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Against the Odds: Improving Survival for Children with Pulmonary Vein Stenosis

ReachMD Announcer:
Welcome to Advances in Care on ReachMD. This medical industry feature is titled “Against the Odds: Improving Survival for Children with Pulmonary Vein Stenosis.” These podcasts are a production of NewYork-Presbyterian with doctors from Columbia & Weill Cornell Medicine.

Here are your guests, pediatric cardiologist Dr. Christopher Petit and health and science journalist, Catherine Price.

Dr. Christopher Petit:
So, like everything in medicine, there's always patients that stand out.

Catherine Price:
That's Dr. Christopher Petit. He’s the co-director of the Children's Heart Center at NewYork-Presbyterian Morgan Stanley Children's Hospital and division chief of pediatric cardiology at Columbia University.

Dr. Christopher Petit:
I am an interventional pediatric cardiologist, which means that I do interventions in the blood vessels near the heart in infants, children and adults who are born with congenital heart disease. And when I was just a budding interventional cardiologist, I met this little child who was referred to our hospital. This child was coughing up blood, had no energy, was not able to breathe effectively, who had to be carried from the bus stop into the house…

Catherine Price:
There was a concern that this child had extra blood vessels growing in their lungs. Dr. Petit brought them in to take a look. But...

Dr. Christopher Petit:
It turns out that the diagnosis was wrong.

And when this child got to the catheterization lab, I found that the child had severe pulmonary vein stenosis.

Pulmonary vein stenosis is a disease of young children and infants where the veins that bring the red blood back from the lungs become narrowed. Just out of nowhere. And it typically starts with one vein is narrowed, and then what happens, it's very unique and sort of bizarre, is that another vein will become narrowed, and so all the blood vessels are really tight and small, and they close off completely, and when that happens, a person cannot survive.

Catherine Price:
In the cath lab that day, Dr. Petit saw that in this child the disease had progressed. All the veins from their left lung were completely closed off.

Dr. Christopher Petit:
And so, what I did was I treated the narrowed but open veins on the right lung so that some blood could get out of the right lung, and that really worked well…

Catherine Price:
After the procedure, Dr. Petit saw a huge improvement. His patient had more energy and even started to walk again.

Dr. Christopher Petit:
It was dramatic.

But sadly, as the disease came back, which it always does, the child got more short of breath. I would bring the child back into the cath lab and reopen the veins, and the veins closed off again, I would reopen them, they would close off again. Do this over and over again, but it got worse and worse, and ultimately the child passed away.

So, it was a lesson that many of us have learned in the field, that pulmonary vein stenosis is a really unique disease. And this is a lethal disease and it comes back and it gets worse no matter what you do.

Catherine Price:
Most people would have been discouraged by this experience. At the time, about 50% of children diagnosed with PVS didn't survive past two years. But it actually had the OPPOSITE effect on Dr. Petit. Instead of running away from this difficult disease, he ran right towards it.

Dr. Christopher Petit:
My mom will tell you I'm very stubborn.

I'm also pretty optimistic. So going into medicine, I felt like families want hope. They want someone to give them hope that their child is going to be okay. Over a decade ago when patients were diagnosed with pulmonary vein stenosis, I think the feeling was that this was a terminal disease, it didn't respond to any therapy. That was not satisfying to me, I didn't want to tell patients we don't have a solution.

And so, you know, in this field you have to be willing to be a little bit stubborn, be persistent. You have to have this belief that patients will thrive despite this disease in the future. I really believed we could do this. We could treat these patients and give them better outcomes.

Catherine Price:
I'm Catherine Price. Today on Advances in Care, my conversation with Dr. Christopher Petit. We discuss how Dr. Petit's years of treating and researching Pulmonary Vein Stenosis have led to innovative treatments for the disease. And how his relentless optimism, and commitment to collaborating with other physicians, have changed the odds for his patients.

So just to give us a sense of the scope of this disease-- how prevalent is PVS?

Dr. Christopher Petit:
We will see at Columbia, and at New York Presbyterian Morgan Stanley Children's Hospital, about two to three new patients every month.

Nationally, it's thought that maybe there are 250 to 500 new cases every year, maybe a thousand, but it's a relatively rare disease.

Catherine Price:
And how is it diagnosed?

