't one of them.**

Sickle cell disease, or sickle cell anemia as it's often called, affects red blood cells. Those are the cells that carry oxygen to all the tissues in our bodies.

Normally, our red blood cells are soft and shaped like a doughnut, so they can squeeze through even the smallest of blood vessels.

But sickle cell disease changes them: Specifically, it causes the hemoglobin proteins inside the red blood cells to change their structure. Instead of being doughnut-shaped - they become curved, like a crescent moon, or as the name implies, like a sickle.

These *odd-shaped* cells are also hard and sticky which means sometimes they can't flow smoothly through blood vessels. And when that happens – they start piling up like cars on a busy highway making it really hard, if not impossible, for oxygen to reach where it needs to go.

It's that lack of oxygen to tissues that causes the stabbing pain.

That's the medical side of the disease, but as Terri mentioned earlier, there is also a societal component.

Dr. Isaac Odame: *To address sickle cell disease, we also have to address the fundamental issues that relate to systemic racism and how it impacts on access to care.*

That's Dr. Isaac Odame. He studies the ways racism and medical care intersect when it comes to sickle cell disease. He is the Medical Director of the Global Sickle Cell Disease Network at the Center for Global Child Health.

Dr. Odame grew up in West Africa.

Dr. Isaac Odame: *Sickle cell disease was something that I was very familiar with. Not only did I have distant family members who had children with sickle cell disease, but some classmates and schoolmates who also lived with the condition. So I was exposed very early to the ravages of this disease.*

The first documented case of sickle cell anemia in America was in 1910 – so just over a century ago. But its history dates back thousands of years.

Dr. Isaac Odame: *Sickle cell disease has been known for centuries in parts of Africa. And if you go into the oral tradition, they did have descriptions of the disease, which typified the chronic and intercurrent excruciating pain associated with the disease.*

Oddly enough, the mutation that changes the cell's shapes was once an evolutionary advantage - protecting against malaria.

Dr. Isaac Odame: *It predominantly affects people of African descent because malaria is very endemic in Africa. It occurs in people of Indian descent, Mediterranean descent, and parts of the middle east, Arabian Peninsula.*

And when you look at the common link between all of these areas, is malaria endemicity. So it was a survival advantage it provided against malaria, and the percentages of people with traits in the population would rise over time.

Having sickle cell 'trait' – that is to say you develop some misshapen blood cells but your body is able to break them down and you don't have any symptoms - is actually quite common in African populations – and people with it are better able to break down the malarial parasites.

But for some people, those traits become too much for their body and they develop the disease with all of its horrible consequences.

That historical context explains why the majority of sickle cell patients in the United States are African Americans.

That means sickle cell treatment provides a clear example of the racial inequities and disparities in the medical system. That includes 'access to care,' and 'quality of care.' Both of which are lower for African Americans.

Dr. Odame is hopeful that sickle cell treatments in development will not just *treat* the disease – but will address those *other complex* issues as well:

Dr. Isaac Odame: *I think more and more, the patients are becoming more empowered. And I think they call themselves warriors, which is the appropriate term. They're not only dealing with the ravages of the disease, but they're also having to fight a system that doesn't recognize their needs appropriately. And so the warriors are beginning to speak out aloud. The system is beginning to respond.*

Vertex Pharmaceuticals is a leader in that response.

Dr. David Altshuler: *For it to actually help people's lives, it has to work for them and it has to work for society.*

That's Dr. David Altshuler, the Chief Scientific Officer at Vertex. They have a unique approach to choosing the diseases they target.

Dr. David Altshuler: *Vertex has decided to focus on a set of diseases where we see great unmet need, where we see the human biology is clear, and we feel that we have the technology, the insights, the wherewithal to make a difference.*

When it comes to Vertex's sickle cell program, Dr. William Hobbs is in charge of clinical development.

