Dallas Reed: My name is Dallas Reed, I'm an assistant professor of OBGYN at Tufts University School of Medicine in Boston. My clinical roles are dual. I'm a division chief of genetics, and a director of perinatal genetics and a general obstetrician gynecologist at Tufts Medical Center. So, I know a lot about pregnancy and genetics. And so, this is sort of why I am here to talk to you all today. And I was asked to talk about family planning and have entitled my top autosomal dominant PKD and pregnancy considerations. This disclaimer that you've probably seen in many of the other talks is here and the disclosure, I don't have anything to disclose. I do have a disclaimer though, that during the talk, I may use the terms female and male partner that is meant to talk about someone's genetic sex and not their gender identity. And we're just going to kind of read through a couple of different topics.

The first is PKD basics, which many of you probably are already aware of. And so, we won't spend a lot of time on that. And then we'll talk about the pregnancy considerations. And then I'll go back to the preconception considerations because I think it makes more sense once we talk about what things you're worried about in pregnancy, or when patients are trying to become pregnant. So, you likely know that PKD is a very common one and 800 to one and 1000 live births have autosomal dominant PKD, and this is the same as a prevalence of about 39.6 per 100,000 people. It's the leading cause of end stage renal disease, kidney transplant and dialysis. And as many of you know, there are manifestations of PKD that are throughout the body, not just related to the kidneys, but as you know, there can be enlarged cystic kidneys, hypertension or high blood pressure, renal pain or cyst pain nephrolithiasis, which is kidney stones, urinary tract and cyst infections, cancers, including renal cell carcinoma, and ultimately renal failure, requiring dialysis if things progress.

There can also be extra renal manifestations including liver, pancreatic, seminal vesicle cysts and arachnoid membrane cysts in the brain. There can be other issues with the vasculature, including intracranial aneurysms and aortic dilation and if the dilation progresses, too far a dissection or opening of the aorta. cardiac abnormalities include the abnormal valves and

aneurysms of the coronary arteries. And then there can also be an association with colonic diverticulosis, and diverticulitis. And PKD, as many of you know, can be diagnosed clinically, there's a few different sets of criteria. But looking at the kidneys with renal ultrasound is the primary way of diagnosing. And depending on how many kidneys you see if they're unilateral, or bilateral, depending on the age of the person can help make the clinical diagnosis. There are also criteria using MRI if necessary. And that's usually in the cases if renal ultrasound is inconclusive, it can sometimes be hard to see little, tiny cysts on ultrasound.

And so, if there's more than 10 cysts in individuals at risk and at risk need someone who has a first degree relative with a known diagnosis of PKD, then that is enough to make the clinical diagnosis. There are also other things that can be seen that can lead to the clinical diagnosis, including extra renal cysts, and some of those areas that we discussed previously. Even just enlarged kidneys or liver that are palpable on a physical exam, hypertension diagnosed at less than 35 years of age, the cysts plus intracranial aneurysms or a family history of PKD. So, if you sort of there isn't necessarily a strict criterion, you need a certain number of these to make the diagnosis.

But if somebody has sort of some of these constellations or features than that is enough for a suspected diagnosis of PKD. But we do know that there's also genetics related to PKD. And there's two genes in particular, we know that PKD is autosomal dominant, hence it's in the name. And for those that don't understand what that means, and how that's different than autosomal recessive PKD. Essentially, we know that we pass on half of our genetic material to our offspring. In this illustration here, the affected parent is in the blue, and this affected parent has one normal copy of one of the PKD genes and one copy with a variant or a mutation. And because we pass on half of our material and it's random, there's a 50% chance that the affected parent will pass on the variant copy of the PKD gene.

And so, what we say is there's a 50% chance that someone who has a dominant condition will pass that on. What we know about PKD is that there's phenotypic variability. Phenotype just means the features of the

condition. And so, we know that individuals within the same family may have different features of PKD. Obviously, those that have the condition will likely all have the renal cysts, but some of the other things related to extra renal cysts, aneurysms, aortic dissection or dilation. Those can vary amongst people and even in the same family. And so, it's really important when people come see someone like me, geneticists, that we sort of dig into all of those possible features when we're taking a family history. And we'll talk a little bit more about sort of genetics role in this.

