SickKids VS Cardiac Collapse

Hannah Bank: It was March 2021, morning recess at Sacred Heart Catholic School in Port Lambton, Ontario. Ten-year-old Seth was playing catch with one of his cousins. In fact, several of his cousins went to Sacred Heart, one of just two schools in the small community. That morning, after a few tosses, Seth missed a catch. And the next thing his cousin knew, Seth was on the ground. Here's how Seth's mom, Tricia, pieced it together.

Tricia: My niece, who was in grade 7 or 8 at that time, saw him fall. She was across the play yard, started to run to Seth because she knew that was an unnatural fall. So, she had started CPR. Kids ran to the principal, got the principal, grabbed the defibrillator. She came out, took over, started doing compressions, then defibrillated him. There's 120 students in that school. They all saw Seth drop. They all saw everybody rush around him. All the teachers rounded up all the kids. Got them in the classes. The paramedics showed up. At this time, Seth still had no heartbeat.

Hannah: When he was a baby, Seth had been diagnosed with a heart disease called cardiomyopathy. His heart was enlarged and wasn't pumping blood properly. As he got older, he had to be careful about certain sports and avoid extreme temperatures. He regularly saw a cardiologist in nearby London, and at SickKids. Over the years, there were ups and downs, lots of scans and medication tweaks. Sometimes he'd get winded and tired. But most of the time, Seth felt ok.

Cardiomyopathy – especially Seth's kind – comes with a risk of sudden cardiac death, when the heart quits without warning. Some people will go their whole lives without experiencing this. Some will survive it. Others will die from it. For patients and families, this uncertainty is unnerving.

Tricia: The uncertainty of him going to school, let me tell you, was scary. I'm trusting people with my child. People that had never had to deal with a child with a heart condition.

Hannah: Before enrolling Seth, Tricia insisted that the school get a defibrillator, and that all the staff get CPR training. She prepared an emergency bag for Seth that contained information about his condition, the names of his medical team, a list of medications – and a teddy bear, in case he ever had to ride alone in an ambulance.

That morning in March, as Tricia remembers it, Seth hadn't felt any different. His body betrayed not the slightest hint that his heart would simply quit that day, causing him to crumple in the school yard.

But what if there *was* a way to know – to know if you were the kind of patient that would probably never have a brush with sudden cardiac death. Or the kind that might. And if you knew these odds, what if you could be ready, and even prevent it from happening?

You're listening to SickKids VS, where we take you to the frontlines of child health. I'm Hannah Bank and this is SickKids VS Cardiac Collapse.

Hannah: Dr. Seema Mital has resuscitated countless patients who've had major cardiac events. And she's lost more patients than she cares to recall. Seema is a cardiologist at the Heart Function & Transplant Clinic at SickKids. The team provides specialized care for children who are in heart failure, or who've had heart transplants. About 80 percent of these patients have cardiomyopathy.

Dr. Seema Mital: Cardiomyopathy is a genetic disease of the heart muscle, and it often runs in families. It is the leading cause not only of heart failure, but also of sudden death in children and young adults. This is a condition where the heart muscle can either get very thin and weak, it can get very thick, or it can get very stiff, and the heart can't pump blood effectively. And currently there are no cures. And that's actually one of the reasons why a lot of the research that I do is focused on cardiomyopathy.

Hannah: Seema is also a scientist. She's spent the last 15 years working to find the underlying genetic cause of cardiomyopathy. There are several types, and they can all be quiet and sneaky. They can present at different times for different patients, and look different, too, even among family members. Cardiomyopathy can lurk in the background, with initial symptoms so mild, they could easily be dismissed.

Seema: It may start out without any symptoms. A child may be doing fine, not even realizing they have this underlying heart condition. And as it progresses, when symptoms develop is when it comes to our attention. Once it starts progressing at a certain point, it reaches a point of no return where there is nothing you can offer outside of heart transplant. And this is because the heart muscle starts losing its capacity to effectively pump blood. It's pumping blood 70, 80, 90 times a minute, all day, all night long. Over time, as it gets weaker, it loses this ability. And sometimes it may just completely give out.

Hannah: Initially, as a baby, Seth had been diagnosed with dilated cardiomyopathy, meaning his heart muscle was weakened and stretched, like a slightly deflated balloon. About a year later, the condition became *hypertrophic* cardiomyopathy, which means that the walls of his heart had become thick. And overtime they also got stiffer, which can cause erratic heartbeats, called arrhythmias. In their worst form, the pumping chambers of the heart quiver fitfully instead of pump. Blood flow to the body stops abruptly, leading to sudden cardiac death.

Seema: Hypertrophic cardiomyopathy is the leading cause of sudden cardiac death in children and young adults. And it *can* be picked up with symptoms as sometimes, like palpitations or tiredness, feeling dizzy, fainting. But it can often be silent and the child may collapse suddenly as the first presenting signs. I would say anywhere around eight to 10 percent of children who have hypertrophic cardiomyopathy can have a sudden cardiac death-like event within five years of diagnosis and or go into this kind of life-threatening arrhythmias, from which half of them may not survive because they were unable to be resuscitated.

