Understanding congenital hepatic fibrosis (CHF)

I’m Michelle Carl and I’m a volunteer for the PKD Foundation. I have two sons with ARPKD/CHF. They are twenty-one and fifteen years old. You have joined us for Understanding Congenital Hepatic Fibrosis (CHF) and Best Practices for Managing Liver Complications in children with ARPKD and ADPKD.

I’m very pleased to introduce our speaker for this session. Dr. Ryan Fischer is a Board-certified Pediatric Gastroenterologist and Transplant Hepatologist at Children’s Mercy Hospital in Kansas City. He has a strong interest in translational research related to liver disease and transplantation, and novel therapeutics to treat disordered information in the liver. Clinically he focuses on the diagnosis and treatment of liver disease in children, devoting time to children who have undergone liver transplantation. Dr. Fisher has done a lot for us with the PKD Foundation. Come to a lot of conferences and always willing to answer a lot of our questions.

So, thank you so much, Dr.Fischer, we’re pleased to have you here and Dr.

Fischer is going to start with the presentation.

Thank you so much, Michelle. That was awful sweet. And yes, I have really enjoyed my time working with the PKD Foundation and being able to give this talk.

I hope it's something that is useful for all y'all.

Make sure you know Michelle if anything comes up as I'm giving this that you let me know because I'm happy to take a break and answer questions.

as they come up, but otherwise, for certain, afterwards well we can chat.

I have given this talk for the PKD Foundation before and do keep updating it each time I give it, because what's been, very cool is that I've learned from the parents in particular, you know what, what extra questions they have and where I need to either be more clear with some thoughts or are actually talk about what we've done our own clinics, and things like that.

So, again, feel free to not just ask questions but to teach me as well, but that said, I'm going to share my screen and we'll get things going. And it looks like it's all good on my end with that, we'll start off.

Activity disclaimer, as well as disclosures, nothing relevant for me to disclose and we had talked about my background already.

So in this talk, about discussed congenital hepatic fibrosis, including its definition, and how it develops and then its association with polycystic kidney disease.

Now, this is in particular with Autosomal Recessive Polycystic Kidney Disease, and not as much with ADPKD.

I don't want to make any parents with children that have a behavior feel left out.

The good thing is a lot of those kids don't develop significant manifestations in development. You will hear me talk a little bit more about ARPKD.

Beyond that we'll discuss some components of the hepatic fibrosis that goes along with it, including how we get it, and really try to understand and unpack those long-term complications. Decide what future therapies might be helpful.

So, first off, when we talk about congenital hepatic fibrosis, we want to know, and if we go into the medical textbooks, it's a developmental disorder of the hepatic portobiliary system characterized by defective remodeling of the ductile plate, abnormal branching of the portal veins and fibrosis surrounding those portal tracks.

If you want to break it down to say, the bile ducts and the veins didn't form right in these affect livers. The whole thing should start developing right around four weeks of gestation in utero where the hepatic duct branches out from the nascent Lumen of the fetal intestine and really becomes well organized within about six weeks. When it's all done, we should see a nice-looking liver. A root-like network of bile ducts going through it.

Those bile ducts are actually mirrored by the hepatic venous system, which comes in and I think, the please correct me if I'm wrong does the pointer show up on the presentation because if it does, you can see that I'm pointing out the liver and system that the hepatic veins started.

The portal vein setup is exactly the same as what, the bile duct set up.

What's kind of cool about the liver is that it's taking everything from the intestines and stomach and (poor audio).

…deliver once it's done processing. Those nutrients will of course send it to the heart through the hepatic vein which isn't shown in this particular illustration.

But again, it's an amazing, you know, if you really nerd out about the liver, like me it, consider something like that a beautiful thing to see.

When we talk about congenital a paddock fibrosis, it's really that early remodeling stage has gone wrong. And what I mean, is that if you go back to that four weeks of age, there is a ductile plate which is this green system that surrounding the growing portal venous system.