In this topic a little bit later. There are two genes related to autosomal dominant PKD type one is caused by a gene called PKD-One, it causes most cases about 90% of cases in which we can find a genetic cause, and it causes more severe disease than type two, the average age of end stage renal disease is depends on the type of genetic change. So, truncating variants are those that stop the reading of the of the gene early and non-truncating variants don't they just change sort of how that what we call how that gene is spelled. So, there can be a difference in age of the end stage renal disease, depending on what type of variant is present. Type two is the less common it causes about 10 to 15% of cases and in those that we know have a genetic cause.

And it has a little bit of an older age of average age of renal transplant, about 80% of patients start dialysis over the age of 45, which is significant because usually people under the age of 45 are in their reproductive prime and are able to have children. And so sometimes people are not aware that they have a diagnosis of PKD. If there isn't a good family history of family knowledge about this condition, and so it's very prevalent, or could be very prevalent in in patients or couples who want to become pregnant. We know that the prognosis is partially based on the molecular cost, molecular cost just means the specific genetic change. But there's also other environmental factors including lifestyle modifications, diet, medications, etc.

We also know that there are some people with autosomal dominant PKD, in which we cannot find a genetic cause. And that becomes really important when we start talking about family planning, because you need to know the genetic cause in order to proceed with some of the options that are out there.

So, we're going to move on to pregnancy considerations. The biggest concern in pregnancy is around hypertension and something called preeclampsia, which we'll talk about a lot in the next couple slides. So, patients who have autosomal dominant PKD have in pregnancy about a 15% chance of developing new onset hypertension.

25% of pregnant people have complications due to hypertension in pregnancy, if they have PKD and 11% of the time, the pregnant person may develop preeclampsia, even patients who come into pregnancy with normal blood pressures, no diagnosis of hypertension with PKD have an 88% chance of developing chronic hypertension if they have hypertension or preeclampsia during a pregnancy. And even if they do not ever develop high blood pressure or preeclampsia during the pregnancy, they have a 62% chance of later developing chronic hypertension after the pregnancy. Obviously, this increases the risk of acute renal failure during pregnancy and the cases that are out there show us that that likelihood is there usually in patients who have had a diagnosis of preeclampsia, so if they haven't had a diagnosis of preeclampsia that renal failure risk does not go up dramatically during pregnancy.

So, pre-eclampsia is something you may or may not have heard of it. The definition is new onset hypertension and proteinuria or other evidence of end organ damage during pregnancy after 20 weeks gestation. So, any high blood pressure before 20 weeks gestation is considered chronic hypertension. And anything after is on the spectrum of gestational hypertension, or preeclampsia, and preeclampsia is when we add in the proteinuria or other end organ damage. Examples of that could be elevated liver function tests, elevated creatinine levels, abnormal blood counts or low platelet counts. Those are all evidence of what we call an organ damage. It can obviously be challenging and people who already have kidney disease or pre-existing hypertension to make the diagnosis of pre-eclampsia.

And that's why there are some important things that we do early on in pregnancy to make sure we can know the difference that this is going to develop for someone. And importantly, although we talked about it

happening in pregnancy, it can occur up to six weeks after delivery. And so, we always keep a very close eye on our patients who have risk factors for pre-eclampsia. Up until that six-week period, the symptoms of preeclampsia that someone may experience are headache but doesn't resolve with medication. Typically, the medication we're talking about as Tylenol, because that's kind of the safe, non-narcotic medication to use in pregnancy, vision changes.