Hannah: Tricia and her family carried the weight of this possibility every day. She remembers a solemn conversation with one of Seth's cardiologists when he was around five or six.

Tricia: I said, like, what does the future look for Seth? Like, can you give me any idea? Can you help me navigate this world? You know, and she says, Tricia, there is like 18 plus roads that this child can take. One being he could wake up tomorrow and nothing be wrong with his heart – like it could all go away – to him needing a pacemaker or defibrillator or ECMO or the Berlin Heart, a heart transplant, to possibly even death.

Hannah: That day on the schoolyard, the family's worst fear had come true. But despite the name, sudden cardiac death *is* survivable with timely defibrillation and CPR. Seth got both in heavy rotation. When the school's principal got word that Seth collapsed, she raced outside with the defibrillator – the

one Tricia had insisted on. The principal shocked Seth and did chest compressions repeatedly until the paramedics arrived from nearby Wallaceburg. It took 40 minutes.

Though Seth had been without a heartbeat for 40 minutes, the chest compressions kept blood flowing to his organs, enough to stave off tissue damage. But, just as paramedics got a heartbeat, they lost it again at the hospital. There, a team worked on Seth and revived him a second time.

By this point, Tricia had arrived from nearby Chatham, where she was working. Her husband and her parents met her at the hospital. Her sister happened to be the ER nurse on duty that day. She was excused to be with the family.

Tricia: And then when we finally got to see him, my heart crashed. You know, it's not every day you see. Sorry. It's not every day you see that picture. And I thought, okay. I'm going to take my first picture of what's going on. So I took a picture of Seth on that table, and I thought, okay, this is at his worst that I've seen. We can only get better from here. Seth still had a blue tinge to him. You could tell he was starting to bruise a little bit from the CPR and the cardiac defibrillation. A very blue. I mean, he's a redhead, so he is very pale. So when he starts to go blue, you tend to notice it a little more, wires everywhere. And then I looked under him and there was his brand new sweatshirt he had worn to school that morning cut off of him. And I was like, okay, we're going to have to buy a new sweatshirt for him. And I mean, that was my thinking is, okay, he's going to survive this and we're going to have to get him another sweatshirt. No big deal, you know?

Hannah: Against the odds, Seth had survived a lethal sudden cardiac event. Seema, the cardiologist we heard from earlier, knows Seth's story well. She has treated him at the Heart Function Clinic, which has been following Seth since he was two years old. And though he was one of the lucky ones, Seema understood the toll of Seth's ordeal. For several years she had been working on a tool to prevent all this.

Seema: This whole episode, it was a catastrophic event and he did require a lot of rehabilitation, but he's recovering now. He's on the right medicines. But it's patients like Seth who remind us why it is so important for us to predict this kind of event before it happens, so that they are not running this risk from where they have these life-threatening arrhythmias from which they may or may not be able to be resuscitated.

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Hannah: In order to predict a disease outcome, you have to collect reams of data on lots of patients so you can tease out the factors that might account for their trajectory. For hypertrophic cardiomyopathy, Seema and her team wanted to find out what factors are important for kids who've experienced a sudden cardiac event. And for kids who haven't.

Seema: The first thing we had to do is to make sure we had access to a large database of patients, not just patients we see at SickKids alone. We had to establish an international and multicenter network, a registry. So now we have 20 centres from across Canada, the USA, as well as Australia.

Hannah: Starting in 2017, clinical teams from all these centres began inputting dozens of data points into the registry about their patients.

Seema: We have several thousand patients in the registry, and from the first several hundred patients, we collected data from the time of presentation to their last follow-up to see what they looked like when they first presented. What were their symptoms? What were their echo findings? What were they ECG findings, family history, their genetic status, how it changed over time and which patients went on to develop one of these events.

Hannah: Cardiologists can (and do) consider these factors when seeing patients in the clinic and assessing their medical history. But physicians can't always be certain enough to confidently counsel a family about the risk of sudden cardiac death for *their* child. So, Seema and her team developed a calculator that could ingest and analyze all this data. And give doctors mathematical validation to inform their recommendations.

Seema: So what this calculator is, we call it PRIMACY – or precision medicine in cardiomyopathy – where the goal is to take all these various features that we consider risk factors for sudden cardiac death and put them into a single model. And we're using mathematical and artificial intelligence approaches that you can make complex calculations to determine what the risk of this particular child in front of you is for having a sudden death event in the next five years. We as physicians until recently, we saw that they have multiple risk factors, but each risk factor is not the same. They're not equal. Some are more serious than others. And the human mind cannot always calculate or compute that. But with this kind of tool, we can mathematically include all that information by studying a large number – hundreds of patients – in order to come up with a precise prediction for that child.

Hannah: In other words, by examining the whole group, you can get a clearer picture of the individual. In this case, a personal risk-score for sudden cardiac death.

Seema: It can range from as low as, you know, two percent over five years to maybe as high as 60, 70 percent over five years. And that's powerful information because it empowers physicians and the families to understand and quantify what the risk is.

Hannah: If the risk score is high, doctors can recommend an implanted defibrillator (or ICD), a small device placed inside or near the heart. The ICD can detect and shock the heart out of a bad rhythm. A literal life-saver.