And usually what's going to happen is that those that ductile plate going to break down into little bile ducts similar and kind of mirror those portal veins.

Typically it looks pretty well organized. You can see those ducts hanging out with the veins. But in congenital hepatic fibrosis, you see, large kind of floppy network of unusual shape ducts there. With that unusual activity you get bile one of the products of the liver that static inside there.

It doesn't get out of the liver as easily as it should and it can cause scar tissue or fibrosis to develop. And cause a lot of the problems that we see for the kids with congenital hepatic fibrosis. And if you look at this pathologically, even if you haven't seen liver under a microscope in your life, what I'm showing here is, this is, these are normal liver cells surrounding what we call the portal triad, which is that, which is that portal vein, right here, this big guy right here, there's a hepatic artery. That also comes into it, though we won't talk much about that.

And then you can see a bile duct. That's kind of that's nice.

And again mirrors, that portal vein quite a bit.

When you go over to the right side, you see that you've got some normal-looking liver cells out here, but that there's a ton of scar tissue a ton of fibrosis and really these floppy large bile ducts sitting out there. That indicate congenital hepatic fibrosis or kind of a fibrous cystic liver disease is present.

So again, if we look at it in another way using Imaging and in this case MRI we can see over on the left side, what should be a fairly normal looking liver so you can you can kind of make that line if you if your brightness on your computer's of enough of a nice pyramidal shape liver here.

It's got right and left hepatic ducts coming down into a common duct.

There's a gall bladder right there, and that all looks good. That's what we'd like to see with little branches of the bile ducts going out to you, that it got really jacked up and you’ve got big, dilated spaces throughout the liver. A liver that's larger than it should be.

And these (poor audio) that you can see, throughout some of which are normal size, but it's some of which are quite dilated and you can infer that there's a lot of fibrous tissue surrounding these.

You know, if we, if we see this on Imaging, this is pretty close to what it looks like if we were actually which again something you can see if we get ugly, does this all happen?

It's a great question. It's unfortunately very poorly understood. It is often related to mutations in that ARPKD gene, that PKHD1 which 1 in 70 in the United States are carriers. And of which you guys hear a lot about, there's a number of different portions of the gene that can be affected to create a problematic gene product or protein from this PKHD1.

And again, that's just fortunate because each, you know, having a copy of the mutation on one gene from your mom and one gene from your dad means you're going to get that.

It's not the only one that is found however. There are a lot of other genetic disorders that can associate with what we call fibrocystic liver disease.

And of course, while we see the polycystic kidney disease is on this list, there's Joubert syndrome, which, you know, I take care of a couple kids with that. Bardet-Biedl syndrome is another one that we'll see and then some conditions that I haven't even seen yet.

As such, you know, it is important for us to talk a little bit about what we mean when we use the language that I'm that I'm kind of bringing up here. Congenital hepatic fibrosis, and if we kind of go back to the slide this Caroli syndrome are pretty much one in the same. Fibrocystic liver disease is a great catch all term, that deliver doc might use to describe this. Where you do have on one end in Congenital Hepatic Fibrosis alone by itself, which we might see with ARPKD.

(Poor audio), or you could have Caroli syndrome which would simply be, excuse me, Crowley's disease, which would be simply all the dilatation without much of the fibrosis.

Honestly, either one of those, it is incredibly rare. What we, what we tend to see is a mix Mash in between both having fibrosis and having the double dilatation.

And then essentially what we're going to call either fibrocystic liver disease, refer to, as congenital hepatic fibrosis, or you might see it referred to as Caroli syndrome where it's not the disease, it's not just the dilatation, but it's that dilatation with the fibrosis.

And again, these are just some examples over on the left of cartoons of what the Imaging by look like in those situations where you've got an, A, a normal liver and biliary tree and, B, that's just fibrosis. So you can see the liver is large base, but you see no dilatation. C, where you've got some dilatation, but let's fibrosis and then be where you end up with both dilatation and fibrosis present to give you that (poor audio).