So, that can be blurry vision, double vision or spots in your vision, acute onset of chest pain or shortness of breath at rest, meaning you weren't doing anything, you weren't climbing stairs, you weren't running after your other child, you just sort of start to develop the shortness of breath, right upper quadrant pain, so the right upper quadrant is right underneath the right breast or the right chest area. And that's where your liver is. And so, in pre-eclampsia, the liver can have bleeding around it into what's called the liver capsule. And that can cause pain in that area. Sometimes it's epigastric, or sort of more towards the midline.

Sometimes it gets what we call the referred pain to the shoulder. So, any kind of acute onset of that type of pain very separate from the uterus. It's not contraction pain, it's very different. Although not strictly in the definition, but something that should be concerning and somebody with risk factors for preeclampsia is sudden onset weight gain from worsening edema or swelling. So, if there's, you know, a three or four-pound weight gain in the course of one or two days due to that extra fluid in the in the body that can be concerning, and especially if that swelling is in the hands or face.

Obviously, the legs can commonly get swelling because pregnancy causes decreased blood return to your heart and all other types of things that can happen in the lower extremities but especially when we see it in the face and hands that can be a little bit of a concern. And pre-eclampsia implies that there is a pre-eclampsia and Eclampsia is when these features or symptoms develop are not cheated and can progress to seizures. So, this is something that we that you know, preeclampsia is something that happens commonly not just patients who have polycystic kidney disease. And it's something we

have our eyes on very closely, but it can be very dangerous. We have this definition of preeclampsia with severe features. And preeclampsia with severe features is what sort of moves us in the direction of sort of more serious management of the preeclampsia.

And that's defined as a blood pressure greater than systolic blood pressure of 160 or a diastolic pressure of 110. So, if either number is elevated, then that's considered a severe feature. Thrombocytopenia, which I talked about before, which is a low platelet count. Usually, platelet counts are above 250. That's pretty normal. Once you get below 100, that starts to be concerning transaminitis, which is that elevation and liver function tests. And the definition of that is twice the upper limit of normal different labs have different cut off values for those labs. And so, it's not sort of just a one set number, worsening renal function. So, doubling of the serum creatinine mean, obviously, people that come into pregnancy with pre-existing kidney disease have a craniotomy level, that's known.

And so instead of, again, using a specific cut off, we talked about doubling of what that number is persistent, right upper quadrant pain, like we talked about before, pulmonary edema, which is fluid in the lungs. And that's what can cause that acute onset shortness of breath, or the visual changes that we talked about before. So, for patient has elevated blood pressures proteinuria and starts to develop these severe features, then we get even more concerned and want to sort of move forward with how we're going to treat them. preeclampsia, as I said, can be very dangerous. So, for the foetus, it can cause growth issues, and that's usually growth restriction. So, babies can be very small or very, very small, which can cause a lot of issues later on, especially after they're born preterm delivery and that could be because preeclampsia is present, and we need to deliver someone prior to their due date or prior to term.

It also could be due to the growth issues with the foetus, the foetus stops growing for example, then that may be an indication for delivery and lead to create, you know, a premature delivery. Abruption, which is when the placenta separates from the uterus. That is an emergency it causes bleeding

into the uterus and sometimes bleeding from the vagina. And the reason that that's the problem is because the placenta is what feeds the foetus and gives the foetus all the nutrition than if that has now separated those connections are no longer there. And it can cause the foetus to essentially haemorrhage because there is no connection between the foetus and the pregnant person anymore. respiratory distress, which just means breathing issues for the foetus. This can be associated with prematurity or can be sort of separate from prematurity even if the foetus is not born prematurely, and then stillbirth, which means a demise of the foetus.

And that could be due to abruption or growth restriction or some of the other placental issues that can occur in preeclampsia. For the pregnant person, the concerns are around high blood pressure during pregnancy. This high blood pressure if it gets to that severe range can lead to stroke. And we also know that people who have preeclampsia have a future increased risk of developing hypertension and cardiovascular disease even they're no longer pregnant. And even when they're done having pregnancies, it obviously can lead to kidney damage. If there's hypertension, and chronic kidney disease, liver failure as possible if those liver function tests become affected, it can also cause the cardiomyopathy which is a enlargement of the heart and it causes the heart to not pump as well and can cause somebody to go into heart failure.

