Welcome to PKD Chronicles, navigating life with polycystic kidney disease.

A podcast by the PKD Foundation presented generously by Otsuka Pharmaceuticals.

This podcast is all about helping you live your best life with PKD. In each episode, we'll explore the stories, science, and support and resources for families impacted by PKD. And here's your host, Alyssa Ealy.

>> Hi everyone, welcome. Today, we're talking about genetic testing and its implications for polycystic kidney disease. We're joined today by Kayla Colbert, a certified genetic counselor with experience navigating these conversations for people affected by PKD. So she'll talk to us a bit today about why genetic testing is an important step in understanding and managing PKD. Kayla, welcome.

>> Hi, thanks for having me.

>> Do you want to start by telling us a little bit about yourself and how you became interested in this field?

>> Absolutely. Yeah, genetic counseling is, it's kind of the, for me, the best of both worlds between science and interacting with people. I'm kind of having that psychosocial interaction and also helping break down some really tough and complex concepts, scientific concepts for people. So that was something that I was drawn to. I kind of grew up around the Mayo Clinic, so I had proximity to kind of the healthcare system and was able to kind of see this job, got into it, and came back to Mayo to be a genetic counselor. And right now, I'm a little bit of a generalist, so I do see patients with all sorts of different kidney diseases, including PKD, and then I also see other types of patients, too, in all sorts of different areas.

>> It's definitely a really fascinating area and so important for patients with PKD. So we're really excited to have you. I guess the biggest question that patients usually have when I see them is, why should they get genetic testing in the case with PKD. So they've been diagnosed. They kind of have this big new diagnosis and they're trying to figure it out. So what is the decision to test for genetic mutations really look like for patients?

>> So if a patient is meeting with a genetic counselor to kind of go over the pros and cons, we're trained to be very non -directive. So we're not here to convince you to do genetic

testing, but absolutely want to make sure that patients are aware of the benefits and limitations of testing. Kind of at the top of the benefits list is knowing what gene, the exact gene that is causing the PKD, and even the exact, you might think of it as a spelling error within that gene, knowing those pieces of information can go into that prediction of disease progression. So There are certain nephrology areas will use something called a pro-PKD score that incorporates lots of different things, images of your kidneys, all sorts of different labs, and including that genetic test result to kind of make a prediction about the progression of disease. So that's kind of at the top. Knowing that specific gene invariant can also play a big role in, you know, if we're talking about a donor situation, we need a transplant. If a relative comes forward, we want to make sure that they do not have the risk to develop cysts. And knowing that genetic component is a really easy way then to rule that in or out in those individuals.

>> Are there any downsides to having the genetic testing done for patients?

>> Great question. A lot of people will ask top of mind is, you know, insurance discrimination and things like that. So there is a law, a federal law called the Genetic Information Non-Discrimination Act that essentially says, if you get genetic testing, you got that positive result that kind of gives you the diagnosis. Your health insurance, your general health insurance can't drop you, can't change your premiums, those kinds of things. And your employer also cannot fire you based on a genetic test result, can't use that information. Now there are some exceptions to those two things, and there's a website, www.ginahelp .org, that has a lot more information about kind of the nuances of that. But the point I'm making here is that this law does not protect when it comes to life insurance, long-term care, and disability insurance, which is to say, if anybody is applying for a new life insurance policy or a new long-term care policy, that company can use genetic testing results just like they can use anything else in the medical record. So they will find what they can, unfortunately, to not, you know, give a policy or to increase the amount, the premium amount that you're paying, that kind of thing.

>> That's a big decision then.

>> It can be, yes. Yeah, it's kind of weighing out the immediate benefit of knowing that result versus the possible long-term kind of that discrimination aspect. I will say they can use just family history of PKD alone without the genetic testing. So for some people they say, you know, I've already got PKD, that this life insurance thing isn't going to make a difference for me. But for a relative who maybe doesn't know at this point, if they have cysts, they want to do testing, that is usually a bigger conversation for them.

>> Is that a conversation that every genetic counselor would be able to have with a patient to rule out the benefits and the cons?