Now, when we talk about, you know, why this happens and where this comes from, you know, why is it that if we don't understand completely where it comes from, why does it keep progressing? And so what ends up happening is a combination of not just having the most abnormal cysts growing but also the bile that gets stuck in there that bile is a digestive enzyme, it's supposed to come out of the liver, if it doesn't come out easily or it comes out slowly, you’re going to drive inflammation damage and the need to repair or that fibrosis that goes along with it.

And so, you know, we truly know that with this remodeling, you got these big, dilated aires, you’ve got bile stuck in there, and then you get the fibrosis to go on with it.

That's not the complete story because certainly these kids just develop extra fibrosis anyway, but it certainly doesn't help that that we have both the fibrotic process there and also, those big, dilated aires.

Unfortunately, now that we do kind of understand, you know, at least a little bit where it comes from and how it progresses, you know, with those different components, we really have a hard time fixing it up.

So, you have to focus on managing his long-term complications.

This includes immunization for Hepatitis A and B, super, super important because if you already have, you do not want to get another disease on top of it. It's not 1 plus 1 equals 2, it’s 1 plus 1 (poor audio).

You do need to monitor growth, development and nutrition in these kids.

When bile doesn't get out of the liver easily, they're at high risk for vitamin supplement. Bile is a digestive enzyme, it’s supposed to help you absorb nutrients, including what we call fat soluble vitamin. Of course, you avoid alcohol and you really do try and live a healthy life style again.

You know, from the kidney side, we always talk about salt and things like that, but the liver has some stuff it doesn't love either. One of them, the liver doesn't love to sit around likes to move. It doesn't want to just store energy for us. It wants to take that energy that it's from your diet and send it back out body. Two, actually, really doesn't love sugar. We find that sugar and alcohol, especially high fructose corn syrup, appear a little bit similar when you break them down.

And if you can avoid table sugar and really sugary sweet or processed foods, you're going to do yourself a big favor, certainly other items like antibiotics or even what we call choleretic agents or kind of biofilters can be useful. And then avoiding things like ibuprofen, especially if your liver disease has advanced become important as well. Again ibuprofen, it's not a kidney friend, either.

So with all this said, you know, if you do have congenital hepatic fibrosis, what could possibly go wrong? Well, it's obvious that you're gonna run into some troubles and that fibrous and scarred liver can cause what we call portal hypertension. And you will remember I was talking about the portal vein there.

Well, that vein running into the liver, delivering nutrients from the intestine is a great little guy, but when the liver is really beat up and scarred up as you can see in this cartoon here, it doesn't allow flow through the portal vein, into the liver, like we would expect. And so the portal vein gets congested, it gets bigger and thicker. And we start to see problems related to that and we call those problems complications of portal hypertension, but what can develop is that blood backs up, is that blood vessels, which would normally flow nicely, become congested all along, not just the intestines but also the stomach and the esophagus we can actually see these gastric and esophageal blood vessels stick out in the form of verices.

You can see a spleen which is a really you know, vascular organ, get bigger and so when you feel on your belly, that spleen gets really big and that's why we have to limit contact sports because that has a possibility of rupturing.

And you can even see, even though it’s not illustrated here, that if this, you know, blood backs up into the intestines that you might get leakage out of those intestines in what we call ascites, or fluid in the belly.

As I mentioned, kids who do have fibrocystic liver disease, can have significant GI issues and one of them is the development of these varices. And I think it's really apparent over on the left hand side, where you can see these big blood vessels. This, these congested blood

Vessels that just can't deliver the blood to the liver, like they want to and so they start to back up. They’re not a big problem, other places in the intestines, but here in the esophagus, where I've got a good picture of the scope there, you can see that they can get really congested and they're close to the surface. If you look up at the top, you can see that there's a little there's a little blood there.