And then obviously, seizure as we talked about as the definition of eclampsia is when seizures develop. In addition, there's this other association with diabetes that can occur after pregnancy. So, the treatment for preeclampsia in pregnancy is very simple, it's delivery. And so, if somebody is diagnosed with pre-eclampsia without severe features, in order to sort of weigh those risks of prematurity, we continue to monitor patients and deliver them by 37 weeks that monitoring could be inpatient, or outpatient. Depending on someone's ability to sort of adhere to the frequent appointments and frequent monitoring, I will say at the institution that I work at. We typically admit patients with pre-eclampsia without severe features to be admitted in the hospital until they deliver at 37 weeks or sooner if things start to worsen.

So, if somebody comes into the hospital at 26 weeks with preeclampsia, then they may be there until 37 weeks to deliver. When somebody has severe features associated with their preeclampsia. Again, we're trying to weigh those risks and benefits of prematurity, we can keep the blood pressures and in the labs are not worsening and everything stays under control, then the decision is made to deliver by three four weeks delivery may be by induction of labor or depending on the urgency of the need of delivery, it could be by a caesarean section. Induction of labor is when we give medications to help somebody go into labor, and optimally have a vaginal delivery. So, it doesn't automatically mean a C section. But it does mean a delivery, probably not at the due date like you were thinking coming into the pregnancy.

And the management also includes obviously monitoring the blood pressure. If the blood pressure spikes up to that severe range, we often give IV medications so that I will act quickly to help lower the blood pressure. And then we can maintain the blood pressures with oral medications for most patients, and then also this medication called magnesium sulphate is given, the goal of magnesium sulphate is to lower the seizure, the lower the risk of somebody developing a seizure. And so, this is a very, very important part of the treatment of pre-eclampsia. Other things outside of the blood pressure and pre-eclampsia risks are obviously related to the kidney function. We know that people who have a significant renal disease before pregnancy have an adverse effect on long term renal and foetal outcomes. And we know that patients who have chronic hypertension that we know about before pregnancy allows us to be more proactive and have a better sort of plan going into the pregnancy and outcomes may be improved if we're able to treat that hypertension early on in the pregnancy.

What we do know from the few case reports and studies that are out there is that patients who have a stable renal function it does not seem to worsen during pregnancy. And for patients who have multiple children, so more than four children, the data has shown that the curiosity may worsen at that point but prior to that likely does not. We know that urinary tract infections can also be common they are common in pregnancy anyways, and in people with

ADPKD they can also be common in pregnancy. It's typical to have what we call an asymptomatic urinary tract infection which means and in fact should with no symptoms you don't have burning when you pee, there's no cloudiness in the urine, you're not rushing to go to the bathroom, and then small amounts of urine come out, you are rushing to go to the bathroom during pregnancy, that's just part of pregnancy.

But because of that reason, we like to monitor the urine during the pregnancy. So oftentimes, when you go to a doctor's appointment, they're checking your urine. One of those reasons is to check for an asymptomatic infection. And if those are not treated, they can ascend. So, move up the urinary tract and get into the kidneys and cause a pyelonephritis, or a kidney infection, that can be very dangerous in pregnancy, it can lead to pulmonary edema, which again is fluid in the lungs and cause breathing problems for the pregnant person. It also can cause sepsis, which is a blood infection. So, if that kidney infection sort of leaks out into the blood, that can be very dangerous. So, we want to take UTIs very seriously in pregnancy. And we treat with safe antibiotics, there are many antibiotics we can use that are very safe to use in pregnancy.

We know that kidney stones can also be an issue in pregnancy and with PKD. And so, we manage that the way that we would normally manage it, we try to do our best to use safe medications and non-narcotic medications if possible, and just sort of increasing the fluids and letting that stone pass. If that's not possible, or we need higher level of pain medication with narcotic medication, we can do that in pregnancy. And we try to do that for a shorter period of time as possible, in order to not lead to addiction issues with narcotics and also to minimize the effects on the foetus. And then the removal of stones if necessary. It can be done with specific types of procedures not every way that we treat kidney stones outside of pregnancy can we use in pregnancy, but there are some techniques that can be used.

