Pressure, Flow and Fragility – Rethinking Hemodynamic Support in Severe CDH - Pediatric Grand Rounds-4-10-2026-Meeting Recording

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So we're going to go ahead and start grand rounds. For everybody, just to remind, so a few reminders to unmute yourselves for people that are logging in.

The for the CME, just log in and check the chat, and the attendance number is going to be there. So, I would like to welcome a special guest for today. We have Dr. Asrafi that has joined us. He

He is a cardiac neonatologist at Chalk, and this is the Children's Hospital of Orange County. And he's one of the few physicians to receive formal training in both neonatal intensive care and pediatric cardiac intensive care. His premier interest is in neonates with cardiac conditions and hemodynamic instability.

congenital heart disease, and he's the associate medical director of the CHOC NICU as well. I just learned that they have 20 NICUs and 80 neonatologists covering all those NICUs across the region. So he's the medical director of the Neonatal ECMA program.

the director of the Neonatal Cardiac Intensive Care Unit, and the program director for the Neonatal Cardiovascular Intensive Care and Hemodynamics Fellowship as well. He is the founder of the Neonatal Heart Society and the chairman of the International Meeting NeoHeart Cardiovascular Management of the Neonates. So Whoever wants to join him in London this year is welcome. If not, then next year, San Diego. Prior to joining CHALC, Dr. Asrafi attended medical school at the University of Utah, followed by the pediatric residency training at Emory University. And then he completed the neonatal intensive care fellowship at UCLA.

where he was recognized as the chief fellow. Dr. Musharof then went on to complete a second fellowship in pediatric intensive care unit and pediatric intensive care at Boston Children's. So this is a special day as well because we are, we have a special

guest. Julian was a patient with us 12 years ago in the NICU.
and we're celebrating his life with his family here. And with Dr. Escobedo, who is also part of a, well, she was part of our family, continues to be part of the family here in the NICU in San Antonio. And we will welcome them also in between. Everybody's welcome to stay after Grand Rounds into the next lecture.
for another hour, so we will have more welcome statements for Doctor Escobedo as well. So, I will ask Doctor Ashrafi to start his lecture, so then we can talk about pressure, flow, and fragility and rethinking hemodynamic support in severe.
Thank you so much for joining us and welcome to San Antonio.
My name is Amir. It's an absolute pleasure to be here. Thanks to the Division of Neonatology. Thanks to Julian here to my right, Dr. Escovedo. Thank you everybody for coming. So it's a pleasure to be here at Grand Rounds here at the UT San Antonio. Now, I know Grand Rounds typically
has a very diverse audience. General pediatrics, subspecialists, everything in between. Diaphragmatic hernia, particularly severe diaphragmatic hernia, is very niche. Typically neonatology, Pete surgery, maybe pulm will dabble in it, maybe cards will dabble in it. Excuse me.
Before we committed to this topic, we were going to talk about septic shock, then we were going to talk about PDA, and it wasn't until last week we landed on this entirely my fault, so...
What I want to do, though, is talk off the slides and make this as relevant as possible for everybody who's outside of the NICU and outside of Pete surgeries. Hopefully, I do a good job with that. And so even if you don't take care of diaphragmatic frenia per se, there will be concepts in there that you can take back with you with other patients you care for.
That is not a typo, PGY 20. I did have to count on my fingers to make sure I got that right.
Full disclosure, I do have 3 relationships. Abbott is trying to make devices not for peds or adults, but for neonates, in particular small babies. So I've been consulting with them about what to do for babies under 1 kilo. Mallinquot, makers of nitric oxide, just got approval.
for treatment of pulmonary hypertension in congenital heart disease in Europe, New Zealand, Japan, and Europe. So they've asked me to help them understand where nitrogosate can be helpful or harmful in congenital heart disease, nothing in the US. And I designed on the data safety monitoring board for a phase three clinical trial of

a rare disease. So those are my 3 disclosures.
Now, diaphragmatic hernia is something that's evolved quite a bit in my own mind over the years. And when I first started as an attending, I had this approach. And this was an approach that was taught to me by my attendings. And I think by and large, this is what everybody in the country did. We recognize that this is a triad that takes place.
between the heart, the lungs, and the pulmonary vasculature. And if you have diaphragmatic hernia, we know that there's going to be problems with the lungs. There's a big hole in the diaphragm, all the abdominal content comes up into the chest. And so there's going to be undoubtedly some ramifications for the lungs. And what's important is this concept of gentle ventilation. In fact, this came up
I believe the term was coined out of a gentleman in Columbia back in the 1990s. And the idea is you don't need to have a pH of 7.0, sorry, 7.4 and a pCO2 of 40. You can let that pCO2 rise a little bit, let that pH drop a little bit. They'll do just fine. Gentle ventilation don't hurt the lungs that you have right now.
Um...
Then the other component was pulmonary hypertension. And this is the part that got everybody's attention, myself included. We wanted to keep our saturations above 90% because we know if they desaturate, it's only going to exacerbate their pulmonary hypertension. There was no evidence for nitric oxide, but everybody used it. And whatever evidence out there existed,
seem to suggest that if you use nitric oxide, increase the mortality and increase the need for ECMO. But we ignored that because clearly there's a selection of lines. If you need nitric oxide, you're going to be sicker. So let's ignore all of that data. And this is the primary reason why any baby would go on to ECMO was pulmonary hypertension or inability to get it under control.
And then when it came to the cardiovascular component of the triad, very blood pressure centric. Make sure we've got a blood pressure greater than their mean gestational age. I mean, their mean blood pressure greater than their gestational age. If not, start dopamine, max that out. If that doesn't work, then go to epinephrine, max that out. If that doesn't work,
start hydrocortisone. And this was sort of my simplistic thinking, and this is what my attendings taught me by and large.
After that, I would call the surgeon. We'll have one of two requests. Either baby looks great, let's go to the OR to repair this congeal diaphragmatic hernia, or baby's not