And what can happen is that these guys can bleed. It's a dramatic presentation when they do because if you imagine blood from say an esophageal or a soft pale soft, you'll Barracks kind of drops into your food pipe goes down into your stomach.

That blood is really irritating the stomach and your kid will throw up and it's going to be bright red blood that comes back up. It doesn't happen often, but it is a dramatic effect. And we do like to make sure we watch our kids with ARPKD and Congenital Hepatic Fibrosis to see if they have any of these varicies developing.

Over on the right this is what you hope to see. This is what the esophagus should actually look like, nice and smooth without any of those blood vessels. Just to give you a frame of reference.

Now when they do develop, like I said, they're difficult but they're certainly manageable and one of the cool things that we can do is if you see over here on the left, that's a picture of a scope.

That goes down into the esophagus, will like I said, we'll do those regularly in some of our ARPKD kids to see if we can find blood vessels.

And if we do, we're going to go down with a special tool that actually kind of sucks those blood vessels into a suction canister on the end of our scope and then we fire a rubber band down around it. So that it basically kind of strangles that blood vessel and takes it away for us.

And you can see over on the right a good picture of that rubber band of kind of making that mushroom shaped appearance of the blood vessel underneath it.

In about one to two days that will be dead tissue and it'll fall off nice and easily and it really limits your risk of bleeding happening in that situation which is great to see.

And as I mentioned, you know, not every kid is going to have these, but they are a relative complication of Congenital Hepatic Fibrosis. So when we talk about their development, you can see that in kids with portal hypertension so with some signs of that spleen being enlarged, about 80% of them, by the 11 to 15 years, are going to have these vericies in place, and it becomes an important, you know, idea for us to really talk about and co-manage with our nephrology colleagues. Again, not everybody's going to do it. But over time, they certainly can develop in those kids who may have some of those findings of portal hypertension.

So, with that said, you know, that's kind of one of the main ones that I talked about especially with parents because, you know, when you do find a, there’s something you can do about it, but b, it's also, you know, quite dramatic.

And it can be pretty, pretty scary like that. And so are there other things that we need to watch out for our talk about?

And yeah, there certainly are.

As I mentioned, fibrocystic liver disease or congenital hepatic fibrosis, you can have those big, dilated areas of bile. Well, those are kind of like those are easy, become infected and unfortunately bacteria, which would normally flow out in the bile would not be able to get up into the liver from the intestines where they normally live can kind of crawl up in there and when they're those big, dilated areas and that liquid just kind of sitting there, the bacteria have a great home, they can replicate, they can cause cholangitis, or an infection of that biliary system.

The infection is most notable for its, what we call the Charcot’s Triad. Named after the Doctor who kind of first described it. But it includes having that fever, turning yellow and having a lot of pain in that right

upper side of your liver. There's other reasons you could get it perhaps a stone has moved through and is blocking things up. But, but when you do have congenital hepatic fibrosis, that's one of the big things that we always think about. And that we worry about when our kids have fever. Especially with elevated, bilirubin levels and that jaundice and that right side of the pain, you know?

Honestly, I tell folks, it's those big, dilated areas within the liver, just kind of like a bacterial hot tub. They love sitting in there and getting with their buddies and it's something that you do want to, you know, be ready for.

As I also mentioned, you know, portal hypertension. This, you know, difficulty of the portal vein getting blood into the liver can also kind of push fluid back and create what we call ascites. We will see that in renal failure as well, but when those livers really beat up in fibrosis, ascites can come from these liver conditions and again, can fill up with fluid.

That fluid is another reservoir for perhaps infection, which we would all bacterial peritonitis. So bacteria not only love living in those dilated ducts, they love living in ascites and it can be something where we actually need to drain the ascites to either help diagnose or manage the problems that a kiddo may be having with it.