And then for cyst pain, we would again want to manage pain, the way that we always manage pain, so with safe, non-narcotic medications, if possible, and then increasing to other medicines if we need to. For liver cyst, it doesn't seem like they will change much during pregnancy. Although if someone has

multiple pregnancies, and there wasn't really a number as to how many multiple is but multiple pregnancies can the studies have shown can you know women can develop more cysts later on. Obviously, if somebody has liver cysts, you want to monitor those for enlargement of the liver. And we know that we can see that when there's increased estrogen exposure. So, whether that's pregnancy doesn't really increase the estrogen levels too much. It's the progesterone that is increased.

But that could be if you're going through a process to become pregnant, that may include estrogen levels or birth control pills, for example. So, something to keep an eye on. And then obviously, there is not just the pregnant person to worry about, but also the foetus and the neonate. So, affected foetuses, foetuses who have inherited the PKD genetic change, have a 2% chance of presenting in the foetal period with enlarged echogenic foetal kidneys. So, we know a lot about autosomal recessive PKD, which pretty much always presents in a foetus, although the cysts and the way that the kidneys look can look a little bit different in autosomal, dominant PKD versus recessive PKD.

But it can be very hard to tell sometimes because the cysts are so small. So, in patients that we see in our ultrasound unit, for example, if we see a foetus with enlarged echogenic kidneys, we always want to examine the kidneys of the parents, because we know that the first instance of autosomal dominant PKD might present at that time, that might be the first time anybody has ever brought that up. And we may find it in the one of the parents. And that's a completely different prognosis. As you can imagine. Autosomal dominant PKD versus recessive PKD, which is usually fatal or has very significant impacts on the neonate in the in the first few months of life. 43% of affected foetuses that are foetuses that are present in utero are within the first few years of life died before age one and that's probably just an indication of how severe that kidney disease is.

And 67% may have complications by three years of age. For foetuses that are not affected that do not have PKD, but the pregnant person does have PKD we know that this can cause some of the things we talked about already small for gestational age, foetal growth restriction, which is different than small for

gestational age based on the degree of growth restriction, preemie prematurity admission to the NICU, there may be some associations with foetal malformations or birth defects. That data is a little bit fuzzy and there needs to be some more are some more evaluation looking into that? But that is perhaps in association and then neonatal death is possible. So, during pregnancy, how do we monitor people, we get what's called baseline preeclampsia labs. So, knowing that these patients are at an increased risk of developing preeclampsia, we want to see what their baseline is of everything at the very beginning first visit.

So, what are their blood counts? What are their platelet level? What are their liver functions, we want to know what the Creatinine level is? And then we typically do something called a 24-hour urine, which you may be already accustomed to. But for that urine collection we're looking at, we want to look at the protein level over that 24 hour. So, once we have these baseline levels, if things start to develop later on in the pregnancy, with higher blood pressures, or the protein in the urine that we see in the office, we can start to re-evaluate, do the labs over again to see if anything has changed. And if this person is just worsening, they're their hypertension is just worsening, or if they're actually developing pre-eclampsia, because they're treated very differently. We also know that prenatal aspirin is a good preventative measure that people can use that maybe developing pre-eclampsia, and especially pre-eclampsia.

That is early onset early onset means kind of like in the second trimester, or early third trimester, before 34 weeks. So, prenatal aspirin is something we recommend that patients take starting at 12 weeks, it's just an 81 milligram or baby aspirin that's taken once a day, every day until delivery. And that has been shown to decrease the risk of developing that early onset preeclampsia. We actually can start at any time between 12 to 16 weeks, but the earlier you started them, the more time it has to act on the little tiny blood vessels that are in the placenta that are starting to sort of make their home into the uterus. We also obviously want to follow the foetus. So, we do the usual ultrasounds early in the pregnancy that look at how far along someone is. And then there's

another one that looks at genetic risk. There's an ultrasound that happens between 18 to 20 weeks gestation, that's called the level two ultrasound or foetal anatomy, ultrasound, which allows us to look at the fetus from head to toe.