Seema: Once we have the results of this calculator to ask the family and the patients what would work best for them, what is most important for them. So, it's no longer a physician telling them, "no, this is what you must do." They need to understand the risks and benefits of an ICD versus the risk of sudden cardiac death, and then make that informed decision.

Hannah: ICDs are 90 percent effective. But not all cardiomyopathy patients should necessarily get one. The implant surgery is not without risks, and ICDs can sometimes fire inappropriately, which can be traumatic. The PRIMACY calculator helps doctors and families weigh these risks. Seth's situation was

more cut-and-dry. Since he'd just had a sudden cardiac event, his medical team recommended he get an ICD as soon as possible.

Tricia: I call it my insurance policy. So when we finally were able to get a defibrillator, like the ICD in him, it was relief. I could sleep and know that it's in there. And if something happens, it's gonna shock.

Hannah: The PRIMACY calculator is the first tool of its kind for paediatric patients. It launched in 2021 as a web application accessible to clinicians around the world. When Seth was diagnosed in 2010, PRIMACY wasn't even in motion. But it's not a stretch to think that such a tool could have predicted this outcome for Seth, and that he could have received an ICD much earlier. And that it would have spared him a near-death experience, a long resuscitation, and the resulting brain injury.

After his horrific experience, Seth spent three weeks in the ICU. He was intubated and needed three attempts before he was able to get off the respirator. He spent another two months in hospital, then several more weeks in rehab. He had to re-learn how to walk and talk and eat. Tricia considers what Seema's tool could have meant for Seth.

Tricia: I think the tool would have been amazing, because the reality of it is we were at the cardiologist two days prior to Seth having a cardiac arrest. He had a Holter monitor on 24 hours prior to his cardiac arrest. If that tool would have been in place, he would have already had an ICD. And then as soon as he went down, he would have been shocked. Maybe he wouldn't have been out 40 minutes plus and sustained the brain injury. And I hope it helps a lot more parents out there.

Hannah: Since the launch of the PRIMACY tool, Seema and the team have been working on a mobile app version. And, in a major technical feat, PRIMACY was recently embedded into SickKids' electronic health records system, which means the tool will pop up automatically for patients with hypertrophic cardiomyopathy. The team is working with other hospitals to embed PRIMACY into their systems. In the meantime, they continue improving PRIMACY to become even more user-friendly and even more precise.

PRIMACY is also a stark example of precision medicine at SickKids, known as Precision Child Health. It's a sweeping new approach to medical care that's more deeply informed by each patient's uniqueness – their genetics, physiology, and even their environment and social circumstances.

Seema: When we think about precision medicine, which is what the field of medicine is focused on, which is giving the right patient the right care at the right time. This is a very important example of that because we are tailoring our recommendations to a patient's unique profile clinical, their genetic, their lifestyle choices. And so translating this into a clinical tool was a big achievement. And that really is what is at the heart of precision medicine is the translation back to the clinic.

Hannah: For Seema – who's seen the toll of cardiomyopathy, who's lost patients to sudden cardiac death – PRIMACY has been a bright spot in her career.

Seema: So this has been, I would say, the most rewarding of all the research that I've done so far. It has been very gratifying, especially as a clinician scientist. The whole goal of doing research is to make sure that it's changing or improving outcomes for patients.

Hannah: Seema's genetics work is also having tangible impact. She and her team have discovered new genetic causes for various heart diseases. And this has meant a four-fold increase in genetic findings that can be returned to families to help personalize care and inform family planning.

In fact, it was Seema's study of Seth's whole genome that uncovered the genetic cause of his cardiomyopathy, which had eluded his medical team for years.

Because hypertrophic cardiomyopathy is hereditary, Seth's whole family is having their genome sequenced. This is especially important for Seth's two younger siblings, who may carry the genetic variation but not feel any symptoms. Cardiomyopathy is a progressive disease, and though medications can slow its effects, there's no way to stop it. As a clinician, Seema has found this reality difficult – and motivating.

Seema: Being in pediatric cardiology, I remember many patients where it was it was heartbreaking where you would see a patient present who thought they were perfectly healthy. They came in with some symptoms, for example, even something as simple as a heart murmur or just getting tired easily and turned out they had hypertrophic cardiomyopathy. Now suddenly they were facing the thought of a transplant and that their heart would not last. And seeing children – families – go through that is a sobering experience. So, I think that is what got me interested, and also just understanding what drives these different types of cardiomyopathy. Because if we don't understand what genes are causing it, then we can't really actually act on it in a way that we can prevent the disease from progressing. So I think that's one of the take home messages, really, is, is to embrace the idea of doing genetic testing for cardiomyopathy, recognizing that we don't have all the answers yet. In hypertrophic cardiomyopathy, we might know the answer in 50 to 70 percent of cases. But unless we do testing and learn more, we'll never get close to 100 percent.

Hannah: From SickKids Foundation, I'm Hannah Bank. Thanks for listening. To support breakthrough research and care at SickKids, please visit SickKidsFoundation.com/podcast. And if you liked this episode, subscribe and rate us wherever you listen to podcasts.

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