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TRANSCRIPT - GR 05 09 25 **"The Highs and Lows of Hypoxemia: How We Personalize Oxygen Targets for Acute and Chronic Hypoxemic Respiratory Failure"** guest speakers Kyle Enfield, MD and John Popovich, MD from the University of Virginia

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Internal Medicine Grand Rounds

- Thank you, everyone, and welcome to medicine grand rails. We're excited to kick off a new type of format that we hope to do several times a year at grand rails called How we Treat. So I'm taking a clinical lecture series that focus on both some of the evidence-based practice as well as focusing on how we manage patients, sometimes, even really, between the guidelines and practice. So we're pleased to have Dr. Kyle Enfield from the division of pulmonary, critical care, and John Popovich, fellow inner division of pulmonary critical care to talk with us about the highs and lows of hypoxemia, how we personalize management of product and acute hypoxemic, respiratory.
- See these slides, presentation objectives, the disclosures faculty planning credits going for today.
- Our chief President will introduce our august speakers.
- Well, good afternoon, everyone. It's my distinct pleasure to formally introduce our speakers today. Dr. Kyle Enfield and Dr. John help. So, starting with Dr. Enfield, originally from southeastern Oklahoma, he obtained his medical degree from the University of Oklahoma. He went on to complete his Internal Medicine Residency, and fellowship in primary and critical care here at Uva, and has remained on faculty where he is. Section 2 for critical care.
- His research is aimed at predicting and preventing hospital infections and complications which has led to an understanding that we can improve survivorship and response to targeted interventions and better understanding the factors contributing to hospital utilization. He's also working to understand how tools like clinical disease support and digital who's sitting right here?
- One of our fellows and esteemed former chief resident originally from California. He made the poor decision to lead the objective paradise of early transplanted Virginian and Triple D, complete Medical School Residency, Chief Residency and fellowship at Uva. Despite many telling him you should go back where he came from. Excellent clinical teaching has made me well up and popular educator. It's not uncommon to hear the voice echo around our conferences and other teaching sessions this year, despite his busy schedule running, for which he wakes up at 2 Am. Daily Yoga and Film. Although this is likely included only because he wants to tell you that he's usually we are very excited to have them join us for grandhouse today, so please enjoy joining and welcome so happy to be here. I'm so grateful to you guys for coming.
- I have previously, I think, distinguished myself in grand rounds space as the chief who sometimes covered for Kara and presided over the most technical difficulties in grand rounds. So I'm kind of hoping for some redaction today. The highlights of my year.

- We don't have any disclosures. I'm gonna immediately take back what I just said. The actual highlight of my year was a couple of weeks ago, sitting in the room and pitching ideas for what this grand rounds could be. I'm happy with what we settled on, but I think we have some other winners, and I thought it'd be fun just to share with you the fun that you could keep having.
- So the 1st was 30 CC's kill per kilogram of fun. How we personalize resuscitation of the septic patient. So salty learning from sweet guys, this was my pitch, and Kyle said to me. We want people to come. I also said that as people who rounded with me in the it, you know, the only thing I like talking about the least is so oops refractory, hypoxemic respiratory failure in the post covid era.
- You're actually gonna need to know this 6 CC. Per kilogram of Ircc per kilogram is not enough. How do we personalize mechanical ventilation and vent liberation in the Icu? We thought that was a little bit too critical care, so we decided to branch out something old, something new, something borrowed from a container's friend and someone that will not be the only political joke today.
- What we're actually going to do for you today is review the means of measuring peripheral oxygen saturation, both noninvasively and invasively. We're going to work to understand the pythiologies of hypoxemia. So we're going to then review the evidence for supplemental oxygen is chronic hypoxemia, respiratory regulator of varying severity and hopefully help you out cases.
- We're going to explore the options of hypoxemia and the experience of altitude with some AI generated images that are extraordinarily flattering. We're going to review the work of the management of severe, acute, hypoxemic, respiratory failure that's coming without hypoxemia. These fellows are a little bit different from what you guys got in the handout. That's because Kyle and I are both in the Icu right now. The world is dynamic.
- The way this is gonna work is we're gonna give you a short case vignette. We're gonna distill that case vignette down to what we hope is a applicable and commonly faced clinical question. We're going to give you some evidence and some experience that will help you answer that question. And then we're gonna still our evidence and our experience.
- We're going to start with someone that they see every day in the Dental Home clinic, and then all of our Residency every week at Uma. It's a 56 year, old lady. She's got a 55 past year smoking history. She comes to the primary care clinic for breathlessness that's developed over the last 2 years or so. She's got a longstanding cough productivity of some sputum, we get pfts on her. She has met Pv, one of 60% predicted and ratio of 65% and a Dlco of 55%.
- She's resting at 86% on the mayor, and that mayor's at 82 during the I would like to point out that I don't know where the rebel alliance doctor is, but I did appreciate that. John squeezed that in there, just for me. So for this patient. The question I'm hoping you're wondering is, how would we appropriately, how we manage and cancel her?
- But really, 1st we've got to figure out, what do we really mean? And what is it? How do we figure out a patient is hypoxic. I get to control this for just a little bit. Okay? So we're also going to try to figure out which one of us can stand still the longest. So. 1st of all, you know the easiest way for us to figure out how someone is hypoxic is non-invasive measurements of hemoglobin using a sat pro or their apple watch, whichever one they happen to have with them at the time but that, as we know, has its problems, and we can also directly measure of oxygen in through an Abg. Now,