That might be where abnormal kidneys are found in a fetus, if they were to develop that. But we also would do what we call growth ultrasounds, which are basically monthly ultrasounds to check the size of the fetus and make sure that growth restriction or small for gestational age is not developing. There also is this other assessment called uterine artery dopplers, which is looking at the blood flow between one of the uterine arteries or viewed an artery and it looks to see how much resistance there is between the placenta to the fetus. If you start to see a lot of resistance, that could be an explanation for growth restriction. And if that blood flow actually starts to go backwards the other way, that may be an indication for delivery because then we know the placenta is not really doing its job. And the more we wait, the longer there is a risk of stillbirth.

They also want to assess the amniotic fluid. We know that the fetus, the amniotic fluid is actually baby pee or fetal pee. And so, if the kidneys are not working well then that may be decreasing the amniotic fluid levels, but in a few years that we know is unaffected with a with a pregnant person being the one that has PKD. We also know that the high blood pressure and the poor placental sort of perfusion can cause those fluid levels to be low. So, we want to keep an eye on that. And that happens also about monthly or so may increase towards the end of the pregnancy. So, for monitoring blood pressure in pregnancy, there are some safe medications that we can use. These two at the top tend to be the two that that most places use either libido law or nifedipine.

Typically starting with libido well in our practice, and it can go from 100 milligrams, twice a day, up to 400 milligrams three times a day. And then nifedipine extended release is also a medication that we typically start at about 30 milligrams. And we usually take that once a day for people that need better control, maybe twice a day. But there are some other medications that

can be used here. And these are considered to be safe in pregnancy. We want to pay really close attention to the blood pressure in pregnancy for all of the reasons we've already talked about. But also, we don't want to overcorrect the blood pressure. We know that in the first and second trimester, it's normal for the blood pressures in pregnancy to be a little bit lower than they normally are. And so, we don't want to be too aggressive about treating the blood pressure and have that blood pressure drop too low because that can affect the perfusion between the pregnant person and the placenta, which affects the blood flow to the fetus.

So, it’s a little bit of tight close management of looking at those blood pressures. For patients without PKD, we typically aim for blood pressure in the normal range with just less than 140s, systolic and less than 90 diastolic. For patients with autosomal, dominant PKD, that range is going to be a little bit lower 110 to 135, over 70 to 80, we really don't want it to dip below 110 over 70, because then we get into the placental perfusion issues. And then delivery, there's no special things that need to happen for delivery. Most patients are eligible for a vaginal delivery, even if they have to be induced or delivered early because of the preeclampsia or other fetal concerns. Patients with PKD are more likely to undergo induction of labor because of the reasons we've talked about.

But also, they are more likely to undergo caesarean section. And that would be done just for the normal fetal or maternal indication. So, it's not that PKD means you need to have a C section or that an induction means you have to have a C section. But we just know, especially with growth restricted fetuses that sometimes they just don't tolerate labor as well. And if we start to notice that that's happening, that may be an indication for a C section. And there's many other indications for C sections that just happen all the time. So, I'm not seeing any questions yet. So, we'll move on to the preconception considerations. And first, we'll start with a male partner. So, we know that there can be some sperm abnormalities due to what's called ciliary motility issues.

So, cilia are like little motors in the body and the sperm have the flagella or the tail that has a little motor that helps it move. The PKD genes can affect that ciliary motor, sort of how that apparatus is put together. And so there can be something called Normospermia in males with PKD, which means dead sperm. And Asthenozoospermia, which means a low motility, sperm with mobility issues. There also can be dilated or cystic seminal vesicles. So, this is just a picture of the male anatomy here. This part here is the bladder, Right here is the prostate, and the urethra, which is where the urine and the semen come out of the penis, the testicle is down here, and the seminal vesicles right here, just behind the bladder, it's basically where the vas deferens start and the vas deferens or where it ends, I'm sorry, which is where the testicles where the sperm are made, and they sort of travel up through the vas deferens, and they have to collect all different types of fluids to help them survive the sort of pH in the vagina and sort of that whole journey that they have to take.