doing so great, we need you to go on to ECMO. And this is, like I said, how we did things. Now you heard, we host this meeting every year now called NeoHeart, Cardiovascular Management of the Neonate. And the idea of NeoHeart was
When I done NICU, you know, there's a very NICU way to do things. And then when I did CVICU, there's a very CVICU way of doing things. And even though you're both taking care of neonates, the way they managed the ventilator was very different. The way they managed inotropes was very different. It's the same one week old baby, but the approach was very different. And so why is that? Well, over time,
As medicine gets more and more sub-specialized, the consequence is, do I admit people from the lobby? Do I say yes? Oh, you're doing it. Okay. Thank you for that. What's the consequence of the...
Medicine, we're getting so specialized.
And now you've got neonatologists talking to neonatologists, cardiologists talking to cardiologists, surgeons talking to surgeons. We have our own journals now. We don't read other people's journals. We only read our own journals. We only go to meetings where neos talk to neos. And we start to get more and more siloed. So the concept of NeoHeart was, let's try to break that silo and break that mold. Let's have neos talk to cardiologists.
Let's have CVICU talk to CT surgery, CT surgery talk to Neo, and have everybody come together and let's talk about these patients together. So that's the concept of the meeting. And it was in one of our early Neo heart meetings. My partner, Dr. John Cleary, goes, hey, Amir, have you heard of this guy named?
Gabriel Bolte.
No, no, never heard of him. Who is he? Well, he's a fourth year fellow at Stanford who seems to think that in babies with diaphragmatic hernia, the right ventricle is not what we should be focusing on. It's the left ventricle that's so telling in babies with diaphragmatic hernia and the need for ECMO. And I thought to myself,
Well, Gabriel's an idiot. Of course, it's pulmonary hypertension. Of course, it's the right ventricle. What does the left ventricle have to do with anything? To which John Cleary goes, no, no, no, you should read it. And it's actually a really good abstract. I read his abstract. It ultimately led to a publication and he won the best abstract of that year. And again, he's saying that it's not the right heart of pulmonary hypertension we need to worry about, it's the left heart of the cardiac output.
Well, fast forward a couple of days, there's this gentleman right here, Dr. Gil Wornofsky. This guy is the GOAT when it comes to CVICU.

double boarded cardiology in PICU, spent most of his career at Children's Hospital of Philadelphia, hosts a lot of the major meetings with regards to cardiac ICU, and just an all-around outstanding, brilliant gentleman. So I was getting advice from him early on in this whole conference planning business. And I was like, hey, Gail, so you know, what do you think about, you know, Neoheart? What did I do well? What did I do?
poorly, and he goes, you know, it's good. I like the concept, but it's still, you're not, you're not breaking the mold. You still got Neos talking to Neos and cardios talking to cardios and surgeons talking to surgeons. We haven't actually, you haven't broken any barriers yet. Okay, well, what should I do, Gail? He said, you know, diaphragmatic hernia is a lot like Shone's complex. What you should really do is talk about what a CVICU person's experience is.
And I heard nothing else after that. He kept talking and I heard nothing else after that.
CDH is like Shone's complex. Has this old man lost his mind? Now, for those of you that don't know what Shone's complex is, small left-sided structures, think hypoplastic left heart syndrome.
What does hypoplastic left heart syndrome, Schoen's complex, have to do with diaphragmatic hernia? But he's Gil Wernovski. I don't want to look like an idiot in front of Gil. So what do I do? I smile it now in my head. Oh, yeah, yeah, yeah, yeah, totally. Yeah, they're exactly the same. Yeah, yeah, I get it. I didn't hear anything else happen up. So conference comes and we go forward.
And there's a young, eager resident by the name of Sharif Jafar. His mom was a neonatologist. He was going into cardiology. He's now a cardiology attending in New York. And he says, hey, Dr. Ashrafi, I really want to do some research in something neonatal cardiac related. Do you have anything for me?
Interesting you should mention. There was just this conference we were at last week, and the abstract winner seems to think that the left heart is more important than the right heart. I think it's a bunch of crazy nonsense. But could you take a look at our data over the last 10 years and tell us what you think? And any residents in the room?
Sharif, take this advice, is a doer. When he says he's going to do it, he doesn't. There's plenty of people that want to do it. He's A doer, be a doer, particularly for residents. So this guy was a doer and he turned it around and lo and behold, after 10 years of data, the degree of pulmonary hypertension

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Right heart function had nothing to do with the need for ECMO. It was all left heart output and left heart function. I was like, wow, are all my attendees and everything I've learned incorrect and ultimately this led to a publication as well. There still is this important triad when it comes to diaphragmatic hernia. I want to spend just a few slides talking about the pulmonary
implications of CDH. Now, never is the statement more true than with the lungs. That function follows form. There's a cast you see in that picture. On the left side is all the airways. On the right side is the arteries and the veins.
Really beautiful picture. And if you look at the human lung, the 1st 16 branches is dead space. It's the last seven branches from 17 to 23 is where gas exchange takes place. We have 23 segmentations of airway and vasculature in the human lung.
And if you look at congenital, I'm sorry, if you look at normal lungs, here's a cartoon. You've got two healthy lungs, you've got a full diaphragm intact, and here's an electron microscope of what alveoli should look like.
But then if you have diaphragmatic hernia, I think everybody knows the diaphragm is no longer fully intact. You'll notice, oh, you don't see my mouse.
You can see that the diaphragm is not intact. And so all the abdominal content, small bowel, sometimes large bowel, lungs, liver, all come up and act as a space occupying lesion on the side of the defect. Now, it's pretty obvious that in this scenario,
the left lung is going to be problematic and is going to be hypoplastic. But, well, actually, let me stop here and say that the consequence of this space occupying lesion now is you have significantly fewer conducting zones of the lungs. They have significant lung and alveolar hypoplasia.
which makes it far more difficult for gas exchange to take place. But it's not just the affected side. The other side, contralateral side, is also affected. Now you've got everything pushed over to the other side. You've got the heart pushed all the way over and it impacts the lungs on
both sides. The other problem with this is not just lung hypoplasia, it's also vascular hypoplasia as well, particularly on the side that's affected. So most of your blood is going to go to the contralateral side. If blood goes to the contralateral side, these