obviously, pulmonologists, we love our abgs. We really do, but we also love our abgs of time, and we usually rarely get them. So the big problem that we have right now is that we also know that the pulse oximature was designed for people that look a lot like the 2 of us and there was not even a single black that was just like completely. So once again my wife is right. I'm not as funny as I think I am, but I'm going to keep going with it because it makes me laugh. So. You know, there's been there was studies actually back into the 19 eighties that really said that pole oximeters have failure points. The failure points had to do with pigment. But then, during, you might remember that there was like this thing that happened a few years ago, about 5 20, where this came to a head again, and we recognize that doing anything with a pulse. Oximeter had problems, and it can lead to different kinds of clinical significance it can most likely underrepresent how hypoxic a patient is.

- Now there's been some work done at Uva to figure out ways to manage it through AI models or other machine learning models. But in general we know that there's some flaws with this. Now, this is a technology thing. This is an area where someone should be able to figure out how to fix it. I'm looking at all of the Mba people in the room who might have access to, you know medical research facility where they can really study this and and engineer, because we should be able to fix this problem. But no one has done that yet. So we're really stuck with a system where we could under represent someone's hypoxemia, or we had to put a needle in their wrist which people don't like, I'm told.
- So what we're trying to figure out is what's going on with oxygen. Once it gets into the body, we know what they're breathing in, and we need to figure out how they're using it. So we're trying to figure out really, the differences between the alveolar calculated with the alveolar gas equation which I know you all have memorized. We're going to do some quizzes here in a little bit on the whiteboard and have Steve have you work this out.
- But that's going to help us understand is oxygen getting into the blood? Because what we really care about is not so much what their oxygenation is, but how their tissues are using it? Is it going to the right place? And then we try to figure out how bad that oxygenation problem is.
- So in order to do that, we really need to actually go a little bit deeper and sort of distill this into the deep, dark, nether regions of physiology. So we did decide to pull out Mary Nadel's and and break it down into this wonderful display of.
- But I'm gonna make it cleaner and cuter and more complicated, high, level anatomy.
- You have ones, those ones have all you live serving. Those alveoli are blood vessels. You have a pulmonary artery, hearing deoxygenated blood pulmonary capillaries where the gas exchange occurs, and then a pulmonary vein that's returning that oxygenated blood to the left side of the heart, and between them you have some sort of diffusion barrier.
- 1st reason a person might be hypoxemic is not our fault. Don't blame us for it. It's low, inspired, partial pressure oxygen. This is hopefully pretty logical. If there's low oxygen in the atmosphere, there's going to be low oxygen in your blood. The lungs don't get inflamed.
- The a ingredient in this case would be normal.
- Second cause of hypoxemia is hyperventilation. This one always caused me a little bit of consternation until a very smart faculty member reminded me to look at the at the alveolar gas equation, which was really frustrating.