And when it comes to, you know, any of these complications, whether it's the varices or the cholangitis or the ascites, you know, we always want to know okay, hey not just are you aware of it and can you diagnose it, but can you do anything about it? And there are a couple things that we can talk about. Things for certain when it comes to the vericies, we do often recommend beta blockers, especially in our older kids, to try to reduce some of the pressure in that portal venous system that seems to help kids not to have any bleeding complications related to that, we typically won't use it until we really do see or have a complicated or have varicies that have actually bled in the past.

But at the same time, we do use it and do find it to be somewhat helpful, at least in our practice. When it comes to bacteria in the liver like cholangitis, IV antibiotics are a must. It's really important to get those sooner rather than later, if that infection is proven.

And then sometimes we do have kids that take antibiotics every day or every other day just to prevent effective infection.

Ascites, same thing when it comes to infections, but that can also be helped by limiting sodium in the diet, even more restrictive then say a kid might be used to. Or, using some of the diuretic medications, like, Lasix and spironolactone to help remove some of that fluid from their body. And then finally, as I mentioned, there are things that (poor audio) is kind of what we call one of those choleretic agents that helps make that vile a little more water soluble.

And we can also to always talk about adding vitamins and to help kids out with their medical care.

And then certainly, we always love to see our PKD kids in our Clinic.

And you know what we'll do is a good clinical exam of course.

But we have some tells that we like to look for. So one is doing notice that the spleen, you can actually feel it sticking out underneath liver of some kids who have portal hypertension that becomes important.

Might see that they have really prominent blood vessels on their abdomen.

Now, if there are pale kid, those vessels may be prominent as well. These can be really striking and an easy way to at least be concerned that maybe portal hypertension is present. Looking at the labs is another great tool. The platelet (poor audio) blood get trapped in the large spleen.

When you kids who've been worked on for thinking something's wrong with the bone marrow or something like that (poor audio).

I really just do a good work out. Looking for that portal hypertension.

Am I back on now?

Yes, you're back on.

Okay, it looks like my connection is good now, so sorry about that. Yeah.

So we look at INR which is a measure of coagulation. That lets us know how the liver is functioning. We will look at platelet count where those platelets can get trapped and go up if that bile is really stuck inside the liver and GGT which is an enzyme that comes from the cells around your bile duct. What we call, when you have a lot of bile stuck in there, are any information on that GGT is an enzyme that may go up. So those are things that we'll check out there.

In our clinic, we always get ultrasound to start off with and see what's going on inside the liver of a kid. I think that's really important.

Then as I mentioned, MRI can be a useful adjunct tool to give us a lot of in-depth looking at that biliary tree. And then finally, as I mentioned with vericies, we do consider the screening endoscopy in kids.

Now no one test is completely predictive, but if you put these all together with your clinical exam, you can really get a good idea of if you think a kid is advancing with their portal hypertension and having problems or not. Some of them aren't easy to do necessarily.

I find that, you know, there's certainly kids who have a hard time with lab work. Ultrasound is pretty painless, but they do have to be able to cooperate a little bit with the radiology tech. MRI and endoscopy are procedures that require sedation. We may not do those in real little kids, just because the value at a young age isn't quite worth it. But we may, you know, move forward and recommend those certainly later in life or again, if we find that, you know, the lab work or the exam is concerning.

There are some, you know, beyond, like looking at an endoscopy or, you know, putting them to sleep so that we can get a good MRI, especially the younger patient, some non-invasive ways to look at the liver itself.

These would be ones that can say measure fibrosis without us necessarily needing even what we would consider like a liver biopsy say.

And so these non-invasive ways can use ultrasound technology like what's an example here where we use a special machine called either a fiber scan, or in this case, shear-wave elastography to measure the stiffness of the liver. When a liver has a lot of fibrosis in it you can turn on your ultrasound machine and measure that stiffness measure the velocity that those sound waves go through the liver. And that gives you a great idea if you're, you know, if you have a lot of extra fibrosis or if perhaps your livers in a little bit better shape, than maybe you thought it was.