And so, when these seminal vesicles cysts are present, it actually decreases the amount of that seminal vesicle or the seminal fluid, which can cause a problem. So, we can see this in 39 to 60% of those with PKD. There was a question in the chat, I'm going to save that to the end, since it's talking about pre-eclampsia, but we will we will get to that one at the end. There can also be a Jak dilatory duct cysts that are present. So, that's what we know about the male partner for the female partner. We don't believe that there are issues with fertility, especially if renal function is normal. We know in other studies that people who have abnormal renal function for various reasons, not just PKD may have issues with pregnancy. That there, there may be this increased ectopic risk and atopic pregnancy is one that happens outside of the uterus.

So usually, that's in the fallopian tubes. It's not exactly clear if that risk is real or not real. But it's been perhaps shown in some studies. So, what we want somebody who a female partner who wants to become pregnant who has PKD, we want them to check in with their nephrologist, obviously, before pregnancy. If they hadn't had a renal ultrasound in the last year, we'd want that done just to assess any cysts size and that way we can monitor that as pregnancy goes on, especially if symptoms arise, like cyst pain or other renal

symptoms arise in the pregnancy. But medication that's out there now tolvaptan is a Class D medication and pregnancy. So, Class D means it may show some harm in fetuses. And so, it's definitely not recommended in pregnancy.

So, if it's something you know, this is why talking about pregnancy with your nephrologist, is important early on, because if it's something that you want to eventually be on or might be eligible for it may make sense to sort of decide about your family planning before that gets started. Obviously, the hypertension piece is important. Pre pregnancy proteinuria. If somebody does have high levels of protein in the urine early or before pregnancy, the ACE inhibitors or angiotensin receptor blockers can be given. So, that's like Lisinopril as an ACE inhibitor, so that can be given until a positive pregnancy test and then switch to one of those safe medications that we talked about earlier. If there isn't proteinuria, early on, or prior to pregnancy, then stopping those medications prior to pregnancy and starting on a safe antihypertensive is what's recommended.

The reason for those that have the pre pregnancy partner aid to stay on their medication that we know helps their proteinuria is that sometimes it takes a while to become pregnant. And we don't want to be losing opportunities to help control the protein levels and the kidney damage if we can happen. Also, important to have a preconception MFM consultation, if you are desiring pregnancy, because we want to talk about preeclampsia, and what we would do in pregnancy, and what's happening with your blood pressures and sort of its kind of it makes sure we have a plan about how to manage the pregnancy and the delivery. For those that don't know MFM stands for Maternal Fetal Medicine, which just is our high-risk obstetrics doctor, so they often do ultrasounds, and they may follow women who have high risk pregnancies or may just give advice to ups to obstetricians that are taking care of patients, it just kind of depends on the practice setting.

It would also be important to meet even though you're you would meet with an MFM. It's also important to meet. And I would say that the MFM consultation could also happen even if the male partner is the one with PKD.

Preconception OB consultation just to talk about the normal things we want to talk about with people like lifestyle modifications and healthy diet and avoiding smoking and drinking, but also to do what's called carrier screening, which is genetic testing to see if people are carriers for recessive genetic conditions, with jarred have a different inheritance than dominant ones, we won't get into the details of that. But that that's an opportunity to do that so that we know what all the risks are going into the pregnancy before someone is pregnant.

