

RODRIGO RUANO: Hi. My name is Rodrigo Ruano. I am a fetal surgeon at Mayo Clinic and chair of the division of maternal fetal medicine. And today, I have the pleasure to be here with Dr. Joseph Dearani and Dr. Elizabeth Stephens, who are pediatric cardiovascular surgeons at Mayo Clinic.

And we are here to discuss today something very exciting, which is the possibility of doing fetal interventions for congenital heart defects. So Dr. Stephens, Elizabeth, which are the main diseases or congenital heart problems that we think we can treat in utero?

ELIZABETH H. STEPHENS: Well, that's a great question. The vast majority of patients with congenital heart diseases, they grow just fine while they're in utero. So they're getting oxygenated blood from the mom, and that goes to the rest of the body and the brain.

But there is a subset of congenital heart diseases where the disease itself progresses or gets worse during development. And it's that specific select group of patients where there's this opportunity to use fetal cardiac intervention to either stop the progression of the disease or even make it better.

RODRIGO RUANO: That's fantastic.

ELIZABETH H. STEPHENS: Yeah. So one of the things that-- there are a few examples that this has been shown to be effective, and one is hypoplastic left heart syndrome, including if they have what's called an intact septum or aortic stenosis, a narrowing of the aortic valve, and then Ebstein's anomaly which, at Mayo, we have a lot of experience in.

So maybe I'll ask Joe, given all our experience here with Ebstein anomaly-- and we get a lot of fetal consults regarding these patients-- can you comment on the referrals we get and the opportunity to intervene on these fetuses?

JOSEPH A. DEARANI: Sure. So this is a great launching pad to talk about a lesion that we really do have a lot of experience with here. And despite this extensive experience, there's still room for a lot of improvement. So Ebstein anomaly is an anomaly of the right ventricle and the tricuspid valve. And it's really the only lesion where the spectrum of clinical presentation can be a symptomatic neonate to an asymptomatic adult that's not even identified until the adult years and everything in between.

And the symptomatic neonate still is sort of the one lesion that really haunts the surgeon when surgery is required, even in the current day where the results of surgery for hypoplastic left heart syndrome have gotten to a very low mortality. When surgery is required in the newborn with Ebstein anomaly, it still carries high mortality. And so we need to make it better. And I know that we've worked together to talk about what those options would be.

And the problem is it's such a drastic anatomic abnormality with the heart that it results in poor development of the lungs. And if we can intervene a little bit earlier on to not avoid the need for surgery but make the performance of the child after birth a little more stable and allow us to sort of collect our thoughts, evaluate, get the proper imaging, and do surgery in a controlled manner as opposed to a chaotic, urgent type of situation, not only will the risk of surgery be lower, but the long-term outlook would likely be better. So I think we have an opportunity here.

RODRIGO Great. And you mentioned about hypoplastic left heart syndrome [INAUDIBLE]. Can you explain a little bit about
RUANO: hypoplastic left heart syndrome and then aortic stenosis? And then we can discuss a little bit about the interventions we can do for that situation or those situations.

ELIZABETH H. STEPHENS: So good question. Hypoplastic left heart syndrome is when the left side of the heart-- so the mitral valve, the left ventricle, and the aortic valve-- are small. And in those cases, they are not able to supply enough blood to the body. So among those lesions, aortic stenosis-- in other words, where the aortic valve is there but it's small-- that's one of the lesion sets where they've demonstrated that intervening as a fetus can be helpful. As Joe has mentioned, they still need surgery after they're born, but that can improve their overall outcome and their stability.

RODRIGO
RUANO: Exactly. This is one example of the surgeries that we are currently doing before the babies are born. So hypoplastic left heart syndrome, the left heart doesn't develop very well. When we have aortic stenosis, we can put a tiny needle inside the heart of the fetus, of the baby before the baby's born, and try to dilate the aortic stenosis or try to dilate the aorta and to improve the heart.

So the success rate of this procedure nowadays is about 85%. So 85%, we are able to perform the procedure. And 50% of the time, we can create a biventricle situation. So we can have two halves. We can save the left heart. And then, this is one option that we are offering now. And then, maybe with Ebstein, we can do something too in the future. So we have some examples of fetal interventions that we can show. But afterwards, I would like to come back to Ebstein anomalies.

So nowadays, we can offer many different types of fetal interventions. We can offer fetoscopic repair where we can put a tiny scope inside the uterus, the maternal abdomen and inside the uterus, and we can treat the fetus. Or we can open the uterus. I have one example. For example, congenital diaphragmatic hernia.

This is an example of a normal fetus, 28 weeks. And then we are going to see a fetus with congenital diaphragmatic hernia, which is a hole in the diaphragm, the muscle that separates the chest and the belly. And then we have the herniation of the stomach, liver, and bowel inside the chest. And by consequence, the lungs and the heart are pushed against the other direction. And the lungs, they don't develop very well. So what can we do for that?

So these babies, they develop something called pulmonary hypoplasia, smaller lungs. So at 28 weeks, we can introduce a tiny telescope inside the uterus. You're going to see now the ultrasound guidance with local anesthesia, so some sedation to the mom. And then we use [INAUDIBLE] inside the amniotic cavity, inside the mouth of the baby, inside the trachea, and we deploy a detachable balloon that will promote lung growth. And this balloon stays there for 28 weeks until 34 weeks.