Dr. Christopher Petit:
It's usually diagnosed in the first year of life, in the first few months of life, but it's not something that a person is born with. That makes it really challenging because a lot of babies will have a murmur when they're first born and we'll do a scan or an echocardiogram in the first week of life and it's normal.

And in a baby with PVS, you can look back and say, oh, they already had a normal echo, everything is fine, but at two or three months of age, things have changed. Now their pulmonary veins are narrowed whereas they weren't before.

Catherine Price:
And so you're not born with it. What do you think causes it?

Dr. Christopher Petit:
There has been a lot of research into this, and we don't know what exactly causes it, but we do know what risk factors are associated with developing pulmonary vein stenosis. Many of these young children were born premature and spent a lot of time in the neonatal intensive care unit, or NICU.

And many of them have lung inflammation. There's a surgeon who has a hypothesis that babies who spend a lot of time on their back who are on the ventilator in the newborn nursery, that means they're always with their heart pressing on their spine.

And that, just that physical interaction between the heart pressing on the spine and the pulmonary veins getting a little bit smushed can

be enough to set this up a little bit.
So, there are a lot of hypotheses out there we just don't know yet.

Catherine Price:
So historically, it seems like this would have been a terminal diagnosis.

Dr. Christopher Petit:
So, the disease has a really high mortality associated with it. When surgeons tried to operate on this disease, it didn't really matter. It came back. And that created a lot of pessimism in the field. Physicians became really disheartened because they knew that no matter what a surgeon attempted in the operating room or what someone like me attempted in the catheterization lab the veins got narrowed, more veins became affected.

Catherine Price:
I mean so if those are the typical outcomes, then what do you do at that point? Can you give us a big picture overview of what PVS treatment actually looked like when you were first starting out?

Dr. Christopher Petit:
So, when I was first taking care of some of these patients with pulmonary vein stenosis. So at time of diagnosis, when I'd sit down with the family at the first meeting I'd say, here's what your baby has. We're going to need to come to the cath lab every six weeks to re-balloon, re-stent, keep reopening, because it's going to keep coming back.

The first two years of this disease are the most active. Meaning progression, where it's getting worse and then recurrence are really at their worst. But if we keep doing this, your risk of death is a lot lower two years later. So, if we can just buy our time and keep this disease at bay, by frequently re-intervening that may be enough.

Catherine Price:
Oh…Ok.

Dr. Christopher Petit:
So doing that, it was sort of a traditional, sort of a conventional approach to this disease, right? You're going to bang away at it with stents and balloons and surgery, just trying to keep these vessels open. In the field like PVS, I think of that as almost being kind of like a caveman approach. This is a complex problem and to sort of throw the same old tools at it is a bit simplistic.

Catherine Price:
I see.

Dr. Christopher Petit:
The equivalent to this is when surgeons used to treat breast cancer with just more and more invasive surgery. Your breast cancer came back, we're going to carve out more tissue.
That's kind of what PVS treatment was like 10 years ago or even five years ago.

Catherine Price:
Right, you just try to make it through the end of that tunnel.

Dr. Christopher Petit:
Yeah. The problem with that is… there's something underlying this disease which we haven't really paid attention to if we're just banging away at the disease and that is, why does it keep coming back?

Why is this disease so unique?

Catherine Price:
Right…

Dr. Christopher Petit:
Like, we owe it to ourselves and to our patients to ask that question. What is going on here?

Catherine Price:
What did you do next to pinpoint what makes PVS such a unique disease? And, you know, find a better way to treat it?

Dr. Christopher Petit:
So, with PVS when you look under the microscope. There's so many cells that they actually grow into the opening or the lumen of the blood vessel. There's an underlying cellular problem that's causing too many cells to grow and grow aggressively.

My team and I decided, well, we ought to offer medical therapy because stents and balloons are not treating the underlying problem here.

And the first thing I did in the spirit of collaboration was I talked to my pediatric oncologist colleague, someone who has a lot of experience with different immune medications. They're used for certain cancers, but they're also used as modulating the immune system, changing the way cell growth happens in inflamed blood vessels. And we decided that sirolimus, which is a medication used for treating the immune system was probably the best medication to use for these children with PVS. And the rationale for sirolimus is that it has a very low risk profile. Very well tolerated in children. It's also very effective in certain blood vessel diseases in children. And so we thought, let's try this.

Catherine Price:
Okay. So, from there you conducted a study to see if sirolimus might be an effective way to treat PVS, right?

