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Steph Dewar: Hi, everyone. I'm Steph Dewar, associate professor of Pediatrics here at UPMC Children's Hospital of Pittsburgh; also, the vice chair of Clinical Affairs and director of the Pediatric Residency Program. Welcome to “That's Pediatrics.”

John Williams: And I'm John Williams, professor of pediatrics and division chief of Pediatric Infectious Diseases. And I am delighted to welcome our guests to today's podcast. Both of them are physicians here at the Children's Hospital of Pittsburgh. Please welcome Dr. Drew Feranchak, who's chief of the Division of Pediatric Gastroenterology, Hepatology and Nutrition, and Dr. Dan Weiner, medical director of the Pulmonary Function laboratory and co-director of the Antonio J. and Janet Palumbo Cystic Fibrosis Center and professor of pediatrics. Welcome to “That's Pediatrics.”

Daniel Weiner: Thanks.

Drew Feranchak: It's great to be here.

Steph Dewar: So we were wondering that we have two very smart physicians from two very different subspecialties, if you could help us to understand why we would invite you to be here together?

Daniel Weiner: That's a good question. I think together, because we both take care of different aspects of children with cystic fibrosis.

Drew Feranchak: I would add that most people think as cystic fibrosis as a disease that primarily affects the lungs, but it also affects GI organs, specifically the liver, the pancreas, and the intestine.

John Williams: So do a lot of patients end up seeing more than one specialist at the same time, or do patients tend to have more lung or more gastrointestinal disease?

Daniel Weiner: The majority of patients have some manifestation both in lungs and gastrointestinal disease, and so some patients end up seeing the CF gastroenterologist or the CF endocrinologist. And all of them will see the pulmonologist.

Steph Dewar: And so tell us a little bit about the center here at Children's in Pittsburgh.

Daniel Weiner: We've got about 260 pediatric patients cared for at Children's and a similar number of adults that are cared for over at Presby. We see patients in four locations here at the main hospital and in three satellites in Wexford,

Monroeville, and Bethel Park. And we have a multidisciplinary approach, so patients will see the CF pulmonologist, a nurse educator, a respiratory therapist, a nutritionist, a social worker -- and all those people coming together for most visits to try to help provide a team approach.

Steph Dewar: So what would you say is the advantage of having all of that available in one location, as opposed to say a patient out, perhaps several hours from here, doing most of their doctoring, so to speak, locally?

Daniel Weiner: Well, for CF, I think we know that that team approach really results in better outcomes. I think there is actually some data to support that center-based care provides better outcomes.

Daniel Weiner: From the patient's perspective, I think, it adds a lot of convenience. And we're very fortunate that we can provide that to families. Wherein some centers you might have to make a separate appointment and a separate copay to go see the nutritionist or the physical therapist, we try to just have that all provided in one stop for the patient.

John Williams: And so both of you are also engaged in research in the area of cystic fibrosis. How much of a connection is there between research that's done here at Children's Hospital and the center? Are a lot of patients involved in research? Does some lab research derive from the patients?

Daniel Weiner: So the research at the CF center, I think, comes in two flavors. So we have a lot of clinical research, much of which is organized by the Cystic Fibrosis Foundation. And a lot of that are clinical trials around new drug therapies for patients with CF. So the patients are really excited about many of those trials because these new therapies seem to be very exciting, improving lung function and weight and cutting down on how often they're in the hospital. So patients are really excited about that.

Daniel Weiner: And then in addition to the clinical research that we are doing that's mostly through the foundation, there's a very active investigator-initiated research program. Drew's going to talk about some basic science stuff. We also do some investigator-initiated clinical research. And so we talk to all patients about research, and we start talking about almost at diagnosis. Because we tell them this is why patients are living longer and longer: Your participation in clinical research is how we achieve that goal. So we talk about it from the time they're babies.

Drew Feranchak: Yes, that's true. As Dr. Weiner reports, the lung is still the main cause of death for the majority of patients with cystic fibrosis. However, the liver is becoming more prominent and is actually the third-leading cause of death in patients with cystic fibrosis as our treatments for the pulmonary manifestations get better all the time. In fact, we don't know what causes the liver disease in cystic fibrosis. And even patients with the exact same mutation in CFTR, such as the Delta

F508, which is the most common mutation, only a small percentage of them will develop end-stage liver disease. And we don't know why that is. It points to perhaps that there's other genetic modifiers or perhaps other environmental factors.