- It's just a crowded issue. If you're hyperventilating, if your tidal volumes are low. If your respiratory rate is low, you're not exchanging carbon dioxide. Carbon dioxide is going to crowd out the oxygen.
- The 3rd cause of hyposemia. I'm going to touch and back away from, because we're going to go more in depth later. It's shunt. You can really think of Shunt as either a literal or a metaphorical separation of the airspace and the blood vessels.
- It's as if the blood never touched that gas exchange surface. So the blood remains hypoxemic.
- The 4th cause of hypoxemia is diffusion, defect. Again, I hope this one's pretty logical in healthy people. The space between the alveolus and the blood vessels is thin and easy, and easily allows carbon dioxide and oxygen to pass.
- Yeah someone is unlucky enough, as in someone with interstitial lung disease to have that become thick and scarred and nasty, makes it hard for gas to exchange.
- The big one is the hardest and unfortunately, it's also the most important. It's the Queue Mismatch.
- What's really unique and really challenging about the lungs is that it requires 2 inputs. There's oxygen input coming into the alveoli. And then there's the red cell input and the hemoglobin seeds in a perfect world, you would have a perfect match of oxygen molecules for seeds on hemoglobin.
- If you have a mismatch in that too much gas for not enough blood, or vice versa. It can result in hypoxemia.
- I find this a really hard thing to think about, or to create an image, for with just one gas exchange. So I'm going to give you a bunch, and I think you should think of it as a situation in which you have some blood vessels that are not served by alveoli or semi that don't have blood vessels serving them kind of on a macro scale.
- Everything I just said will cover 100% of all of your acute and chronic hypoxemic, respiratory failure
- for most of the chronic hypoxemic, respiratory heart failure, though I actually find it a little bit easier to say it's generally going to be vq mismatch. There's generally going to be some diffusion defect involved. Let's just take a step back and think about gas diffusion. Instead, if you look back at the way the gas diffuses across the surface, it's related to the amount of surface area. You have to do that exchange and the thickness of the barrier, more surface area to exchange more gas exchange. If it's a thicker surface that you're trying to cross. That's going to allow less right?
- Most of the people with chronic hypoxic respiratory failure have a problem with one or or both of these things.
- Folks with Emphysema, both with these kind of moth-y maple sees that have been destroyed by smoking for many years, have lost alveolar surface area. So they have chronic hypoxemia from an area problem.
- Folks with Ilv folks with scarred down services have a thickness problem.
- The thing that I'm missing out on. Here are folks with pulmonary hypertension who have a complex mix of those. I called it a Mahalic problem.
- So for this person did that for a little late use. I think it's really important that we be really specific in what we name our problems. This is a woman who is hypoxemic. She has severe hypoxemia because her virtual stats were less than 88.
- And it's a resting hypoxemia, and that it's not just within. But how would we cancel this person.
- The answer comes from way back in the 19 eighties. This is the not trial out of annals. It took folks who met the same criteria as this woman did folks who were

chronically hypoxemic at rest and randomize them to receive oxygen 24 HA day, or oxygen just at night and they found a pretty good mortality benefit for oxygen 24 HA day. So supplemental oxygen for people who are chronic oxygen has saved their lives.

- Our practice has been changed a little bit recently with the redox trial. Redox was a little bit more lenient, and it compared continuous oxygen in just 15 HA day for the same group of patients, more or less and that not a lot of us. So we can actually give our patients a bit of a break and say, you need to be on your oxygen for about 15 HA day, including while you sleep. But if you're hanging out on the couch watching TV. It's okay to take a break.
- So for this 1st case, which is our longest one, because I had to show you my animations, supplemental oxygen for patients with chronic resting hypoxemia is gonna save lives.
- They need to wear it for about 15 to 24 h, including Mobile.
- We're gonna lighten up a little bit. Give you a lady who's 63. You'll notice she's in athletic clothes because she's healthier than our last person developed over just about a year. Her pfts are better than the 1st person I gave you in the resting oxygen of 92% and is matering at 86 during a 6 min walk.
- So how would you handle this person?
- She sounds like a difficult problem, but it's more moderate. Her verbal status greater than 88%. And it's really only exertional.
- What would we do with someone like this?
- The answer is, you probably don't need to do much.
- Imagine in 2016 for payments like this who are more moderated and very hypoxemia and give themselves mental oxygen, did not get that same mortality benefit, did not get that same hospitalization benefit.
- But maybe they really like their oxygen. Lots of people really like their oxygen. Why, 5 insurance will cover it. You can give oxygen to these folks, but if they don't want it, I don't. I find I don't really have a leg to stand on on telling them they have to use it may give them a little bit of quality of life, may give them a little bit of exercise tolerance, but it's not going to get the same benefit for the chronic, severe bipocc.
- So the best part about this grand rounds is really, we got to dig into medical history. We got to go all the way back to the 19 eighties. And there was just some fascinating research done in the 19 eighties, apparently.
- But this time we're also going to bridge into the area where there's not a lot of research for us. And this is actually not an uncommon patient that we will hear about. So this is a in this case we're taking a 37 year old patient with idiopathic pulmonary hypertension who comes in to you. They're pretty well controlled. They're on Ambersenton and Daffinil, and they're living pretty stably, but they want to go to Colorado to visit some friends
- and maybe do a little hiking they're an active person here in and around Charlottesville, and the question is, Well, what should they do? What? How would you manage this person?
- And that opens up a lot of things? Now, if you look at the guidelines right now, that's published by the Wilderness Medicine Society and by ats, they would say, recommend something like, probably you shouldn't go. They're actually, and it really sprays it as probably. And the reason for that is because it's been really hard to do research on this population for years. No research was done because we thought it was too risky for people.