>> Absolutely. Yeah, their GINA, this this federal law is is something that every genetic counselor is aware of and can speak to. I will say we're not lawyers. So to some degree, if there's questions about, you know, well, what about my insurance or if I'm a federal employee, there's some exceptions to that. All that, those nitty gritty details may be something you wanna chat with a lawyer about, but we can at least speak to this law on a very general level. And that definitely is something that's brought up for those asymptomatic relatives coming in for testing. Let's say that a patient is seeing a provider who is not linked to a center that has genetic counselors available. Is there a national resource where people can access genetic counselors outside of their medical providers and the health system they're in?

>> Yeah, that's a great question. I know there need to be more of us. There is a website to find local genetic counselors. If you type in find a genetic counselor .com it'll get you there. I do know that there are also these so there's more and more of these telemedicine companies. I'm not affiliated with any of them. I can't speak to them other than the fact that they will offer, you know, virtual visits for people who don't have a genetic counselor in their area. So looking up things like that could be really helpful for people who can't travel really far if there isn't a genetic

counselor nearby.

>> This is all really interesting. So let's say that patients with PKD decide to proceed with genetic testing. What does that process look like for a patient?

>> Probably depends on the place. Some nephrologists may be comfortable ordering a genetic test themselves. I know where I'm at, the nephrologist is referring that patient to a genetic counselor for really a discussion about informed consent because we want people to know what they're going into and what they're testing. This is a little bit more complicated than just your simple blood test for, I don't know, you know, something in the blood or protein in the urine or things like that. So there's a conversation on the front end usually with a genetic counselor and that's gonna, we're going to go over kind of the scope of the testing. So are we just looking at PKD genes? What PKD genes are we looking at? Because there's quite a few that can be tested. And then we want to go over what kinds of results can come back from that. And sometimes isn't straightforward. You know, you think, well, we'll find it or we won't find it. Well, sometimes we actually find what you might consider a spelling change in one of these genes. And we just don't have enough data on it. We don't know if this is the cause of the cyst or if it's just a normal spelling variation that this person happens to have. So sometimes there's additional things that can be done at, you know, family studies. If there's other relatives who have PKD, we can see if they also have that uncertain finding. All of these kind of extra things that you might not think about on the front end need to be discussed on that pre-test visit. And billing is also another big topic of conversation. People kind of wanna understand what they're getting into with genetic testing and the genetic counselor can certainly speak to kind of how that test will be billed. It varies depending on the lab, depending on the institution, but a lot of labs that will do PKD testing kind of have a billing process where

they can reach out to the patient's insurance and get an estimated out of pocket ahead of time, that kind of stuff.

>> So is this usually a blood test for patients or can they do it any other ways, like a saliva test that they can send out?

>> Yeah, both of those, I mean, it depends on the lab, but at this point, most labs can do both blood and saliva. I mean, one or the other, you don't need both, but they can do either or, and that's why, you know, those virtual visits are actually much more convenient now because a saliva kit can just be sent to your house after you have the visit and just drop it off in the mail. Usually they come with everything you need, you know, pre-labeled package, all that kind of stuff. So it's pretty, it's pretty slick now.

>> Yeah. They've really simplified the process for patients. That's amazing.

>> Yeah.

>> Really speaking to efforts to increase access with some of this nuanced care that isn't always available in more remote areas. So how long does it usually take for patients to get the results from their genetic testing in your experience?

>> Yeah, another great question. And it depends on the lab, the ones that I'm familiar with, we're talking usually one to two months, usually more on the one month end, but I've seen it go longer. And that's really a matter of, you know, It's not just that the lab has to sequence the genes, but they also have to interpret what they find, and that can be a process in itself. So that is a little bit why that timeline isn't just a one-day test, it really takes some time to go through the data.

>> Takes a while. And so when the lab is sequencing these tests and learning and analyzing what they find, what kind of reports do they provide to the

patient and provider after they're done?