Drew Feranchak: In larger genetic studies, no single factor has proven to be the main determinant of the development of liver disease. Perhaps being a carrier for another liver disease may in fact impact the development of cystic fibrosis-associated liver disease, or perhaps it's an additional environmental factor. Recently, the microbiome in the intestine has gotten a lot of highlights in that regard. And in fact it could be that one's intestinal microbiome may affect the development of several diseases, including an impact on cystic fibrosis-related liver disease.

Drew Feranchak: Alternatively, other inflammatory conditions anywhere in the body, such as lung infections, can affect the development of liver disease through effect on circulating cytokines, which may have dramatic effects on the expression and function of liver ion channels such as CFTR or alternate chloride channels, which may be functioning in cystic fibrosis.

John Williams: Drew, I know from collaborating with a couple of people in the center here, in the basic research, there's a lot of different people around the university in pediatrics, of course, but in adult pulmonary and in microbiology and cell biology. Could you talk a little bit about the different kinds of basic research, and how does that come together in the center?

Drew Feranchak: Sure. There's a lot of basic research that takes place here on the University of Pittsburgh campus, at Children's Hospital here in Lawrenceville, at the basic science research buildings in Oakland, and then at the basic science research buildings down by the river in Bridgeside Point. So that's one of the challenges, is getting all of these scientists together to study a particular problem, in this case cystic fibrosis. And so we have basic scientists in the area of infectious diseases, basic scientists in the area of understanding how this protein functions as a channel, basic scientists in various fields of epithelial biology, in infectious diseases. We all study the same disease and study the same part of that, but you really, in lots of different ways, study different aspects of this disease. So it's an exciting environment to be in.

Steph Dewar: So, I'm just curious. I look around this room, and none of us are overly young physicians, and I'm wondering if you could describe for us how the outcomes have changed for these patients over your careers?

Daniel Weiner: Yeah, I think when I was a fellow in training, which was about 20 years ago, we had quite a number of pediatric deaths when I was on service. And that's essentially unheard of for our trainees to see a pediatric patient die from CF. In the '30s, the average survival was about 2 and the predicted survival now is in the mid-40s. And we do have adult patients over at Presby that are in their 50s, 60s, and 70s. So that's a change that just within my relatively short career, survival has improved dramatically.

John Williams: Steph, I like to think of myself as young at heart, if not actually young. We're all pediatricians, remember. So maybe you could tell us a little bit about your own areas of sort of interest, and what are the things that you do in each of your realms that you're excited about, in the clinical realm, in the basic science realm, in your research?

Drew Feranchak: Sure, John. My area happens to be the liver associated with cystic fibrosis and the disease the patients get that actually occurs within the liver. It's still really unknown; people don't know why patients with CF even get liver disease. The basic defect is not even found in the majority of cells in the liver or the hepatocytes. It's only found in the bile duct epithelial cells known as cholangiocytes. So why patients even get liver disease is still a big question mark. So we study the basic defect that occurs within the liver and cystic fibrosis, looking at the channel protein and studying other channels that may serve as a therapeutic option for patients with cystic fibrosis.

Drew Feranchak: As Dan pointed out before, these new medications, new drug therapies are exciting, but yet there's still probably about 10 percent of patients that they just won't help because they have mutations that just will not be amenable to treatment with these. Our research specifically targets non-CFTR proteins in the cells, and so any potential therapy that we derive from this research will benefit all patients with cystic fibrosis. So it's a little different.

John Williams: Dan mentioned that a lot of patients have manifestations of both, but is that why some patients have more liver disease than others? They may have more of these other mutations in different proteins?

Drew Feranchak: Well, they could. People have looked at other genetic modifiers of CF liver disease in lots of large studies. Nothing has really shown up that's been consistent with all of the studies. People know that people with other tendencies to get other liver diseases, like Alpha-1 antitrypsin deficiency or some of the other rare diseases, may be more susceptible if they also have cystic fibrosis to get CF liver disease. It could be that perhaps it's an environmental factor, which causes worse liver disease in some patients. For instance, inflammation or infections or other environmental factors that may play a role in causing worsening liver disease.

Daniel Weiner: I get excited when I can sort of marry two of the loves that I have, which are pulmonary function testing and CF. So, I mean, I really love the pulmonary function lab because it's a way to apply the pulmonary physiology that I like so much, and when I can then apply that to CF even more so.

Daniel Weiner: So some of my clinical research is on developing new pulmonary function tests that may help detect lung disease early because we know it starts in infancy. So applying different kinds of tests to infants that are too young to cooperate with standard lung function testing so we can respond to changes in lung function before they become severe.