- Because there's this thing that happens to normal people when they go to altitude. When you go to altitude you go from sea level, where you have a pao, 2 of 100 of mercury down to about 60 of Mercury at around 3,100 meters, which is about 10,000 feet, so one could hypothetically be going to a research conference in Colorado and say, wouldn't it be fun to watch your 24 h oxygen saturations?
- Anybody? No, one's never done that before. And what happens is you find this really cool phenomenon, where you actually see desaturations at night, desaturations which, when you send it to your pulmonary critical care, friends during the conference they go. Oh, my gosh! What's wrong with you, and then you send it to your sleep College. And they're like cool, periodic sleep disorder. And that's what happens during the day when someone is at altitude, they have an increase in their respiratory rate. They blow down their Co. 2, and they maintain their oxygenation during regular movement. But at night. What happens is that stops the drive to breathe faster goes away, and your oxygenation saturations drop down and every once in a while they pop back up because your body goes. Wait, 85% is not a good place to live. And we know that this is going to happen, not only for normal individuals. But it's going to happen to people that have pulmonary hypertension as well. And so then the question becomes, what happens to them that exercise. And so this is research that has been done mostly in Switzerland. Thank God for the Swiss for doing this research.
- They've taken both patients with Copd and pulmonary hypertension. They've studied them at 460 meters, and then take them up in altitude to 3,100 meters again. That's around 10,000 feet for those of you who are not comfortable with meters, and they put them on bicycles because everyone likes to go up into 10,000 meters or 3,100 meters and get on a bicycle, have an art line placed, and breathe into a machine to figure out what happens for those of you who don't read. For those of you who don't normally read. This is a part of the Cpet test, and what you see in the area. The blue is the same individual at altitude as the red for them. You see that at rest, and you can look at their Vo 2 mass. You can look at their oxygen pulse, which is another measure for Fatty.
- And then, if you look at their Pao 2, which is the easiest thing for us to measure, and what you see in all of these, both at rest and exercise and before exercise is, there's a drop. In general, what happens is people become more hypoxic. Well, there's no shock there, right? We know that the Pao 2 at 3,100 meters in the atmosphere is about 60 of mercury. So there's less.
- There's not less oxygen percent. Oxygen is the same. But the partial pressure has gone down. So there's fewer molecules of oxygen to move into the alveolar spaces. When they exercise, they actually have to do more exercise, they end up using more oxygen to do the same amount of exercise, and in general, their exercise capacity drops down a little bit, but not a whole lot. In fact, most people maintain their exercise capacity as they begin to move.
- The question then, is, should I give this person oxygen? If they have mild symptoms? So these are people that are well controlled have pretty good functional status. These are not your severe Copd patients, and they have looked at this as well. They've given people oxygen to wear at night, and they looked at non-invasive, systolic and diastolic blood pressure as well as heart rate. And what they found is that if you do nocturnal oxygen you, your physiologic variables return closer to what they would be at baseline at sea level, which also makes sense. If you've got enough oxygen for everything to work, then your body at night doesn't become

hypoxic as much as it does. If you're not breathing oxygen, Aka, me! At my last conference and

- Your blood pressure and pulse will will follow that the challenge with all of this is, these studies are done in about 27 individuals each. These are great, large, non randomized, controlled trials. And so we're still left with basically expert opinion.
- And the way that I approach this now, as people do know, like my pulmonary practices have gone increasingly small, I've actually increased my psychiatric practice. It's become very large. It's every Thursday in the long Covid clinic. But I have a lot of people who ask me questions about this, because I also like wilderness medicine. And so occasionally people will ask me this question, and there is some some pre-travel risk assessment. You can do. You can look at the person's abg at Baseline. You can look at their functional capacity, and you can actually do an altitude challenge on them to see what their oxygenation would do with altitude. Those are all great ways of handling these things. They're actually not as predictive as we'd like them to be. And so it's generally not what I would do unless someone's kind of on the edge. If you have someone with mild to moderate disease most likely they can go to oxygen, they can go to altitude. I do recommend that they have baseline lower pao, 2 s. Or baseline. Their sats run in the 94% range that, having nocturnal oxygen when they go to altitude is helpful, it's going to make them feel a little bit better because they're going to not be sat overnight, and it's going to control their blood pressure and heart rate overnight a little bit better, so they'll probably sleep better overall. They need to be monitored, and be ready to leave if necessary. So if they get too hypoxic, they need to come down, or if they start developing symptoms of high altitude, pulmonary edema, or high altitude cerebral edema. They need to come down. But that would be true for other people. But really it's an individualized program, right. We can't say universally, all patients like this should not do this. It really requires us to think about the person that's sitting in front of us right now so what we're basically saying is, yeah, people that have copd and pulmonary hypertension. They can still go to altitude. And they should still continue to do that.
- Our next case is is getting us back to where we live, which is really patients that come into the emergency department with different things. So we're gonna take you to a 75 year old that's brought into the emergency department for fevers and confusions. Has anyone seen this patient this week?
- 2 h ago. He gets intubated in the emergency department. His T. Max is 39, his master 65. He's put on some Norepi peripherally because he doesn't need a central line yet, because his Norepi is less than 10, he's got good veins. His spo 2 is about 93% on a volume control with a respiratory rate of 18 tidal volumes of 350 up to 80% peep of 8. His white count is 30 Cta. His pulmonary of the very dense left upper load consolidation and diffused ground glass capacities.
- So what spo? 2, should I target?
- So this came up. This actually became a very popular thing to talk about in critical care for a couple of reasons. One. There was a concern that if we allow people to have a Pao 2 that was too low. They were getting less oxygen to their brain, and it might cause more delirium and more dementia following their Icu stay. But we also know that if we over oxygenate someone, we make their alveolar oxygen tension too high. If we actually for the development of aerobic bacteria in the lungs, if you take brass and put them in space and in an oxygen, rich environment, they actually develop ards.