blood vessels are also going to be affected. Here's a light microscope. You can see how thick and how dense the septi are.
how difficult is for gas to take place. This is on the contralateral side, not even the affected side. So it's bilateral disease, but they're both affected differently.
And this is kind of the most done study of all times. The bigger the defect, the more lung hyperplasia, the more likely you'll need ECMO and the more likely you will not survive. No surprises there. Here's a nice video of what alveoli look like. You can see alveoli inflating and collapsing, and then you can also see
Blood vessels lining up a single file line, going through, and having gas exchange take place.
Here's a cartoon of it. You'll notice in this cartoon that blue blood comes in, exits red, no surprises there. Carbon dioxide, gas exchange happens early. Oxygen gas exchange happens a little bit later. So now let's put this into a graph. If I were to put time on the x-axis,
and partial pressure of gas on the y-axis, you'll notice that oxygenation and ventilation do not have the same curve and the same pattern. If you were to take a normal neonate, heart rate of about 130 to 150, red blood cell transit time through a capillary takes about
0.25 to 0.3 seconds through that capillary.
Adequate gas exchange, specifically oxygenation, takes approximately 0.2 seconds, which doesn't give you a lot of reserve time. That oxygenation has to take place over the course of that entire path that that red blood cell travels.
Carbon dioxide, on the other hand, gas exchange occurs very quickly, less than 0.1 seconds, plenty of reserve time. So why the difference between oxygenation and ventilation? Well, if any of you were nerds like me in college and were biochem majors or took P chem, you learned about orbitals.
and you learned about structures of different molecules. Absolutely as nerdy as it gets here. You'll notice that carbon dioxide has a higher molecular weight than oxygen. Obviously, it's two oxygens on a carbon compared to two oxygens. But because of the electron orbitals set up, carbon dioxide can traverse across tissues 20 times more readily
than oxygen. To all the neonatologists in the room, this is why you have T-COM monitors and you don't have T-OM monitors. You can measure transcutaneous CO2 for those that are in the NICU. We have a device we put on baby skin where you can measure their carbon dioxide level. It's like a pulse oximeter because carbon dioxide

diffuses so readily
across tissues as compared to oxygen. So this is why there's a difference in transit time.
So now what if you have a sick baby and they have a heart rate of 200? Now your RBC transit time gets critically low. Is it possible that tachycardia could be a cause of hypoxia? I don't know. There's never been looked at, but it's an interesting concept to think about as we move forward.
But let's now take it even a deeper step. How do molecules diffuse across a membrane? Well, you've got fixed laws of diffusion here, fancy math, the difference between partial pressure of a molecule times the area times the constant.
Obviously, the constant of these two are going to be very different, divided by the thickness of the membrane. Basically, when you do all the math, what it amounts to is more often than not, not always, but more often than not, hypoxia results from diffusion limitation, whereas hypercarbia results from perfusion limitations.
And so we could spend a whole lecture talking about how to optimize oxygenation in some babies, how to optimize ventilation in other babies. And when it comes to congenital diaphragmatic hernia, ventilator strategies that need to account for, excuse me, lungs that have low compliance, high elastins,
load time constants, abnormal diffusion limitations. But that's a talk in and of itself, and we don't want to go there. What we're here to talk about is how do we think about the hemodynamic impact of this mass occupying lesion in the left or the right chest that we call diaphragmatic hernia. Excuse me.
So.
If we take a look at normal fetal circulation, I think this is something that everybody knows.
The lungs are not the site of gas exchange for the neonate. It's sorry, for the fetus, I'm sorry, for the fetus. It is the placenta. Placenta is low resistance, lungs are high resistance. You want to send blood to the placenta so gas exchange can take place.
So in utero, how do we do that? We have something called a patent ductus arteriosus, and that's why it exists.
It sends approximately, if you average nine months of gestation and nine months of flow, 85% shunts right to left through the duct, meaning only about 15% goes to the lungs. Those 15% then come back to the left heart.
In diaphragmatic hernia, however, the more severe it is, the more lung hypoplasia, the more increase in your pulmonary vascular resistance, you could get upwards of

95% shunting right to left, meaning you get less blood to the lungs, less blood that comes to the left heart. What does that mean? Reduced volume loading of that left heart throughout nine months of gestation.
It's not just the patent ductus arteriosus, it's the patent ductus venosis flow as well that becomes important. Once the blood goes, the placenta gets oxidated, it comes back through the umbilical vessels.
This highly oxygenated blood then comes in. The ductus finals is oriented such that the blood goes directly into the left heart. Left heart into the first branches of the head and neck vessels goes to the brain. And so the highest oxygen in the fetus goes to the brain. Approximately 70% is oriented right to left through the PFO, and only about 30% goes to the right heart. But what happens to diaphragmatic hernia, particularly in right-sided diaphragmatic hernia? Now the liver comes up into the chest. It reorients the ductus venosus. So now all of that oxygenated blood, rather than being oriented through the PFO, now goes directly into the right ventricle and only 30% volume loads that left ventricle. Once again, you get underloading, volume loading specifically of that left ventricle. Now, why do I specify volume loading? We know from hypoplastic left heart data that how do you grow a left ventricle?
It's not a pressure phenomenon, it's a flow phenomenon. And again, this is where cross-discipline interactions become important. We can learn from one another. If you want to grow a left ventricle, which many centers are doing now, it's a flow phenomenon, not a pressure phenomenon. Well, now that old guy was starting to make sense.
Maybe diaphragmatic hernia is kind of like Shawn complex a little bit. It's underloading of that left heart. It's small, it's stiff. Now again, you may not be totally familiar with Shawn complex, small left side structures. It can range from mild to severe. In the mild form, some small hypiplasia of the left side anatomy.
In the most severe form, we got ductal dependent circulation. I'm not making reference to the severe form. I'm making reference more to the mild form. But now it starts to make sense. And we have known since the mid 80s that neonates with diaphragmatic hernia by autopsy data in the original studies have smaller and stiffer left ventricles than their healthy counterparts.
So let's go to the literature. Maybe Dr. Wardofsky was onto something. What papers out there do look at this concept of LV failure and the need for ECMO in diaphragmatic hernia? This isn't all of the papers, but these are the ones I like the