It has been proven to be pretty good at identifying kids with portal hypertension.

What you can see here is that in kids where we measured the in blue, the left lobe of the liver and red the right lobe of the liver and then in green the spleen. When we did those liver measurements in kids without ARPKD and kids with ARPKD, those numbers do go up. And then if look over, I'm going to try and minimize this graph on the right, you can see that when you have kids without ARPKD, and then in the middle here kids with ARPKD, but without portal hypertension. So not a lot of fibrosis in that liver and then when you have kids with ARPKD and with portal hypertension,

you get stepwise, you know, incremental increases in what we call this Shear wave speed or this measure of liver stiffness.

So it does seem to work relatively well for letting us know, you know.

Hey, is this liver really beat up or is this liver still feeling okay?

That's it. Are there, is there anything else that we need to be ready for with our kiddos?

And if we take a moment to talk about Autosomal Dominant PKD, absolutely. There's some other, you know, non-kidney, non-liver, manifestations of ADPKD, those include aneurysms.

I think that's a really big one that we talked about. Cystic disease of not just the liver but you know, even the pancreas or sometimes issues with the lungs themselves, and ARPKD some features as well. You can have underdeveloped lungs, cerebral aneurysms have been reported, so it’s not just an ADPKD thing.

High blood pressure happens, pancreatic cysts, or of course, the hepatic manifestations where you have either those enlarged cysts in the liver, or those developments of varices, again not as big, a deal for ADPKD kids as it is for the ARPKD kids.

So while the liver’s, of a kid with ARPKD or CHF, does have issues. It really still usually functions quite well. Meaning that those liver cells inside there are in good shape.

They are capable of doing all the things that, you know, liver cells should do just because they have that scar tissue around them doesn't mean they don't work, they can work really well, but it's just that the complications of having that scar tissue, that portal hypertension that really drive us to need to be careful with it.

One of the thoughts is that well, okay, if you can, if you can get around the (poor audio), can you perhaps eliminate some of these complications that we see, whether that's the varices or the ascites in the belly or the large spleen, and the short answer is yes. In some cases, you can

What this represents what we call a shunt surgery, where a surgeon takes (poor audio), and instead of sending it into the portal vein, which is having trouble getting through the liver, they go ahead and put it into one of the renal veins.

Now this may or may not be the best idea in someone with say, like a severely affected ARPKD, but there's some other options where it saved us. You can do like a spinal cable right into here. Regardless, when you get that blood supply going in a different direction.

It doesn't go through the liver first; it goes actually around the liver and then gets into the liver through the hepatic artery on kind of a second pass.

This ends up being physiologically pretty good for a lot of kids.

Now that said there's there are some you know things that we need and bacterial products that are supposed to go to the liver first without going to say up into the heart in the brain first and so you know, it's not perfect in that you do put kids at a little bit of a risk for what encephalopathy where some of those either bacterial products or breakdown products aren't getting metabolized by the liver right away.

There are getting metabolize but just not right away and that can affect say maybe like school performance or create a little ADHD in some of the patients that we see.

So, you know, it's not an uncomplicated surgery from that perspective but it is one that especially if you're having a lot of trouble with either bleeding, or the the fluid in your belly, you might take a look at.

But beyond that, you know, if you really do run into trouble with your general hepatic fibrosis and it's complications related to portal hypertension, transplantation does have to be thought about.

Complications that we see when we would say talk to a family about, hey, you know, this this liver in this setting isn't doing the trick. Would include recurrent episodes of that GI bleeding, especially if you can't fix it with our scopes. Recurrent infections, or perhaps the fact that the livers pretty Advanced, and, you know, while it hasn't had many complications, the kidneys are looking like, they might need to be removed and transplant in. So, doing want to consider doing both of the same time.

And you know, just to kind of put it in perspective when it comes to, you know, ARPKD, we do see types of transplants in these kiddos.

We lost you there again.

We can't hear you, Dr. Fisher.