>> Yeah, there's a report that comes out. It will say, you know, the patient's name. It will talk about the exact genes that were covered. And report format varies widely. Some of them have a lot of science and genetics jargon in them. Some of them are a little bit more friendly to the lay person, but somewhere there will be a table typically. If there is our variants found, if there are genetic variants found, there'll be a table with those variants and

it'll list the gene and it'll list the variants and then it'll also have a

classification. And classification is really referring to what do we think this

variant means? Do we think that this is the cause of the PKD? Is it uncertain or

is it benign? We think this is a normal change. Usually normal changes aren't

reported on those reports, but typically we're only seeing those uncertain variants.

You'll see VUS, which means variant of uncertain significance, or a positive result

can fall into the likely pathogenic or pathogenic classifications.

>> Okay. And so when you say likely pathogenic or pathogenic, so you're referring to that is

what the suspected gene is that's causing the PKD to happen for patients.

>> Yeah

>> That when they see that report, that's what it's telling them

>> Yes, and I would caution people reading a report if they see that word pathogenic or likely pathogenic not not too overinterpret it till a genetic counselor nephrologist is is interacting with them only because different genes require different numbers of variants to cause the condition. So if if you happen to have a pathogenic variant, so there's there's evidence that it can cause disease, but it's in a gene that requires two pathogenic variants in order to have the condition, like in recessive PKD, then this is not a diagnosis

for you. This is not explaining the cysts that are going on so it's really important to

have have someone with expertise to kind of interpret that

>> Yeah, I think now with these these days of being able to see all your lab results yourself immediately It's so tempting to search things. I myself have done the same thing on genetic testing where I got mine back and I searched for it and I said I have no idea what this means. That's a really important thing to consider is that, you know, you should really talk to that genetic counselor, or provider first.

>> Yes. Yeah. And I will say, I say to people all the time, you know, you will be able to see your results. You are welcome to take a look. You're welcome to read through kind of everything that it says. Some labs will give a better breakdown of what things mean. But just exercise caution. Please, please wait to give your final, you know, if there's panic or if there's, you know, relief or whatever you're feeling about it, kind of try to try to wait on that until you do have that conversation to really clarify what that finding means.

>> Yeah, absolutely. And so you mentioned these variants of unknown significance. So that can be very concerning when patients see those kinds of things. So it's kind of the same concept of waiting until it's explained by a genetic counselor or provider. So what kind of information can come out of that VUS section, though? Is there anything you guys can glean out of it that might help a patient with their care?

>> Yes, absolutely. So these variants of uncertain significance, again, it means your spelling of This gene is a little bit different than most people, but whether or not that actually means it's the cause of cysts, it really is up in the air. A lot of times a variant of unknown significance, over time we gather data, we end up saying, this is benign, this is normal. Other times we gather enough data and sometimes this can take months, can take years. We find out, yes, this was the cause. This is a pathogenic variant, we didn't know it, we didn't have enough information at the time, but now we do. But when we're in that space of not knowing yet, sometimes there is a little bit of evidence that can that can lean us one way or the other in terms of suspicion. And so again, if we're finding an uncertain variant in a gene that requires two pathogenic variants, well, that's not very interesting to us because even if this was pathogenic, you'd still need another one in order for this to be the answer. But if this is in a gene where you only need one pathogenic variant, and maybe we've got a little bit of evidence that says, hey, we've seen this in one or two other people with PKD, that makes it a little bit more suspicious for us. And that's probably the point where we're saying, hey, do you have other relatives with PKD that we could check

out, that we could see if they have the same thing and we can start gathering evidence about whether or not this variant is kind of traveling with the disease and the family.

>> Yeah. So this is what you were referring to with the family studies of continuing to check everybody related or many people related to see if the patterns exist?

>> Exactly. Yes. And a lot of labs will offer like free, like little freebie testing just for that variant for one to two relatives. And so if you're strategic about who you test, sometimes you can get a ton of evidence and that can actually upgrade that classification to pathogenic, you get that final answer. Other times that's still not gonna be enough to get us that final answer. And maybe other relatives at that point are also willing to test and to see a genetic counselor to test or we gotta kind of wait for more data and more studies to come out.

>> Genetic testing is really just such an important piece of the puzzle.