Dr. Christopher Petit:
Yeah. That's right.

Catherine Price:
So, tell me about how you got that study off the ground. Like, where did you start?

Dr. Christopher Petit:
So, I only treated patients with the most severe disease.

Patients in whom, despite all the balloons and stents and all the frequent re-interventions that I was doing, they were still having progression of their disease. These are the patients I thought were at most risk of dying.

So, I talked to those families.

Catherine Price:
…of the most severe cases…

Dr. Christopher Petit:
Yeah, your child has severe PVS. It's getting worse despite the fact that we're trying everything we have in the cath lab. We're offering this medication called sirolimus. Here's the side effect profile. Here's how we would sort of keep a close eye on if your child is tolerating this well. And so, we're hopeful that you will be part of our research to advance this field.

And so, in that study, we treated 15 young children. They were almost all of them were less than 2 years of age. Most were infants.

And we treated them for between 6 months and 2 years.

Catherine Price:
With the sirolimus?

Dr. Christopher Petit:
With sirolimus. Yeah, we treated them with the sirolimus therapy oral. They're taking this by mouth taking it twice a day, we're checking levels once a month to make sure they're on the right amount of medication. And we're using that for between six months and 24 months. Those patients continue to get the balloons and the stents and the interventions in the cath lab.

Catherine Price:
So, what happened?

Dr. Christopher Petit:
We had a hundred percent survival in the patients who got sirolimus. Even though these were the patients with the most severe disease.

Catherine Price:
So you're saying the treatment group actually had a 100 percent survival rate, at the end of the trial. How did that compare to the other group who didn't get the medicine?

Dr. Christopher Petit:
Yeah, the other group, the survival was about 57 percent.

So that study, it really changed the landscape in PVS. That study was published in June of 2021, in the journal of the American College of Cardiology. So that came out and that fall, in September, three months later…

Catherine Price:
Okay.

Dr. Christopher Petit:
There was a PVS conference that I hosted. We had about a hundred specialists, whether they're surgeons, neonatologists, cardiologists, or interventionists like me. And someone asked for a show of hands, how many people here are treating patients with sirolimus? Half the group was already using the medication based upon that half.

Catherine Price:
So this is a therapy that no one was using, and just three months after your study came out, half of all these specialists were using it?

Dr. Christopher Petit:
It was a little astounding. The adoption of sirolimus therapy since that study was published has been pretty wide, I'll say.

Catherine Price:
But how does it actually work? Do you need a particular kind of team in place in order to properly dose, and deliver the sirolimus treatment?

Dr. Christopher Petit:
That's the most important lesson that I try to tell clinicians. As you can imagine, after the study, and even now, I get emails and phone calls and text messages from colleagues who are thinking about starting a PVS program, or they have a baby and they're thinking about starting sirolimus, and they're asking, well, what dose, when should I start it, what would you do?

And the first thing I tell them is, find a colleague who can help you with using the sirolimus, because as a cardiologist, you probably don't have the experience or the expertise to look for the complications from this drug.

Catherine Price:
I see.

Dr. Christopher Petit:
So you have to have experts who really know how to communicate with the general pediatrician who's giving vaccines. You have to know what to do if they have a fever and they're on sirolimus, all these things that as cardiologists, we don't think about. So they need to find that colleague, that partner who can help them avoid the complications and dose this the right way.

Catherine Price:
So you're saying a treatment like this really isn't possible without some kind of teamwork and collaboration.

Dr. Christopher Petit:
Yeah, so collaboration is really important for patients like this, because not one person is going to discover all of the important components to therapy. One of the advantages of I do is that I can take care of and open up vessels that are severely narrowed, like they're almost closed or completely closed off. If I can see the target, I can usually push through with a novel kind of wire. We call these CTO wires, Chronic Total Occlusion wires.

And so this can revascularize parts of the lung that didn't have blood flow for a month, couple of years. And they've revolutionized what we can do for children and young adults.

But there are some vessels that I can't get to. There are patients where the anatomy or their size makes it so that it's better if I work with a surgeon, for example.

Catherine Price:
Yeah, I actually wanted to ask you about that actually… because I understand you've collaborated with Dr. Emile Bacha on cases like this. And I was wondering, how do you work together to get these totally closed-off vessels open?