And then the lungs expand, increase, and grow. And then these babies, they will have a better chance to do better after birth. And then, at 34 weeks, we remove the balloon using the same technique. And then those patients can have vaginal delivery. The babies with congenital diaphragmatic hernia that underwent or undergo this procedure, they still need to go to the NICU, but they have a better chance of survival.

And then another example is that we can open the uterus and sometimes expose, for example, the back of the baby. And we may be able, when we want, to expose the heart of the babies. So the next video that I would like to show is about spina bifida. So we do a laparotomy, so we open the mother's belly. And then we open the uterus. We use ultrasound guidance, and then we just open the uterus a little bit. We identify with the baby's back up, and then we identify the defect in the baby's spine or the baby's back. That's the image.

So the baby's back doesn't close very well, we call it spina bifida. And using special devices nowadays, we can safely open the uterus and expose the baby's back. And then a neurosurgeon can come and close the defect in the same way that we would do postnatally. And by doing this, we improve a lot the outcomes of those babies. So those are the examples of surgeries that we can do, we can offer in utero. How can we improve the condition before the babies are born?

**JOSEPH A.
DEARANI:**

Thanks, Rodrigo. You've alluded to, indirectly, the personnel that are involved. You've mentioned NICU and surgery and, of course, your team. And the success of all this, it depends on teams, multidisciplinary teams where you're bringing various specialties together, each sort of bringing a particular skill set.

And I think one of the things that you will appreciate is the number of people involved. And everybody has a specific responsibility. And each role that that person or that group of people plays is essential to the outcome. And so now we would be taking that squad of personnel, and we would be trying to do what we have been doing postnatally prenatally. And we have a protocol in place to do this for Ebstein anomaly.

And you and I have worked together in the operating room. The three of us have seen what's possible. And this is something that I think could be a game changer for these babies. And we have not been able to dramatically change the mortality for surgery with this newborn lesion. Despite the advances and the improvements with so many other lesions, this one is still the one that keeps us up at night the day before surgery. And this is a chance, I think, to make it better.

**RODRIGO
RUANO:**

Thank you, Joe. And how do you think it's going to improve that?

**JOSEPH A.
DEARANI:**

Well, I think that the fundamental problem is the heart becomes so large. They develop heart failure from the heart problem. But also, in addition to the heart being large, it compromises the development of the lungs. So if we're able to, perhaps at the 28-week mark-- I mean, we would have to defer to your judgment about what would be the best time.

But if we're able to reduce the size of the heart at a time when it's very, very large to allow space for the lungs to develop during the remaining portion of the pregnancy so that, at the time of birth, the lungs are large enough that they can support the circulation with the defective heart to allow us to not rush into surgery, let the dust settle, stabilize everything with the neonatal ICU team, and then proceed with surgery in a more controlled fashion.

And there might be some situations where you'd actually sneak through the newborn period without needing surgery. That, of course, would be the dream because the risk of surgery drops dramatically once you get beyond the first month or two of life. So all of this would be a step in the right direction for improvement, and we can do this.

RODRIGO RUANO: That's amazing. So as you mentioned, a multidisciplinary collaboration is crucial for the success of those procedures. And here, we are discussing about a situation that is very severe because of heart and lung problems. So if you can improve at least the lung condition and minimize the cardiac complications, that would be fantastic.

And we have the tools to do this here. And we have, as you mentioned, a protocol for that. So we are starting this protocol, and hopefully we will be successful because our main goal here is to keep delivering hope to the patients and to the families and to give a better chance for those babies and for those mothers.

Elizabeth, anything you wanted to add?

ELIZABETH H. STEPHENS: Well, I think we touched on this some, but these fetal interventions, for the vast majority, are attempting to either slow down the progression of the disease or alleviate some of the disease, but it's not the be-all or end-all for most of the cardiac lesions. So these are things that enable the prognosis to be better, but the family should still expect, postnatally, that the babies will require surgery. But again, the overall goal is to improve the prognosis of the babies.

RODRIGO RUANO: Thank you.

JOSEPH A. DEARANI: You said hope, and I think that is our departing word because there still are a fair number of mothers that choose to terminate pregnancy because of this lesion.

RODRIGO RUANO: Exactly.

JOSEPH A. DEARANI: And we don't want that. We want to come up with a strategy that provides hope with a predictable and reliable chance for a good outcome. That's our goal here. That's what we want to do and that's what we are going to do.

RODRIGO RUANO: And we are studying that a lot, and we are studying prenatal imaging, methods that we can use to predict the lung function, predict heart function. And also, we improved this cardiovascular surgery technique, so we are progressing very well.

JOSEPH A. DEARANI: The future is here today.

RODRIGO RUANO: The future is here today. So I would like to thank you so much, Joe. And thank you also, Elizabeth, for all your work and collaboration with [INAUDIBLE]. And then I would like to thank everybody who listens to us. And then, if you have questions, we'll be happy to answer those questions afterwards. So thank you.