- Right? That also is true. If you take humans and do the same thing, or if you took rats and change the partial pressure of oxygen on earth, you can create pneumonias in those rats just by depriving them of oxygen. That's research from 1,81876, so if you want to go to history of medicine, oxygen therapy which is not regulated by the FDA does have its complications.
- So what we're really trying to get out here is the delivery of oxygen appropriate, and everyone loves talking about cardiac output which we know is heart rate, time, stroke, volume, but not really. And I'm not going to debate it right now, or did I want to change the slides, because that would be no fun.
- And then the consumption of oxygen and the carrier capacity of oxygen, which really is measured by the hemoglobin that we talked about below, and a very small fraction of oxygen that gets dissolved in the blood.
- And we want to know, are we actually getting enough oxygen in the tissues. And so there was actually a couple of oxygen saturation targets for critically ill patients receiving mechanical emulation that came outand in general what they found is we still don't know. I'm just going to cut to the chase because there is maybe some differences, but the large outcomes, which is death as well as neurologic outcomes. There was very poor differentiation between those with higher spo, 2 targets versus lower spo 2 targets. Now I would argue that one of the problems here is that we're talking about Spo 2, which may not actually reflect truth, right? Because there's a difference between an spo 2 of 97%. When my Pao 2 is 98, and my spo 2 is 100. When my Pao 2 is 600 right? And so this is not actually necessarily a perfect study, but it is what we have right now, and in general it gets into the idea that oxygen therapy is probably grounded in the idea of giving them enough.
- Wanna get to the fun stuff a lot of slides in here about this. We're going to skip this one, too, and we're going to get down to the last part of that, which is that there's no recommendation actually for sepsis, for oxygen targets in the most recent guidelines that have been produced. For this. It's true for Ards as well. You should use the oxygen targets appropriate for your patient, which may be individualized for each of your patients. And generally, you know, we like to get around 94%. But if you tried to actually get someone to 94% of the Icu and achieve this because I see our patients at 2 levels, 96% and above and 70. And below
- Don's. Gonna take our next case
- I love this case. This is a young woman. She's here for shortness of breath. She has decompensated cirrhosis. We don't know why, yet prior known decompensations are ascites and Evs. She's on appropriate meds for that. She's really hypoxemic. She's requiring high flow at 40 liters at 80%. It's not all right. Pleural effusion. She's got some interstitial edema. She gets a big thoracentesis. She gets some diuresis. Her chest X-ray looks pretty much clear after this despite that she's still on high Flony's leukemia.
- So really, the question I'm trying to use this case to illustrate is, when should we consider shunt physiology, which I kind of foreshadowed at the beginning. And how do you get about that? How do you get to that diagnosis?
- This is my current program. Director, boss and mentor, Tim Siella seen here on a fancy day.
- He has a habit of speaking in these like aphorisms or things that he thinks are universally true. And what's really, really frustrating about that is that often they're really helpful and universally true. I really like to just kind of got them away, but they work. One of his is about diagnosing shot physiology. What he says is that if you

meet a patient and the patient looks great, but their chest imaging looks terrible that's a person whose hypoxemia is very likely caused by Dq.