Dr. Christopher Petit:
Dr. Bacha, of course, is the Chief of Cardiac Surgery at NewYork-Presbyterian and Columbia University. Dr. Bacha and I have collaborated on a number of these procedures now with veins that are completely closed off, he's able to reopen them surgically and then I put a stent into those vessels right then instead of waiting until they come back to the cath lab.

We call that a hybrid procedure because it's both surgery and cath in the same sort of theater. And the patients come out with open vessels with stents.

Catherine Price:

So you're essentially next to each other in the OR doing this?

Dr. Christopher Petit:
Yes.

Catherine Price:
Okay.

Dr. Christopher Petit:
And Dr. Bacha does one step further. So he puts a little hole in the heart so that I'm able to get through that hole into those veins much more easily. So he's setting up the future interventions for those patients as well.

Catherine Price:
Oh, wait, tell me more about that. So you mean it's a hole that you then can use later if you have to go back in to reopen the veins?

Dr. Christopher Petit:
Right, and when I do a heart catheterization, in order to get access to the left side of the heart, I need to go through a wall that separates the left and the right sides. Some babies are born and have a hole in that wall, but in many babies and children, that wall is completely closed off. And so to get over to the left side, I need a hole. I can either create it myself, but if the surgeon creates it, that's fantastic, because then that hole is going to stay there and I can use that for future heart catheterizations.

Catherine Price:
Gotcha. Okay. Is there anything about Dr. Bacha in particular that makes him a good collaborator? We, as I think you know, interviewed him earlier for this podcast.

Dr. Christopher Petit:
I mean everything about Dr. Bacha makes him a great collaborator. There aren't that many amazing technical surgeons who do congenital heart surgery. There are maybe four or five on the planet and he's one of them.

And then you combine that with his attitude. When he was interviewed by you I’m sure you got the sense that he is just a lovely, enjoyable, very generous, and a very humble person.

Catherine Price:
Oh, I, tears were shed by me. Yes, listening to him.

Dr. Christopher Petit:
He's amazing. And he is always thinking, “what's the best way to treat this patient?” Not, “how can I treat this patient?” or, “I should do operations on this patient,” but, “what's the best, least invasive way to take care of this child with heart disease?” He approaches every patient that way. We sit next to each other in our patient management conference, and all the time he's looking over at me, “what can your team do in the cath lab? Can you take care of this?” So he's always thinking in a collaborative way.

And it resonates with my team, I should say, because the cath team is the same way. We look to the surgeons to collaborate, “hey, we should do this together.”

Catherine Price:
I mean that’s just really cool the way that you’re collaborating with all these different people. I understand you're also working with your colleagues in the genetics lab at Columbia to find genetic connections or causes of PVS. So can you tell me about that research?

Dr. Christopher Petit:
So, like you asked me before, who gets this disease? And the short answer is we don't know. We know kind of, if we look back, we'll say, oh, there's a common thread here, but there's not one characteristic which defines the risk factor.

We believe there has to be some sort of genetic or molecular profile. Some sort of signal. Maybe there's a blood test that we can do in the future so that babies who are in the NICU, or a baby who's had heart surgery, we can test for this, detect it early, and say, “hey, it looks like you have a blood test which is suggestive of the development of PVS.”

Catherine Price:
Hmm.

Dr. Christopher Petit:
What's that going to look like? It's probably going to be what we call a biomarker.

Catherine Price:
Uh huh…

Dr. Christopher Petit:
Biomarkers which tell us that there's the early development of PVS. We're also hoping that using biomarkers, we can measure the progression, and we can have a blood test to tell us, ah, things are cooling off now, your PVS is at bay. I'm an interventional pediatric cardiologist. I know that such things exist, but I don't know how to do all the testing. So, we have specialists and experts in genetics and in genomics and in proteomics who will help us discover what that molecular signature is for patients who are at risk.

And that's next, that's what's next in this field. That will help us be more specific about frequency of re-interventions, type of therapy one gets, how much surveillance, and then when to slow down all that surveillance.

Catherine Price:
I mean I can see why that would be the next step forward, if you could actually, you know, tell ahead of time when to intervene instead of waiting for it to flare up again. And also, speaking of that future research, are you planning to build on that original study where you treated the patients with Sirolimus? I know there were some unanswered questions.