(Poor audio.)

We're not hearing you.

Yes, I think so. Try again.

Now, are you able to hear me now?

Oh, yes. Yes. Now we can

Nope, we don't hear you at all.

We don't hear you at all Dr. Fisher okay.

Yes, I did. I get back in.

Yes. Okay, sounds great.

Okay, I'll keep going. And just holler at me.

If it if it pops out again.

Right about that. You're breaking up a little bit right now,

We have about 10 minutes left.

What I can do is try and wrap up real quick here then.

Okay, we do have a couple of questions, so hopefully we can get to that.

Obviously, when it comes to talking about transplant, early disease predicts a lot higher likelihood. So the kids at present later in life, or maybe, aren’t noticed right away, are going to go a little longer without transplant, especially liver transplant than those who are maybe caught a little bit earlier, or noticed a little bit earlier.

But that’s it (poor audio). It's truly excellent. In kids whether we're considering a kidney transplant only, or liver only, or combined, liver and kidney. And certainly over time we’ve gotten better at it, which is great to see.

So does this mean that we can talk about normal living for kids with ARPKD? And yeah, I always tell folks that this is completely what I expect, 100%. Normal life span. Now you may have medications and bumps in the road, but at the same time getting to do, what you want to do is going to be important.

And so with proper surveillance, you know, I really do think that we can we can get close to having just a super good life for these kiddos.

So again, when it comes to looking for liver disease, we like to use our physical exam and lab work as well as the Imaging.

And then if you know what is it kid say that we would have here in Kansas City, once the renal Doc's have decided that it's a good time to maybe have come talk to us. We would have that initial visit that would include that lab work that ultrasound. And then, you know, MRCP if they're usually if they're old enough to do without anesthesia. And endoscopy, if they've got some signs of portal hypertension, and then we set them up for those annual visits with lab work, vitamin studies, ultrasounds, and those liver stiffness measurements whenever we can, you know, every three years. And in our system, we do like to repeat those MRCP is an endoscopy, and in addition to having that those annual visits.

And so it does tend to be something where we love to good, (poor audio), long-term relationship and (poor audio) every step of the way. With that said, since we just have a few minutes left, I'll go back over and stop sharing now and we can chat a little bit about, you know, what kind of questions you guys may or may not have. Sorry for the audio there.

It's ok.

So the first question is, when do you, when should you start doing a scope on a child with ARPK? What factors do you look for to know if one should be done?

And then I'd like to add how often would you do them?

Yeah, no I think that's a, it's a great question and kind of going back to that last slide there is one that we've tried to at least make a you know, a protocol for the kids that we see.

The one thing that I can't say is that I know, you know, that there is an age where you need to do it and it really isn't like that.

What you do need is you need that clinical suspicion to start doing the type of those type of cares that you want to do.

For us that clinical suspicion comes, usually from the kidney doctors when either they're like hey I did an ultrasound in the liver, and it looks really bumpy, you know, it looks really affected, okay? That would be a good reason for them to come see us. If they feel an exam that the liver super large or that this spleen is super large.

Yeah, you know what, I think it's good to get checked out by your liver, doctor for ARPKD. If they have a large a hepatic cyst and you know, the kidney docs are just are like, hey, will you guys, please look at this.

That's one where our door is always open for kids with ARPKD. And so, we love to see them, even, even if the liver hasn't been affected by anything yet, we're all in right away. Now that said, when we might to kind of take it further, when do you, when do you do all those things?

For us, we decided that we're going to do an MRI or that or what we call the MRCP, which is MR Cholangiopancreatography. But it gives us a nice look at that biliary tree every three years.

I won't do that, a, before usually age, seven or eight, unless a livers, really affected because it does require a little kid to be sedated to get good images.

Now, once they get to be seven, eight years old, they can lie in the MRI machine and watch a movie for about 45 minutes. And then it becomes a lot easier to do it without any kind of anesthesia.