- If, on the other hand, you meet a person who's looking terrible and requiring lots of oxygen, but their chest imaging is pretty clear.
- That's the type of person in whom you should consider physiology as well.
- I told you before cataphysiology is basically a literal or metaphorical separation of the Gas Exchange surface in the blood.
- This could be anatomical. I'll give you examples of that in a moment, or it could be the metaphorical example of someone with horrible, dense, consolidated pneumonia. Horrible dense Ards! There's really no gas in here at all, so the blood may as well not have been there.
- Some really intense anatomy lungs, a heart and muscles between them.
- Part is separated by a septum.
- You can have Intracardiac shunts the blood just skipping from the right side to the left without going to the lungs. Congenital heart disease that do this. If you have elevated right-sided pressures and a Pfo can pop open that the right side pressures can pop open the Pfo and allow shunting to occur.
- You can have intrapulmonary shunts that are things like I just highlighted really dense pneumonias, really dense ards, really bad atelectasis or mucus plugging or you could have a communication in the vessels that allows that blood to skip the pulmonary capillary or pulmonary capillaries. 2 classic examples of those would be hepatopulmonary, syndrome, or pulmonary avms the intrapulmonary shunts are called physiologic shunts because the anatomy is correct is normal. The bottom 2, the vascular and the intracardiac ones are anatomic shunts. There's abnormal anatomy that's allowing that blood to shunt from the right side of the left.
- The 1st test to diagnose Trent physiology is a tte with bowel study. The way that that works is, you take a syringe full of saline. Take a syringe, you shake it up real good.
- All those bubbles go into the right side of the heart and hopefully you'll be glad.
- What you're looking for is bubbles to pass from the right side to the left.
- Bubbles should not pass at all. They should get caught in the pulmonary capillaries. They pass really quickly, as they did in this one. You should think about an intracarthy action. Yes it's trying.
- It takes longer for bones to appear on the other side. You should think about some a something that's outside of the heart, intrapulatory.
- That is a screenshot of my desktop. I don't know why that's there.
- Okay, that's what it does, that is. Make sure. You review all the slides, not just most of them.
- You can see, there's physiology in patients whose chest imaging does not match their degree of hypoxemia, people whose chest imaging looks great and their hypoxemia looks terrible, and order a Tt. With bubble. Study the other learning point there is that if you had to choose between Dq. Mismatch and Shunt, always try to get yourself a Vq. Mismatch, because shunt is very difficult to treat. It's very hard to oxygenate someone who has a lot of shunt physiology, and that can also be diagnostic if you turn up the oo's and their pao 2 doesn't go up. They probably have a shunt of some sort, so we couldn't leave this talk without talking about Covid at least once, and talk about what we do for patients with severe hypoxemia. Now I'm recognizing that we have about 11 min left, and John and I somehow have 2223 slides. So we're going to go real fast. We go to 1, 15. 0, we go to 1 15. 0, yeah, we

got 25 min. Everyone hold on now. So what support it really exists to treat these patients? What are we going to do for refractory hypoxic respiratory. We saw this a lot from 2020 through 2025. We see it less commonly now. But it still happens.

- And this is, we're not even do that. So we already have stages. Right? So we have things that we recommend against. We have some conditional recommendations. And we have things that we really, really like. So everybody likes lung protective ventilation. I mean, it seems like it is everywhere these days. Some people may argue what you mean by lung protective ventilation. Some people are going to talk about your driving pressure all these things, but really, what we're wanting to say is that we don't want to over in the lungs. We don't want to cause harm to the lungs while we're oxygenating them, which can also cause from too much oxygen, and we want to make sure that the patient is during that time taken care of.
- The other one that we strongly like like to talk about is prone physiology, and then we talk about high peep steroids, because, as Dr. Bevel like to point out when he says that he wants to do pulmonary, consult steroids, and then we can talk about a little bit about Ecmo and neuromuscular blockade. So this is sort of where we fall. Currently in Virginia. We'll think about steroids first.st In fact, I think every time someone comes to the Icu someone does mention.
- Well, should we add steroids? And you know it's something to talk about, at least on rounds, because, you know, there's lots of evidence in both sides, and so it gives us something to argue about. Paralysis will come soon, that thereafter followed by prone positioning and Ecmo. Now we have sort of a cultural norm that you have to have someone paralyzed to prone, and this actually dates back to the early days of sepsis, and we have not been able to break this. You do not have to be paralyzed to be prone. Okay that is what we do, but it's not what you have to do. And there there may be some reasons to prone people before we paralyze.
- So the 1st thing we're going to talk about is cortical steroids, actually what the slides look like.
- But yeah, so we're talking about steroids, Ards, which was in a randomized control trial, I mean, steroids and statins have been tried for about every disease known to man in the Icu. If you have a critical illness, you should probably get a steroid or a statin at least once in a randomized control trial. This was what we found. This is the Dexamethadroxone group and the control group, and what we are looking at is, do they get off the ventilator faster? Well, we should. Ventilator 3 days. This is sort of the common nomenclature in critical care trials is, does someone get off the ventilator and stay off the ventilator for 28 days? So if you are extubated on day 3. But got reintubated on day 26. You don't really contribute ventilator free days. What we want to say is, you stay off the ventilator. The next one is all cause mortality of 60 days, and then icu mortality and hospital mortality. And really what this study ended up showing is more ventilator-free days, and there's a lot of discussion about is ventilator free days, the right endpoint for Icu studies right? Because if the mortality is about the same, but they have more days off the ventilator. Is that really good for the patient?
- I would argue, yes, because even if the mortality is the same, they've gotten off the ventilator. They've stayed off the ventilator, and maybe they've had a chance to interact with their family. But other people would say, Well, if you're not keeping, if more people are not surviving their hospitalization, then really, all we're doing is increasing the risk for infection. But the nice thing is that the adverse events