John Williams: I just have to say, I mean, I think that's, first, amazing that you could even do a pulmonary function test on a baby that can't sort of follow commands. At least none of my kids ever could. But the passion of our pediatric colleagues for their research, you're not the first guest to use the word “love” applied to your research on this podcast. I think that's amazing.

Steph Dewar: I agree. And I'm curious. I mean, I sit here and I'm listening to you and I'm curious about your stories: Dan, how you came to pulmonology and Drew to GI, and then subsequently to CF and to Pittsburgh. I'm just curious if you could share with us what that journey was like.

Daniel Weiner: Yeah. So I think I got interested in CF almost before pulmonary. My mother used to do sweat testing when I was in high school in Detroit, and so I got to meet her boss, who was a pediatric pulmonologist who did CF work and I did some computer programming work for him, and that's sort of my introduction to CF. And I think over the years, I sort of evolved from wanting to be a pediatric surgeon into becoming a pediatrician. And this gentleman was a fantastic mentor who sort of convinced me that pulmonology would be really exciting. Taking care of people with CF offers you the opportunity to take care of lots of different parts of the disease. So you have to sort of be a little bit of a jack of all trades to do some CF work.

Daniel Weiner: So I was doing that happily in Philadelphia for about 10 years, and we moved to Pittsburgh when my wife got a better job here in Pittsburgh.

Steph Dewar: Excellent.

Drew Feranchak: I guess I originally got an interest in pediatrics through my mother. She was a speech therapist, and she even worked at Children's Hospital for a while. And she would bring home lots of games and fun stuff that when I was just a child, it really got me interested in a career that we could just play games all day. And subsequently, I went to medical school here and I did my residency here in Pittsburgh, but then went away for fellowship training and was gone for about 23 years or so and I finally moved back. And I guess they always say you always come back to Pittsburgh, right? And my parents are still here, and so it's nice to return home after all this time and to set foot in Children's Hospital once again. It's a lot different when I was here before. It used to be in Oakland and now here it is in Lawrenceville, but some of the same people are still around and it's still a fun place to come to work every day.

Drew Feranchak: I probably got interested in gastroenterology during fellowship training. I knew I was going to be a gastroenterologist, but I thought I was going to be a clinical gastroenterologist. And I really had not a lot of interest in research until I went into the lab for the first time and just fell in love with it. And so now here I am, years later, where I do mostly research, and I love it.

Steph Dewar: What a lovely testament to your mothers and the influences that they have on your life choices.

John Williams: Mothers and parents and mentors. Well, it's really fortuitous. I mean, many of us end up in these careers simply by chance: interaction with a mentor or something like that.

Steph Dewar: So, I'm just wondering: Is there anything new on the horizon that we should know about with testing or training or something that you would like to share so that people are aware of it?

Daniel Weiner: Yeah. I'll mention that within the last couple of years, the state of Pennsylvania has made the algorithm for screening newborns a little bit more sensitive, so we are seeing a lot more babies that are being considered as having possible CF. So we're seeing a lot of those babies. And it's a challenging time for families with a new baby to have to worry that their apparently completely healthy-looking baby might have a chronic disease, and we really do try to partner with the pediatricians to make sure that families are prepared with a little bit of information when they come to Children's for their sweat testing.

Drew Feranchak: I would also add that part of the excitement around the field is to get that next generation of physicians interested in research and cystic fibrosis. We have a very active research center here, and we also take trainees that are interested in the field. We just sponsored our first CF-sponsored fellow in the GI world, and I know that in the pulmonology world that's something that they've been doing for a while now. And so getting that next generation of doctors interested in it as well. So if there's trainees that are listening to this podcast -- students or residents -- it's an exciting time to think about careers in gastroenterology or pulmonology to focus on cystic fibrosis.

Steph Dewar: Well, I really do appreciate both of you coming. I mean, this is a disease that I agree has just -- the outcomes have improved significantly in my little bit longer career, but it's so exciting to know that there's new things coming down the pike and that you guys are involved in this research and care of these patients.

John Williams: Yeah, we're very fortunate to have teams like this of multiple specialties, both taking care of the patients and doing the research. So thank you both for being here.

Daniel Weiner: Thanks for having us.

Drew Feranchak: Yeah, thank you.

Steph Dewar: And thanks everyone for listening. Look for us, “That's Pediatrics,” where you download your podcasts. And please don't hesitate to send us comments and recommendations for future topics. Thanks for joining us.