And then genetics may play a role in your evaluation prior to becoming pregnancy. Becoming pregnant, I'm sorry. So, if you wanted to do any type of fetal or embryo testing, you need to have a molecular diagnosis. If we don't know the genetic cause, there is no genetic testing that can be done for a pregnancy. And the genetic counselling encounter has some several aspects. One is a pre-test counselling session where we obtain a family history and draw something like this, which is called a pedigree just gives us multiple generations of one's family, we ask questions about healthy people and people with illnesses so that we can know sort of the full range of what's happening in a family. It's also a time when we talked about the risks and benefits of genetic testing, we talked about the types of results that can be present.

So, it's not just always positive and negative, there can be other types of results that can be hard to interpret and may actually require us to test other family members to be able to come up with a clear yes or no answer. And we talk a lot about insurance coverage. Unfortunately, for some genetic tests for PKD, the insurances are often not covering the testing, because it's not needed to make a clinical diagnosis.

And so in in some of their minds, it may not be necessary for you to know your genetic risk. From the genetics perspective in in sort of medicine in general, we think that's a little bit of a flawed theory. But we do know that there are some relatively affordable ways to get genetic testing where prices are capped at, $200 $300. And so even if your insurance doesn't cover it go

into genetics professional can help you really understand the true cost of testing, and it might be more attainable than you think.

Speaker 2: Dr. Reed, we have three minutes left.

Dallas Reed: Oh, jeez. That's not a lot of time. Okay. I will skip through this. But essentially, we do the testing, and then we would talk about the results afterwards and can help coordinate testing for family members. If you wanted to do in vitro fertilization to become pregnant. That is a process where we stimulate the ovaries, retrieve some of the eggs, mix them together in the lab with sperm, and then let them grow for a couple of days. And then for those that want to do IVF, with pre–Implantation Genetic testing, we can actually send those little embryos to a specialized lab where they can do genetic testing, they do a little biopsy of the embryo and genetically test that embryo. And then at the end of that which am reels have the PKD mutation and which embryos do not.

And then you can choose to implant the ones that do not. The pros of doing that is that it prevents passing on the condition to your chalk child also freezes time. So, for people that are approaching sort of their 40s, it allows you to sort of freeze time and not have the risks of Down Syndrome and other things continue to progress as time goes on. You can also screen for things like Down syndrome or other genetic conditions. The cons are that it's costly, may not be covered by insurance. And you may have extra embryos leftover at the end, when you're done building your family, which can make it you know, a decision to make about what to do with those embryos.

Obviously, there's also the option of prenatal diagnosis, which allows us to just do a test either called a CVS or an amniocentesis where we put a needle into the belly either to take a sample of the placenta or the amniotic fluid, in order to test that for the DNA and that genetic change that we can see in PKD. Unfortunately, and then once you get that information, you can decide how you'd like to proceed if you'd like to proceed with the pregnancy or not, if you want to deliver at a specialized center where they're able to sort of evaluate the fetus early on. Unfortunately, with the Supreme Court ruling

today, this is obviously going to be a limitation for a lot of families that if they decide their fetus has PKD, and they decide not to continue the pregnancy, they may not have options that are nearby that allow them to make that choice. And that's really unfortunate.

There are other reproductive options, obviously, like IVF, with donor gametes, which means the partner who has if it's the female partner that has PKD, you could use donor egg, or if it's the male partner donor sperm, there's also adoption or somebody asked a question about surrogacy, which is where you have someone else carry the pregnancy, even though it's genetically your embryo, someone else carries the pregnancy, which is also an option, or somebody may choose just to not have children. And finally, there's obviously a lot of feelings associated with all of this decision making, it can be very hard to decide which way forward to go. And so, I think it's important to remember that these are complex decisions, and everybody's care should be individualized. And you should really make sure you find providers who help you feel supported and the decisions that you want to make.

And then this is my contact information. If you have questions on those that I couldn't get to your questions, please email me, I'm happy to answer them. This is my little guy. He's about to be one year old. And I put him here because he was brought to us by IVF done because my husband has PKD and so we did IVF for that reason in order to not pass PKD on to him. So, I know about this stuff from the first-hand level. And I thank you guys for your time and I'm so sorry I talked too much and didn't leave enough time for the questions.

[Audio Ends] [01:06:22]