between the 2 groups are about the same. So we didn't see more infection. We did see more effort on Cba etc, etc.

- So corticosteroids, yeah. And we also know that steroids did show benefit in patients with Covid. Right? So this was sort of one of those findings that we didn't expect to find steroids, for Ards had kind of sort of dwindled off in sort of the normal findings. But then, when Covid came out, there was a study that showed that patients who got steroids for severe hypoxemia seem to have a benefit for duration of mechanical ventilation, and probably some survival benefit as well. So during the pandemic. Anybody who is hypoxic almost got steroids, because that was what we did to prevent people from going on to fire mechanical ventilation and survival. The challenge is that that may not always play out for all patients with critical care. Illness. So we do know that in patients with severe community acquired pneumonia came cod steroids which confuses me. It's just steroids for pneumonia. We don't have to give it a fancy name. This is a study where hydrocortisone was given to patients with severe pneumonia, and there was a survival benefit. I think they were able to get this study to go through because of the experience with Covid, where we saw a benefit.
- And now most of us in the Icu who see someone with severe pneumonia build their steroids for those patient populations, because it does seem to have a survival benefit.
- Paralysis has been one of the biggest challenges in critical care. Paralysis has been in favor, not in favor in favor again, not in favor again all through different randomized, controlled trials. So the idea behind this is, if you paralyze someone, their oxygen consumption goes down. Their diaphragm no longer has to work, all their muscles get relaxed, and so they will have more oxygenation for other tissue use.
- There the rose study came out with, This is not Rose. Sorry I can't remember what the name of the study is, but this was the 1st study of neuromuscular blockade for acute respiratory distress syndrome, and, like many early studies, it showed a survival benefit and there was a lot of questions that came out of this which led to the rose study which it was done by the archnet later on, which looked at neuromuscular blockade versus not neuromuscular blockade in patients that were sedated, and their differences were no difference. Right? So there didn't seem to be any difference between these 2 groups.
- Now, there's a lot of questions because sedation practices also shifted around here. And so the question is, was it just because everybody that was in the Placebo group here was sedated to a ras of negative 5 being deeply sedated, or was it because of something else? And that's been? The question is, why did this 1st study? Maybe those patients were not sedated enough. If you sedate someone enough, do they still need paralysis? Is the question.
- The the challenges is that in some patients the only way you can really get them to be able to be comfortable on the ventilator, or look comfortable on the ventilator. Probably even the more important work is to paralyze them. They will become dysynchronous with the ventilator with cause. Other harms like hypoxemia, hypotension, etc, and so we still do paralyze patients. But our 1st goal is to deeply sedate them.
- So it gets us to prone positioning, which was also something that is actually a historical intervention that was used back in the 19 hundreds and the 18 hundreds for people with severe pneumonia.