For Endoscopy, we will wait until they have some signs of portal hypertension on their exam, or on their lab work or Imaging. We've got to see some kind of indication before we’ll say, you know, we need to go use our scope. But once we've seen that, for us it does become important that we go ahead and take a quick look, we'll do those looks every three years if kids have had varices present, we might go and look every year or two, if they've actually had done a rubber band on them, done that band ligation on.

We may come back within three months after that band ligation to see how things are going and perhaps repeat it until we get rid of those various all together. It really just depends on the patient.

But again for the most part referral to a liver Clinic sooner rather than later is great. But, when it comes to, you know, what's the age where you need, say the MRI or the endoscopy or this, or that, those more invasive tests that that still has to rely a little bit on the clinical situation.

Great. Thank you.

And the next question is, have you had patients with CHF who have developed liver nodules, and if so, how often do their liver modules need to be removed?

You know, we have not had any of our patients, say, develop liver nodules, and would this mean like a liver cancer? I think per se, because what we'll see is that, you know, they can certainly get large cystic disease where the cyst is so large on one side of the liver or the other side of the liver, and people think about taking that portion of the liver out and then leaving behind a relatively unaffected side of the liver if that's if that's the case.

So let's say you're getting a lot of infections and you have this huge cystic dilatation on the left side of the liver, it's possible to remove that side of the liver. Let it grow back.

And, in theory, take away some of that infectious risk.

That's only everything else looks really, really good all throughout the system. It's a rare step to take and I've really only seen it in one patient. Now, as far as developing say like a liver nodule, you do have to worry about cancer development in the liver and that's something that I didn't get to share a bit.

You know, we do need to be aware of some of the risks for what we call cholangiocarcinoma.

This is a special cancer that happens with inside the cells that of those bile ducts.

And you can see here, you know around gosh in ARPKD they start to pop up and you know, in the fourth fifth sixth decade, where you get, where you get, those cleaned your carcinomas.

We do have some case, reports of them happening in kids as well and so it's one of those things where we don't necessarily plan on say removing nodules from a kid with ARPKD and congenital hepatic fibrosis, but we are looking for nodules because we want to make sure that there wouldn't be say a cancer developing.

Okay, great.

The next question is do you recommend long term use of reflux medications, and is there one that performs better than another for these kids long-term?

Yeah. And that's kind of going on to the GI side of things which is you know its a big deal for a lot of ARPKD kids, and sometimes the ADPKD kids that we see.

I don't recommend any antacid over another necessarily and I don't think that they have to be on, but you in situations where, you know, either having this huge liver is making it so that your kid is throwing up or having some reflex type symptoms. Can be a really helpful medication for those kids.

We have a few different categories. We used to use a lot of Zantac had actually got a black box warning because of EDTA, that was kind of a preservative found in in the Zantac they didn't want to keep giving that to people thinking that it could in fact create a cancer. Well, there's no direct correlation that anyone's found it was enough of a risk that we've stopped using that. And instead we like to use Pepsid, which is basically about the same type of medication. A little bit more effective, but also more expensive alternative to Pepcid, or what we call famotidine would be

the proton pump inhibitors like in you've heard about all these, you know, Nexium, Prilosec. A lot of them are over the counter now, but those tend to be really good acid blocking medications and if your child does have symptoms of reflux, or general abdominal discomfort, using them and seeing if they work for your kid is a really good idea.

Now, there are some people who advocate for them in kids who have those varices that I described as you're like, well, what if you reflux into your esophagus and that irritates those big blood vessels could that make them bleed? And some people do think that that's possible.

So, you know, if we do see, you know, really bad redness and irritation of some of those blood vessels but maybe not perhaps anything else going on there, we might, we might go ahead and prescribe the that the, you know, an acid blocker, whether that's the famotidine or one of those proton pump inhibitors for those kiddos.

I'm glad everyone came.

Thank you very much, Dr. Fisher for your time.