

Targeting the Toughest Diseases

Script: Episode 2 – Targeting Sickle Cell Disease

Terri Booker: *And it's like if someone grabs your body and twists in the opposite direction with each hand, it's 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 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 100,000 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're even born.

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

Terri Booker: *They pricked my finger and, 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 fifth 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?"

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 donut, 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 donut-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's 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's 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, it's 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' is actually quite common in African populations. It evolved over time because it prevents the development and spreading of malaria.

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

That means sickle cell care 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. Bill Hobbs

You know, I started in medicine being interested in hematology and sickle cell disease in particular, mainly from a research standpoint. And that was because sickle cell disease has long been considered a disease where the underlying cause of disease could be targeted if innovative approaches could be identified.

And so I really came at it from the scientific point of view. And then along the way, I started to meet sickle cell disease patients and their families, coordinate their care, and realize there was really a lot more to it than just a scientific question.

Early on in my academic career, as a physician scientist, I started an adult sickle cell disease treatment center. And I still remember this. One of the first patients that I started seeing was a woman who had longstanding and severe disease. And at her first clinic visit with me, she walked in, sat down and said, Hi, Dr. Hobbs, I've just got to know one thing. And that is if I ever need you, if I'm in an emergency room or a hospital, it's two in the morning, it's a night, it's a weekend. 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 awareness that I realized at that point that if you're going to take care of patients living with sickle cell disease that you really need to be all in.

Jordan

That's a big ask.

Dr. Bill Hobbs

It was a big ask, but it's actually a fair ask. And 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 really asking for equitable care and what we would offer to anyone else with a chronic severe disease.

Jordan

So, what treatment options are available for patients with sickle cell disease?

Dr. Bill Hobbs

Yeah, you know, the causal biology of sickle cell disease has been known for many years, but for a long time, the only therapies available were able to reduce, but not really eliminate complications of disease in some, but not all patients. And we've come a long way in the last few years, but there's still a lot of work yet to be done.

And I often think about the sickle cell disease patients that I've cared for over the years, knowing that they were in desperate need of new treatment options. And so, you know, we continue to look at multiple angles and innovative options with the goal of treating the underlying cause of the disease.

Jordan

I'm curious from Vertex's point of view, why has Vertex decided to invest so heavily in R&D, specifically with sickle cell?

Dr. Bill Hobbs

For the most part, sickle cell disease has been largely ignored by the pharmaceutical industry for a long time. And I think there's 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's based on solid biology and recognizes the unmet need that exists in sickle cell disease where there's millions of patients waiting worldwide, it becomes very compelling to do it. And so this is really about patients. It's understanding the medical need, it's understanding the causal biology, and then innovating on treatment approaches, which is what we at Vertex do. And you could say that this is in our DNA.

Jordan

Sickle cell isn't a new disease. There's been a lot of work done and a lot of innovation. What is Vertex bringing to this that's new?

Dr. Bill Hobbs

Our aim is to investigate multiple different types of approaches that can give us the best opportunities to hopefully treat the causal biology of sickle cell disease for as many patients as possible.

Whenever you do something like that, there are a number of unknown questions that have to be answered, both scientific and medical, and we're learning to understand what all of those are. And I think what we're also understanding is that for diseases like sickle cell disease, where there's such a huge need for treatment options, that serial innovation is required. And I think this is a focus for us to continue to innovate because, you know, as we all know, technology doesn't stand still, and so neither should we.

Jordan

That's the approach philosophically, but what does it actually look like when you put it into practice?

Dr. Bill Hobbs

We've learned a lot from natural history studies and a lot of other data about how we hope to be able to target causal biology with the aim of treating the effects of sickle cell disease. So for Vertex, it really begins with a deep scientific insight into causal biology and then serially innovating using all available tools and modalities to identify potential treatment options. And so it's essentially identifying the right tool for the job.

And one of the things that's unique about Vertex and the approach is just that it's so completely focused on the patient and what the potential treatment outcomes could be. And so the focus is really 'have we identified and cracked the right science that can translate into something that could be meaningful for patients?' So the goal is a high bar and we do that relentlessly, we do it very aggressively and we constantly strive to out innovate even ourselves within our own programs here. And that's how we do science and develop medicines.

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.

If you like what you hear, subscribe and leave us a review.

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