most. There are a few others out there.
But basically, if you look at everyone, Gabriel Altman, that fellow from Stanford, was on to something. Everyone shows statistically significant values that if your left heart, either output or function is not optimal, your need for ECMO goes up in this patient population. Not pulmonary hypertension, which we always thought it was, but it's the left heart is what these papers are looking at.
So why is that? Okay, that's an interesting correlation, but we still need to ask the why. Well, the most obvious explanation is if your LV output is low, your cardiac output is low, which means your demand is more than your delivery. BO2 greater than DO2. And this is really the premise of ICU medicine. If anybody's interested in ICU medicine,
or if anybody's interested in neonatology, this is really the premise of the cardiovascular system. You have a certain need for oxygen, your VO2, your metabolic demand of oxygen, DO2 is your delivery. And it's all about manipulating your VO2 and your DO2. If not, that's what we call shock.
So if you have reduced cardiac output, your delivery does not meet your demand, leads to end organ function, and you have a cascade effect, and that's why you need ECMO. All right, makes sense. We'll roll with that.
Now, even though Dr. Wardoski was on to something, there's a lot of similarities in left heart phenotype between those two disease processes, you still cannot neglect that there is still pulmonary hypertension. Okay, we can't totally ignore that. It's still there. So how do we reconcile this? Well, everybody is guilty of this, myself included, but every NICU, every PICU, every
cardiologists, we're all guilty that when it comes to pulmonary hypertension, we start to get our blinders on. And we think there's just one size fits all. There's pulmonary hypertension, and we all know what to do, give oxygen, nitric oxide, it's sildenafil, et cetera, et cetera, et cetera. We sort of have our mentality of how we do it.
But obviously, that's far too simplistic. And even though there's one diagnosis, there are five phenotypes to pulmonary hypertension in the neonate. There are more in adults, but in neonate, this will encompass 99% of all pulmonary hypertension. You can have lung causes of pH.
Vascular causes a PH and cardiac causes a PH. By far and away, the most common is lungs causing pulmonary hypertension and a concept known as hypoxic vasoconstriction.
So what happens here?

Well, it's simple. Let's say your alveolar PO2 is low for whatever reason. You've got pneumonia, you've got Laconi aspiration, baby's born premature, not enough surfactant, those alveoli clothes. The alveolar PO2 is low. Well, the body is sophisticated. It says that there's no gas exchange that's going to take place here. I'm not going to send blood there. Instead, what I'm going to do is send blood to areas that are well oxygenated, well ventilated. They're in FRC. They're fully inflated. Makes sense, right? Hypoxic vasoconstriction. First, you have hypoxia, second, you have vasoconstriction. This is a reactive phenomenon. And what the body is trying to do, you guys have heard the term VQ matching to the ICU people in the room or to everybody else. This is what VQ matching is, ventilation perfusion matching. Send blood
where gas exchange can take place.
This is by far in the way the most common cause of pulmonary hypertension in neonates. And this is usually the funnest to manage. I don't want to say easiest, but oftentimes the most satisfying because the vessels are doing what they're supposed to do. They're supposed to vasoconstrict. There's no oxygen there. So all we got to do is outsmart those blood vessels.
We could do that.
Whereas that's the most common cause, it's not the only cause. You get vascular causes as well. I've made reference to this several times already, but pulmonary vascular hypoplasia. This is a baby we had with diaphragmatic hernia and congenital heart disease. Went to the cath lab, you can guess which side the diaphragmatic hernia was on. Look at how much smaller that left
pulmonary artery as compared to that right pulmonary artery. If you have to send an entire cardiac output instead of through this much pulmonary vasculature, let's say pulmonary vascular real estate, so to speak, compared to only this much pulmonary vascular real estate, it's going to be under much higher pressure.
So pulmonary vascular hypoplasia. To the NICU fellows in the room, how good do you think nitric oxide is at growing blood vessels or sildenafil? Or we got to keep that sat above 90, otherwise the pulmonary hypotension is going to get worse.
It's kind of like saying, oh, this is my favorite line, actually, when other attendings or fellows, and I'm guilty of saying it as well, I don't want to just pick on other people, this patient's a nitric oxide non-responder or a selenophil non-responder. It's kind of like giving a cyclovir to somebody with gram-negative rod sepsis and going,
He's an acyclic or a non-responder. I don't know what to tell you. Well, obviously,

nitric oxide doesn't grow blood vessels. So this is a fixed pulmonary hypertension, not a dynamic pulmonary hypertension. And if you really want to practice state-of-the-art medicine,
Your approach to treating pH in vascular hypoplasia is going to be different than treating pH in a kid with a dynamic vascular bed.
Who gets this? Trisomy 21 is the most common one we see. I said earlier, there's 23 branches to the pulmonary vascular airways and vascular tree. Trisomy 21 is known to have fewer segmentations, anywhere from 17 to 22, depending on how few
Their segmentations all will determine the severity of injury.
Ohh.
following up, hydramnials, Potter sequence, but of course, obviously diaphragmatic hernia as well. You can get abnormal vasoconstriction.
So what ends up happening is we know we've got a muscular layer to all arteries. Now, what happens in diaphragmatic hernia when all the blood can't go to the left side out of the right ventricle, it almost forced to go to the right side. There's this concept of Ohm's law, pressure is flow times resistance.
So if you've got more flow, there's going to be more pressure. What happens to muscles under pressure? You go to the gym, and what do you do? Your muscles hypertrophy. When blood vessels hypertrophy, they don't hypertrophy out, they hypertrophy in. And when they have hypertrophy in, you get a reduction in internal diameter. That reduction in internal diameter increases your point of vascular resistance.
Pastelier's law and you get increase in your pulmonary pressures and pulmonary hypertension. Again, to the NICU fellows, how good is sildenafil at causing muscle atrophy?
right? That's not what is intended to do. So this person would be a sordenafil non-responder, I guess. But again, the approach to how you treat hyperplasia of the muscular layer of the artery, different than hypoplasia of the vessel, different than a reactive vascular bed. And so the nuances become important. And of course, diaphragmatic hernia on the contralateral side,
is at risk of developing this phenotype.
This is the one, the more we look, the more we find. Not necessarily pulmonary artery hypertension, but pulmonary venous hypertension. And you get a damn effect. If you have an accident on exit 10, well, if you backed up on exit 5, you're going to have traffic. Same type of thing here.