>> It really is, it really can be. And I think it feels like this space is a little bit unique because the health is also the family's health. Like it's not just one person's genetic information and one person's health. Like the whole family is involved and affected. And when we're thinking about like HIPAA and legalities and all that stuff, there's lots of authorizations that we're having people sign so that we can talk to each other. So it feels like a lot of red tape, but that's kind of how our system is set up.

>> Absolutely. So if somebody with PKD has a parent who also has PKD, would they have the same mutation? Or is there a possibility that they could be different types of mutation and still have the same disease process?

>> I would say it would be highly unlikely that a parent and child who both have PKD have different causes of their PKD. Is it possible? Sure, it could be possible. Maybe, maybe parent has a variant in PKD one. Well, their other copy of PKD PKD1 is normal, does not have the variant. They pass on that copy, but there's such thing as a de novo mutation,

which means this was brand new in somebody for the first time, it wasn't inherited. And that child could have a de novo mutation happen really early on and, you know, when forming in utero. I think if someone comes to me and says, my dad also has this, my mom also has this, we're pretty much talking about the same gene that there's, there's not a lot of, of room for something different, even though maybe that's rare, but possible.

>> Yeah. Okay, that's very interesting. And so I think a big question that is probably weighing on everybody's mind, as a parent with PKD, should they have their children tested for genetic mutations? What is your take on that?

>> Yeah, that's it's a good question And it's not as easy and straightforward as I think maybe a lot of people think it is What what we think about right now when we think okay, should we test children and I'm specifically speaking about minors so young kids Who we don't we don't have any knowledge that they have PKD We haven't looked for cysts and nothing like that should they be tested. And right now, there's actually a position statement by the National Society of Genetic Counselors. There's also a policy statement by the American College of Medical Genetics that kind of gives guidelines on when we think about genetic testing for children. And we're really prioritizing, one, is this gonna change anything for their healthcare right now. If there's a drug that could delay onset, that could prevent onset, that's a situation where we think about testing. Right now, with PKD, there isn't. So there aren't early prevention or delay management strategies. Now, that could change. I know that there's a lot of research right now in that Tolvaptan drug, if I'm pronouncing that right in kids and early symptomatic kids, that kind of stuff. But right now, there's not a lot that would be recommended until adulthood. So right now, the priority is kind of the autonomy of the child. So can they wait until they are old enough to understand and make that decision for themselves, especially given some of those insurance things that we talk about before they get tested. So right now it's the it's the blood pressure monitoring is the main recommendation starting at age five.

>> That's excellent. I think that's tough because I think everybody wants to make sure that they're taking care of their children to the best of their abilities. And I think, as a whole, we like information as a society, we like knowing what's going on, especially when it comes to kids.

>> And I find that too, you know, a lot of parents want to know and know that they want to know. Other times people will say, you know, I don't want this hanging over our head as a family. We know this is going to happen. When is it going to happen? How is it going to happen? That kind of thing. So they're okay with kind of that monitoring of blood pressure until and unless, you know, of course, if a child is symptomatic, is having pain, those kinds I think that's when things should be checked out, could get an ultrasound, or could go ahead with the genetic testing.

>> Great, thank you for that, 'cause I think everybody would really wanna hear about that. I think testing kids is a big, important topic. Is there anything else that you feel like people should know about genetic testing, any big take-home messages that we should make sure are included?

>> Great question. I feel like we've covered a lot of good topics here today. I guess just knowing that genetic testing is out there, it's available, it's relatively easy to do in terms of just the logistical process, but that interpretation piece can be a little bit tricky, so really rely on someone with expertise in this area.

- Well, thank you so much for all this information. I know I personally learned a lot. We use genetic testing a lot in my practice, but there's so much nuance to it, so many details. And I think it's a big question mark for patients. So this is really, really helpful. We really appreciate you taking the time to be here today and sharing all of your wisdom with us.

>> Well, thank you so much. I appreciate you being here and saying that. Thanks for doing this for patients. I'm sure this is going to be really, really cool and helpful for people.

>> Thank you so much.

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