Dr. Christopher Petit:
Absolutely. So, I work with a team of clinical scientists called the CCRC or the Congenital Cardiac Research Collaborative, who are focusing on PVS as our next disease and population to study. The CCRC is a group of 15 centers and growing every year by one or two more centers. Columbia and NewYork-Presbyterian are the data coordinating center, or kind of the hub of all those centers. So the data come here, we analyze the data.

So, one of the best things about working with a collaborative of 15 centers, is that because centers vary in how they treat patients with PVS, we can take advantage of that variation in the approach to PVS to look for what's the right approach here. Because at one center all you know is what you know. But as a collaborative within the CCRC, we can get a lot more data from a lot more patients. So, it really empowers you to conduct more meaningful and more generalizable research.

Some of the questions that we had from the original study, was it the drug or was it the frequency of the interventions? Should we offer this drug to patients with moderate disease? Some of those questions we will absolutely answer with this CCRC data.

Catherine Price:
I mean, putting this all together… can you tell me a bit about how outcomes and prognoses have changed since you started in this field, considering all these advances. Like, if you saw that child from the story you told at the beginning of our conversation today, do you think that the outcome would have been different?

Dr. Christopher Petit:
I think so. So, first off... at the time, I didn't have any belief that we could open a completely closed vein. I look at the pictures from the cath, I still have the pictures on my computer, and I can see the angiograms, and see the outline of the veins on the left lung, which was closed off. And today, I would have reopened that, and if I couldn't have, that child would have gone to surgery, and we would have done a hybrid surgical approach. Dr. Bacha would have opened it, I would have placed a stent, and the left lung would have come back. Yeah, that child would be alive now.

That was 15 years ago. But, I think about that child a lot, and I think about the lessons we've learned. I can't think of the last time we've had a patient die with PVS here at NewYork-Presbyterian. So, I think it reflects the fact that outcomes are better. I don't know anybody who is as pessimistic about PVS as they were a decade ago.

I mean, I don't feel like we've achieved what we want because these patients still go through a lot. I mean survival is just the tip of the iceberg. Now I think we have data and I'm much more confident about your child will survive. And we believe your child will thrive.
The other thing that's changed is that you know, there's the patients that you treat with your own hands or with your own skills that improve and that's very gratifying.

The space that I'm in right now is differently gratifying, but it's really meaningful. Where I have colleagues calling me from Dallas or Virginia or South Florida. I've got a patient with PVS. Can you look at the pictures and give us your advice on what to do? And we talk about it. And I have the understanding of the disease, and I know enough of the people in the community, nationally, that, you know, I think I can give them the guidance. And they carry out great clinical care.

Catherine Price:
I mean that’s just wonderful that it's a collaboration on so many levels between the patients and the doctors, between the doctors

themselves, between different hospitals, initiated by you. Also sounds like maybe your stubborn optimism is contagious a little bit in a good way?

Dr. Christopher Petit:
That's nice to say. I think that there were a few scattered seeds out there across the nation of people who had optimism and a little bit of stubbornness and rose colored glasses like me. And as that started to take root, yeah, then those seeds scattered more and more widely. So now it's a little bit more densely covered.

There's more of us now than there used to be. And it's a rare person who would, who would be so pessimistic as to say it's not worth treating children with PVS.

Catherine Price:
You're like a Johnny Appleseed of optimism.

Dr. Christopher Petit:
I mean, I think mindset is everything, right? If you believe patients with your disease are doing poorly and will do poorly, that's exactly what you'll find. But if you believe that they can do better and they should do better, you'll probably be part of the team that brings outcomes up with you.

I mean you can imagine that these parents grasp onto that hope. And so, our team that offers that hope they really rely on us and we're their partners.

Catherine Price:
That must be really motivating for you too.

Dr. Christopher Petit:
Absolutely. Yeah. It means a lot to mean that much to a family. Right. And the patients that I take care of, even if it's been years, I still will get emails and I'll see their children now in kindergarten or in first grade. And to know that you had a small part in that success is just, there's no words for how meaningful that is.

Catherine Price:
Well, thank you so much, both for making the time to speak with me today and just for being an optimist. It's really wonderful to speak with you.

Dr. Christopher Petit:
Yeah. Thanks so much. I enjoyed it too.

Catherine Price:
Thanks so much to Dr. Christopher Petit for speaking with us today and for his stubborn optimism, which has helped revolutionize the outlook for kids with PVS.

I'm Catherine Price.

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