This is one that we always thought was just for grandma and grandpa with their HPEF, what is it, preserved ejection fraction and diastolic failure that grandma and grandpa get, and we didn't think it was anything to us. In fact, the more you read about neonatal cardiovascular physiology, grandma
and neonate have a lot of similarities. No joke, I really do. So what happens is, well, what if you got a small, stiff left ventricle because you're premature or you're broken? Well, it's like a traffic exit on exit 10. Your left atrial pressure will go up.
If your left atrial pressure will go up, your pulmonary venous pressure will go up. If your pulmonary venous pressure will go up, it backs up and you start to get pulmonary artery pressures. And again, to the NICU people in the room, this is the theory about why extremely preterm babies are at risk of pulmonary hemorrhage.
Now, I'm not talking about diaphragmatic hernia now. I'm talking to the neonatologist in the room. You've got PDA,
A bunch of flow going in, you got a traffic jam, no egress, flow goes in, it can't go out, it's gotta go somewhere, and you rupture, and that's where pulmonary hemorrhage comes from, but going back to diaphragmatic hernia.
We see this a lot, of course, in congenital heart disease, but we're starting to see it more and more in neonatology. And most certainly in severe congenital diaphragmatic hernia, you can have this phenomenon. So now you start to notice that, wait a sec, we're juggling a lot of different physiologic balls, so to speak.
What exactly is going on in the neonate with severe diaphragmatic hernia?
I also, you can have cardiovascular causes, anatomic causes. We're not going to focus too much on that for here. So let's go back. We said, well, the reason for LV failures reduce cardiac output and inability to meet metabolic demands of the body leading to end organ and ultimately ECMO. Well, maybe that's part of it, but maybe there's this other component too, where it's not
Systolic dysfunction, it's LV diastolic dysfunction leading to elevated LV EDP. That's an acronym for left ventricular and diastolic pressure, code word for diastolic dysfunction, which leads to elevated left atrial pressure, pulmonary venous pressure, and it's the combination of
pulmonary arterial hypertension and pulmonary venous hypertension that leads these babies to need ECMA. So maybe my attendees weren't totally off. There still is a component of pulmonary hypertension that we have to manage here.
But now what about nitric oxide? That's what we do with pulmonary hypertension. You're supposed to give nitric oxide. Everybody knows that to be true. Let's give it.

Now.
There's this Punnett Square, this hemodynamic Punnett Square that I give to all the fellows that rotate through our CV MCU. And what sets neonatology apart, again, now talking to the residents in the room, what sets neonatology apart from other subspecialties, if you decide to take that route, is that neonatology is very physiology driven.
You go to hem op, there's all these, you know, different gene mutations and it's very pathology driven and very cool stuff. Neonatology, it's very physiology driven. What is the aberration? What's the immaturity? What is not exactly working right that I need to manipulate? And in our world, what is babies born, they have two fetal shunt. They've got a ductus arteriosus fetal shunt.
and they have a pain foramen ovale shunt. And depending on the directions of these shunts, we can then identify what's the physiology happening in the baby.
the hemodynamics specifically of the baby. So if you've got a left to right PDA and a left to right PFO, that's normal. Your systemic vascular resistance is higher than your pulmonary vascular resistance. Your LVEDP, or the compliance of your left ventricle, is less than the compliance of the right ventricle.
This is normal. This is what's supposed to happen. But what happens if your PFO shunt remains left to right the way it's supposed to, but your PDA shunt is now right to left? Well, then now your PVR, your pulmonary vascular resistance, is higher than your systemic vascular resistance. Ventricular compliance is appropriate.
but vascular resistance is off. You can see this in severe pulmonary hypertension.
congenital heart disease that causes obstruction to systemic blood flow. These are your Shone's complexes, your hypoplastic left heart, interrupted aortic heart, et cetera. But you see it with diaphragmatic hernia and severe LD failure.
Well, what if our PVH shot stays left to right, but now our PFO is right to left? What does that mean? Well, your systemic vascular resistance is still higher than your pulmonary vascular resistance. Oh, sorry, that's not supposed to say RVR, that's supposed to say PVR. But now the ventricular compliance is altered. Again, you typically see this with
congenital heart disease, right heart failure, right heart cardiomyopathies, and then you go to the most extreme, where everything is right to left, and it's not going the way it's supposed to. Again, severe pulmonary hypertension and diaphragmatic hernia. And that's what we're talking about today. So let's
just focus on these two for a moment. Now, in the interest of time here, I'm going to

skip over these next couple of slides that just talks about, are pulmonary vasodilators a good thing for babies or not? I said baby and grandma have more similarities than than meets the eye originally. What's the best way to hurt grandma or grandpa who has diastolic heart failure? Volume. Give them volume. That's the worst thing. A heart with diastolic function does not want volume. So now you give sildenafil, you give williamtscoutenmilhealthmil nitroxide, you give supplemental oxygen, you give whatever point of vasodilator you choose.
You get increased pulmonary blood flow, stats go up, you give yourself a high five, we did great. Then the next team comes on and now all that blood flow that goes to the lungs, where does it have to go eventually?
to the left atrium, to the left heart. And now that left ventricle goes, wait a minute, I can't tolerate all this volume. This is too much for me. So then what's the first thing we do? Blame the night shift. That's what we always do. Those idiots started nitric oxide. Don't think, no, you're not supposed to start nitric oxide. There's not, there's no joy better as at attending than blaming the fellow on the night before.
So, of course, that's what we're gonna do.
Again, how do you reconcile vascular disease with heart disease? There has to be this common ground. There has to be a tightrope that we should be able to walk. And again, in the interest of time, there's been a few studies that looked at this, and basically the punchline is, we have no idea what we're doing.
But it makes sense that if you're going to give nitric oxide.
to a baby, and you're worried about downstream ramifications, well, you can blame the pulmonary vasodilator, you can blame the ship that was on, the personnel with the ship on before you, or you can say, wait a second, again, this is neonatology. There's no mystery here. This is all physiology.
We can fix that. We just have to manipulate the which way blood goes. More and more diaphragmatic hernia is being thought of as a ductal dependent lesion. This is now the first disease process in which we start using PGE, not congenital heart disease. This is the first one. Why do you use prostaglandin?
for diaphragmatic hernia? Well, I'll get back to that in just a second.
What oftentimes happens, and again, everybody's guilty of this, is we get very black and white. Is this right heart phenotype? Is this left heart phenotype? Is this lung disease? Is this vascular disease? Is this heart disease? And we try to like put these in boxes because it makes it easier for us to understand. And in all honesty, it's a continuum. It's a little bit of lungs, it's a little bit of vasculature, it's a little bit of heart.