Dr. William Hobbs: *I started in medicine being interested in hematology and sickle cell. And so, I came at it from a scientific point of view in terms of gene therapy. And then along the way I started to meet sickle cell disease patients and their families and realized that there was a lot more to it than just a scientific question.*

Dr. William Hobbs: *Early on in my academic career I started an adult sickle cell disease treatment center. And one of the first patients I saw there was a woman. And she walked in, she sat down, she said, hello, Dr. Hobbs. I just got to know one thing. If I ever need you, if I'm in an ER at two in the morning, I just need to know that you're there on the other end of the phone, 24 hours a day, seven days a week, whenever I need you. Because if you're not, then there's no reason for me to be here. And it was that sort of dawning awareness for me that if you're going to take care of patients living with sickle cell disease, you have to be all in.*

Jordan Gass-Pooré: *That's a big ask.*

Dr. William Hobbs: *It was a big ask. However, I think if you look at the history of how sickle cell disease patients have generally been treated by the medical system, I think sickle cell patients aren't asking for anything unique or above and beyond or special, they're just asking for equity care and what we would offer to anyone else.*

Jordan Gass-Pooré: *What treatment options are currently available for patients with sickle cell disease?*

Dr. William Hobbs: *We've come a long way just in the last few years. For a long time, there really were no therapies available. In the mid 20 teens, there were three available therapies. And those therapies were based on potentially reducing, but not eliminating the complications of disease in some, but not all patients.*

Jordan Gass-Pooré: *I'm really curious about why Vertex has decided to invest so heavily in R and D into sickle cell disease.*

Dr. William Hobbs: *For the most part, sickle cell disease has largely been ignored by the pharmaceutical industry for a long time. I think there is always historically been a perception that it's a very difficult disease to go into from a commercial and marketing standpoint. However, if one has an approach that is based on solid biology and recognizes the unmet medical need that actually exists in sickle cell disease, where 100,000 patients are waiting, then it becomes very compelling to do it.*

Fetal hemoglobin is the protein that transports oxygen from the mother's bloodstream to organs and tissues in the fetus.

Dr. William Hobbs: *We know from natural history studies and a lot of other data that fetal hemoglobin is protective against the effects of sickle cell disease.*

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.

Dr. William Hobbs: *Whenever you do something like that, there are any number of unknown questions that have to be answered, scientific and medical. And we're learning to understand what all of those are. What is the behavior of a gene edited stem cell? How does it work once it goes back into the body?*

A lot of questions – but also a lot of possibilities.

Dr. William Hobbs: *I think one of our challenges, which is not really a Vertex challenge, but it's a society challenge, a government challenge, a healthcare system challenge, is how do we make these types of therapies accessible and available to the patients who need them? I mean, I think one of the things that's unique about Vertex and the approach here is just that it is completely focused on the patient to the exclusion of just about everything else. The focus is really, "have we identified and cracked the right science that translates into something that meaningfully changes the outcome for patients?" And we do that brutally and honestly, and very transparently within our own programs here.*

Jordan Gass-Pooré: *And what is the timeline for this? So say for instance, I have a friend or a family member who has sickle cell disease. How long should they expect to wait for this treatment?*

Dr. William Hobbs: *Yeah. We know that there are people waiting and there always are in drug development. I think one of the things about this program is how quickly it has progressed to the point that it's at now. We're hopeful that it's not too long.*

The research, the testing, and the potential approvals are moving forward as quickly as possible. And in the meantime, Terri Booker is just trying to live her best life.

Terri Booker: *I exercise, I hang out with my cat, Lewis. Who I love and who ... He always knows when it's something wrong 'cause he'll stay under me a little bit longer or a little bit more, and, I cook often. I cook most of my meals, and when I say I cook every day, I cook every day. And I, uh, I pray.*

What she is praying for, ultimately, is a cure. Terri says until that happens – she'll continue to keep the faith.

Terri Booker: *My faith has grown so much through this process because I feel like … As a human, I feel like it's no way I could be going through these things. I should be in a hole crying somewhere.*

So, our pain is real, and we cope and we do what we have to do to try to live a "normal life," but our pain is real. And when people understand that, I feel like you can understand a sickle cell patient.

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

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

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