What's true on Monday isn't true on Tuesday.
And it's a very dynamic process. So there's all these different variables happening at the same time. And the most important thing is to be aware of it, be open-minded to it, and not get trapped into a certain thought process. Now, the neonatal heart is distinctly different from the pediatric and the adult heart. I just want to spend a few slides highlighting how it's different and why this becomes important.
We know that the neonatal heart contains about 70% water compared to the adult heart, which is only 30% water. Well, what's the implication of more water and less myo size? Less contractile force. It has disorganized myofibers. The adult myocardium and pediatric as well, all the myofibers are oriented
parallel to one another. So when they all contract, they're working harmoniously together to produce maximal contractile force. The neonatal myocytes are haphazard. And they've got myocytes going in all sorts of different directions so that when they contract, not only are they not working in harmony, in fact, they're impeding the progress of one another. One's pulling this way,
One's pulling that way. What does this mean? It can't generate a lot of force. You have smaller myelocytes. Go back to med school, back when I was PGY1. Frank-Starling curves, length-tension relationships. The smaller the myelocyte, the less force it can generate. And of course, rudimentary sarcoplastic reticulum, that's where calcium is stored. You need calcium for
or actin myosin interaction without calcium, you can't have contractility. This is why neonates are believed to be more dependent on extracellular calcium because they don't have as much intracellular calcium as peds in adults. So what does all of this mean? It means that it's afterload sensitive. Fancy way of saying it's kind of like the skinny guy or the skinny girl in the gym that just can't bench press a lot of weight. If you put a little bit of weight, you'll be fine. If you put a lot of weight, they're going to fail. The LV myocardium is exactly the same. Let's highlight the right ventricle specifically. The right and left ventricle are very different from one another. For the one hand, the right heart, well, by the way,
If.
You believe in evolution, the right heart is 85 million years evolutionary behind the left ventricle. And it was the development of the right ventricle that allowed animals to go from water life to land life. If you believe in creationism,
God didn't spend as much time designing the right ventricle. I don't have a better answer than that. A lot in multiple ways.

On the one hand, highly trabeculated. What does that mean? Per square unit of area, you have fewer mile sites in the RV than you do in the LV. Think of it as a very thick, compact, dense structure versus sponge in your kitchen. It's just very porous. It doesn't have a lot of mile sites per square unit of area.
It's triangular in shaped, not conical in shape. If you take, if you speak to any, let's go ahead and skip to this right here. If you talk to any physicist or any engineer, a conical or bullet-shaped structure can generate substantially more force than a triangular-shaped structure. And the other thing that's really interesting,
Is that in the RV, 80% of the muscle fibers are oriented in the longitudinal direction? So most of its most of its movements happens in a single plane. If there's any cardiologist on the line.
or anybody that's interested, we can check RV function by something called TAPC, but you cannot check LV function by something called a MAPC, tricuspid versus vitral valve systolic plane excursion. It's much easier to check RV function because it only contracts in one plane. You compare this to the LV now,
that contracts longitudinally, circumferentially, and radially. So now you start to say, wait a second, this is why the RV is so much more susceptible to failure in various disease processes than the LV does. Now it starts to get, it starts to make sense. Why were we so preoccupied with the RV? I don't think we were necessarily
wrong back in the old days of 2017 when I think just the story was incomplete. Again, we sort of get into our, we get our blinders on and we just start to talk about what we know.
But again, nothing is ever that simple. So clearly it makes sense that the RV can be affected just as much as the LV. So let's go back to those papers that I like. Again, there's even fewer papers looking at the implications of RV failure in severe diaphragmatic hernia and need for ECMO.
None of them are statistically significant.
Wait a minute, huh? So all my attendees were propagating information in the absence of data?
You never do that.
So, let's come back to the go, Dr. Gail Wardovsky. He's got these three rules of hemodynamics.
Number one, and this applies for anything. If you're taking care of a PDA, hypoplastic left heart, anything in between, this applies for all of them.
If there's a hole between 2 chambers, the pressures will equilibrate.

Number 2, blood always follows the path of least resistance.
And #3, blue is better than gray.
It's better to have a desaturated baby with good profusion, good circulation than a dead baby, which is great. So let's see if we can start to put all of this together.
in the 12 minutes I have left here.
There's a lot of stuff going on. And when he starts to deal with things like diaphragmatic hernia and he starts dealing with multi-organ disease, lungs, heart, vasculature, he's trying to juggle all the balls, it can sometimes get a little bit overwhelming and you can sometimes start chasing the wrong thing.
I don't know if this is the right way. I don't know if this is the wrong way, but this is sort of our way, where we've landed with all of this. And I think, again, this is pretty representative of what most people in the country do. Maybe not everybody, but I think it's kind of general gist of where people are going.
I completely ignored the impact of lung hypoplasia and what we need to do on that. That was a different talk. So I'm going to summarize it into one line and just say if they've got lung hypoplasia and respiratory failure, you need to give gentle ventilation, which we've known for decades now. And if that doesn't work, go into ECMO, we'll simplify it into one line and not go any more depth than that.
But what if they have pulmonary hypertension and or right ventricular failure? Well, what we started doing in our unit, and I think this is a little bit unique, is that now neonatologists perform their own echoes.
By no means are we trying to encroach our cardiology. By no means are we trying to take over what they do. What they do is very important for anatomic heart disease, but for physiologic heart disease. The neonatal ICU physician, the pediatric ICU physician,
We just need more insight into what is happening to physiology. Again, neonatology is very physiology focused. That's the pathbone of neonatology. And so if you do an echo.
Assuming there's no congenital heart disease, baby diaphragmatic hernia, and you see something like this.
Left pulmonary artery in blue, aorta in blue, they're both traveling downwards. You've got the red flow, which is the PDA going the other way. It's all left to right ductus arteriosus flow. This tells you that the pulmonary vascular hypoplasia isn't that bad. The pulmonary hypertension
isn't that bad, it's less than systemic, chances are you're going to be fine, barring that

fellow last night that messed things up. You're going to be fine.
However, if your PDA is bidirectional, that tells you that now your pulmonary pressures are equal to your systemic pressures. And if this PDA closes, we don't exactly know which way it's going to go. Are things going to get better? Are things not going to get better? We have no idea. It is not unreasonable. I put IN out here, but you have to substitute.
any pulmonary vasal dilator you want here, sildenafil, EPO, inhaled EPO, supplemental oxygen, whatever pulmonary vasal dilator you need here is fine. It's not unreasonable to do it, but be very careful. If that increased pulmonary blood flow leads to increased preload,
to a left heart with diastolic dysfunction that doesn't like volume, and the baby gets worse, well, then you have one of two options. Either stop the therapy,
or outsmart it, keep the PDA open and start prostaglandins. I'll get to that in just a second. I'm going to take this example because it'll make more sense here in the most extreme form. What if you have something like this? Again, we do our own echoes. This is a baby that was getting ready to go to surgery, just about
about a year ago, getting ready to go to surgery. Everything was doing fine. We asked one of our fellows to go in and one of our fourth year fellows, hey, can you go do a quick hemodynamic echo and make sure this baby is set up to succeed before they go to the OR, or they operate at the bedside, before they go do the procedure. And the fellow comes back and goes, the duct is closing and now
everything is right to left. What does that mean? Your pulmonary vascular resistance is now higher than your systemic vascular resistance. This baby started out in this middle slide and then moved to this far right slide. So now it's got super systemic pulmonary pressures. This is where if that duct closes, the RV is not
Build is not conditioned to tolerate that much afterload. It's not going to be able to tolerate that. And those are the kids that are going to crash on to ECMO. And so if you can give prostaglandin, that offers you 2 benefits. You can pressure offload the RV, that's afterload sensitive,
and you can volume offload your LV that's got diastolic dysfunction. So now for the first time, we're using prostaglandin outside of congenital heart disease.
That old guy knew what he was talking about. Gil Roski was onto something in a hallway conversation.
There's still a component of low cardiac output state, LV diastolic dysfunction. I won't spend too much time here. And typically, you know, we give volume, basal active

medications, we need to go into ECMO, ECMO, but really approach it like a Schoen's complex, approach it like a small left-sided structures, and you'll be better. So in the final few minutes in conclusion.

I didn't spend too much time on this, but it goes without saying, optimize alveolar recruitment while maintaining lung protective strategies and make sure we have an appropriate definition of success. What is successful management of these patients? I love this sort of, we're all guilty of this.

dog mouth hypoxia. If they're hypoxic, it gives them oxygen a more mean airway pressure. If that doesn't work, switch to a high frequency. If that doesn't work, give more oxygen, give more mean airway pressure. How do you know when you give enough mean airway pressure? When you get a chest x-ray and their diaphragm is down to the pelvis, then you give it enough, then back off by half.

Um...

Inhale that to go outside in ECMO. The problem with this, oh, obviously, you have to, heaven forbid, they should move a finger or a toe. You have to give them so much sedation that they're completely knocked out, obviously. And the problem with this is that it lacks any sort of precision.

do it. Make sure you optimize right and left ventricular function. Again, we're all guilty of getting blinders on, and we think that we know what we're doing. Look at everything in its totality.

Here's a here's an example of what we do. This wasn't a diaphragmatic hernia, but it sort of highlights the point here. If again, we'll call one of our one of our fourth year fellows, hey, can you go do an?

Yeah, can you go do a hemodynamic echo on this baby and they'll come in?

You'll get this view right here, right ventricle.

Pulmonary valve, main pulmonary artery.

And that's what you see there. And then what we can do is we can put a Doppler on it and see how much blood is going through there. Here was a patient where this was not a diaphragmatic hernia, and I'm actually going to highlight this in the next talk, but my division chief specifically was like, oh my God, you know,

Doctor Ruffy, you need to get, you know, ECMO initiated. This kid sent her in the toilet. Hey, you know, can I just go do a quick study here? No, no, no, don't waste time. We just need to go on ECMO. No, no, I won't waste any time, I promise.

I was maybe like PGY 13 at the time or something like that. Just still pretty new in my attending career, maybe less than that, 8, 9, 10, something like that. And so this is

where we were. I then went to the RT and said, hey, you know, could you take the kid off the oscillator? Bad faster, bad slower, more eye time, less eye time. I forget exactly what we did, but within a matter of about 10 minutes, we had substantially improved our pulmonary blood flow that you could actually objectively measure.
stats come up, you leave the baby, fortunately never needed ECMO. So just objective data is important in what we do moving forward and not just operating in the dark.
Pulmonary masal dilators absolutely can improve pulmonary vascular resistance in some patients who have a dynamic reactive vascular bed. If you have a fixed Pulmonary hypertension, again, some drug is good, does not mean more is necessarily better. You want to monitor for hemodynamic instability. And if they don't do well, either stop the medication or strongly consider prostaglandin, again, as a pressure pop-off for the RV that can't tolerate that type of afterload because it's not designed to, and an LV pop-off or a volume
pop up for that Alpini.
And again, CDH is a ductile dependent lesion. Now, I've been told that I need to ask you 3 MLC questions to all the trainees in the room. And then this will be it.
Which of the following statements best reflects the approach to pulmonary hypertension? A, all neonatal pulmonary hypertension can be treated with the same standardized therapy. B, inhaled nitric oxide is an effective form, oh, is effective for all forms of neonatal PH. Neonatal PH consists of multiple physiologic subtypes and identifying the underlying mechanism is essential.
To guide appropriate therapy, obviously, is the longest answer. We don't even need to go to D.
Which of the following statements best describes key physiologic properties of the neonatal myocardium compared to that of the older child? Let's go straight to the punch line. The neonatal myocardium is preload resistant after load sensitive. And lastly, which of the following statements best describes the relation between the right and left ventricle and neonates?
The RV is anatomically and functionally distinct from the LV with its own unique geometry and greater sensitivity to afterload. Thank you to the UT San Antonio and Division of Anatology for the invitation to be part of a grand round today. I appreciate you guys.
Okay, any questions?
So the one thing that is, you know, and I think the reason general ventilation works so well, is when you're having trouble and you're increasing ventilation, then at some

point what happens is you start over the segment and limit fusion, you make all your vascular function worse.
because you're over distending the alveoli and pressing the vasculature around the alveoli. You're exactly right. I had a video, I had a little, one of my cartoons early on, it's exactly that point. Doctors West's zones of ventilation, I think it was the 80s or 70s, he came up with that. Exactly what he said right here.
Your alveoli, you see how closely your alveoli and your blood vessels come in connection to one another. If you over-distend the alveoli, not only are you causing damage, volume trauma, barotrauma, you're now compressing those blood vessels, then you're actually shooting yourself in the foot and you're making your polar vascular resistance higher. So that's why again. But those were the right pressures, oxygenating ventilating well yesterday with those.
I may have been good yesterday, it's not good today. Things are dynamic, things change, but also don't be the cat that chases their tail around as well.
I don't know where this line came from, but one of my attendees said it to me, and it stuck with me. "Ashrafi, don't just do something, stand there." Oh, okay. I was like, what did he just say? Don't just do something, stand there. His point was, neonates are resilient.
Just kind of give them some time. They'll work it out. So both of them are true in finding when to do something and when to just put your hands in your pocket and wait. That's where the art supersedes the science of medicine.
With your chemodynamics, do you ever echo shortly after a vent change to see how that vent change affected refusion? More and more, more and more. There's no science on it. I've been looking at it right now, but more and more we're trying to change median airway pressure, change on time, and then Doppler how much flow is coming out of the right ventricle to see if it's getting better or worse. What we started doing with our cardiologists, and they were actually super supportive, is in the cath lab, they do what's called basal reactivity testing. Well, they'll go in the cath lab, then check all the hemodynamics in the cath lab, which is the gold standard. 100% oxygen, then nitric oxide to measure everything. We are now doing that at the bedside with Echo, recognizing it's not the gold standard, but now we're starting to see who's got a fixed pH and who's got a dynamic pH. What ventilator settings are better, what ventilator settings are worse. So as of right now, it's just a cool project until we publish it, but we have fellows that are trying to work on that right now.
Yeah, my last question is in

In Bronco Fulman and Displaysia, what you see is that the...
papillaries are normally at the tips of the septa and the alveoli over time, you know, with chronic vent injuries. Have you seen any EMs of babies that die of diaphragmatic hernias or early on? Because obviously after a course, you're going to get some chronic lung injury. But I'm curious if
In utero development, any of that happen, so that's capillaries are actually not positioned. No great question. I had no idea. Great question. I'll have to look at it and look into that. I never even. This is why these things are so great and so important is this cross cross.
Idea collaboration is great. That's great. I have no idea. Because it's almost a pseudo alveolar papillary dysplasia. 100%. I totally, I hear where you're going with that entirely. That's a great, that's a great theory. I don't know. Great present project. Great present project. I have one question from Doctor Assanasen.
Can you discuss any role of manipulating blood viscosity in cardiovascular systems? If so, how would it be managed directly in the NICU and CVIC you said? Excellent question. I don't know how to answer that question. So if you look at passive liaise law and you look at, again, the concept of pressure and of blood pressure,
blood viscosity becomes an important component. So a blood transfusion, for example, not only increase your blood pressure because of the volume you're giving, but the increase in viscosity as well. This doesn't answer his question. I'm trying to cheat and buy time before I can actually come up with an answer because this is a good question.
There was an idea postulated by a neonatologist that if you could increase the viscosity of blood, that would reduce the shunt burden through the PDA, which would make less flow go through the PDA, which would give it more susceptible to closure. If there's less flow because of higher viscosity, it will close more quickly.
So they started prophylactically giving a bunch of small babies a lot of blood to increase the viscosity and it didn't make any difference to their PDAs. But the question is a good one. How does manipulation of viscosity affect it other than increasing your
Fresher, I don't have any good answers, but I'd be interested to hear what other people think if other people have tried that.
I don't think we have a good answer either. Yeah, that's a good question. I should expect those babies with like a hypoplastic LV or poor function, if they're able to survive, if you found over time, does that increase preload everything back part

eventually from that ventricle or help remodel or help it function or heading mister window? Phenomenal question. In fact,
There's 2 people, one here in Dallas, Kara Goss and Adam Lewandowski in London that are doing phenomenal work on.
neonatal origins of adult diseases and specifically with the cardiovascular system and looking at different neonates, how they are now, particularly preterm neonates, and what they're like when they're 30s, 40s, and 50s. And the LV never fully normalizes. It starts to develop more of a globular type shape.
it still always has some sort of diastolic dysfunction to it. So it's normal enough that they can go to school and they do fine for the first several decades of life. It's not until later that we start to get worried. And Kara Goss and Adam Landowski, they're doing more work on this than anybody else. It never fully normalizes. But of course, that depends on the severity of injury. But
You can bunk growth.
If you talk to the pulmonologist, up to about 8 years of age, you can get good physiologic growth, at which point everything about that is just pathologic dilation of alveoli. The left ventricle is no different. Up until about 8 years, you can get good LV mass and growth. Anything beyond that tends to be just pathologic dilation or hypertrophy and not better. So up to about age 8.
is what we think.
Very good. Well, thank you so much. Thank you, everybody. I appreciate you. Thank you.

Calderon, Delia stopped transcription