- I came back again because of this idea of trying to reduce the amount of vq mismatch. So if you redistribute the fluid from covid-nineteen ards, etc, into a space that is not getting as much blood flow, you improve Vq matching, and so you improve oxygenation. And and the end of the result is, yeah, we don't have the. We don't have the.
- What we really have to learn from this is John made all the slides except for like 5, and I just reviewed them. So I can't remember where everything is. This is an Icu patients where people are either put in prone position or in a supine position, and we see that the cumulative probability of survival is much higher in the prone position patients. This was popularized early in covid-nineteen actually led to people trying to have people self prone that have lesser oxygen requirements. The data on self-prone is not as good, probably because we're allowing people to roll back and forth, however, they wanted to, whereas in patients that are mechanically ventilated to prone them requires an organizational effort to actually flip them, which is also why we paralyzed them because we didn't want them to flip themselves back once they were prone. But there is a significant survival benefit. And in my mind this is a therapy that we should be moving up in our armamentarium for severe refractory hypoxemia before paralysis. But it's not quite there yet, in some ways, because I think it has a lot of benefit for those patients.
- And then we get to Ecmo. So
- Ecmo, is this concept that if someone is profoundly hypoxic, if we just take means for oxygenation out of their lung, and we bypass that into a machine, we can get them to survive longer. There is one really large study for Ecmo in Ards patients. It's called the Caesar Trial. It showed that what it showed is if you were transferred to a center that could provide you with Ecmo, you had a survival benefit.
- Okay, so this is an intention to treat trial. But everybody in the intervention arm those transferred for Ecmo. Didn't get Ecmo. And so it has left a lot of questions around what we should do with these patients. Because there is this because part of it could be that if you're at a center that provides Ecmo, you have other things as well that you're doing. That's different than centers that don't provide. Ecmo
- What I would also say to this, though, is that you still have to individualize to our patients. We found definitely during the pandemic that there are patients that have severe refractory hypoxemia that truly benefit from being on long course in the backbone and actually do very well afterwards. It is hard to identify what patients those are, because we don't have the right studies to do that. And so you are still stuck with thinking about your patients.
- What are the other organ failures they have? How many other problems do they have? And where can we go with them.
- But in the end, what we're going to say is that the strongest evidence really is for cortical steroids and proning and paralysis may have some benefit in there, and you may be doing it just to be able to get them to prone or be synchronous with the ventilator and Ecmo. We should think about it. But it's also a fairly intense resource utilization. We have about 8 circuits that we can run at the University of Virginia. There's lots of reasons to do it and not to do it, but it is an option that is out there, and we should think about it. Sometimes we're in on sort of the other extreme, and that is the dyspic patient that comes in that is not hypoxic. We see these, you see these in your uma clinic. These are patients that come in. They're always short of breath. They don't have hypoxemia, they don't fail on their 6 min walk. They have

some exercise limitations. They have normal pfts, and you're left stuck with what to do with them.

- We see them a lot in the long Covid clinic. You can talk to Dr. Coddle about that later. But this is a fairly large population of patients, and what do we do with them?
- It is a common problem, and it probably occurs in about 8 to 10% of the general population is much higher in people with other respiratory problems. And it's actually something that we've known for a long time. It's called dysfunctional breathing syndrome or dysfunctional breathing disorders. What this means is we'll get into in just a second. But it is one of those problems that is difficult to diagnose because you have to think about it. And most of us are not trained in it is a real problem. It is not a some sort of fictitious syndrome that they have. It is a issue where the respiratory function that they have with their entire respiratory system, the lungs, the chest wall, and everything is not working to meet the needs of the patient. For once. I am not going to blame the heart though it's really fun in pulmonary claims. Say, there's nothing wrong with you. You should go see a cardiologist, but there are some things that we can do. When we think about dysfunctional breathing, we have to sort of think about all the things that could go into. We see one of the most common is people with restricted lung disease without impaired diffusion. How many people have gotten dfts and seen that? Besides, John sure you've gotten that in Uma Clinic? I know that when I was in Uma Clinic someone would come in with Dyspnea, and I would see, you know, get pfts on them, sure that I was going to get Copd, and they would have restrictive lung disease without a diffusion. Everybody and I did not know what to do with that other than tell them to lose weight. It's not just weight loss. It can be other neuromuscular disorders. So kyphospholiosis can cause this problems. Some of the other joint disorders which can cause frozen joints in the rib cage, allowing them not to expand correctly, can cause a trapped chest just like you can have any other trapped joints like in your ankle or your knees, you can have trapped joints for your rib cage. It is commonly when you see this, you also see that they have very large scale muscles because they're using most of their upper respiratory system to breathe. And that means that they're breathing at the top of their respiratory cycle, which means that when they walk, when they go up and saliva stairs they don't have anything else to do. They've already maximized that out. What they can do with their breathing drive, and so they feel short of breath very quickly.
- That leads them to become tachycardic.
- They feel bad, and then they start doing less, and this cycle becomes sort of perpetuates itself.
- The other thing that we can see for this is people that actually have fairly good respiratory drive, but they tend to hyperventilate at baseline for reasons that are not very clear. A lot of these patients feel anxious all the time, and they get more anxious, because then they hyperventilate because they hyperventilate, they get more anxious, and it just also becomes this fulfilling circle. These patients tend to not be able to complete sentences, they will start a sentence and then they will have to breathe, because they also, with their hyperventilation, are sort of breathing at the end of their respiratory cycle these very, very small fast breaths. If you get abgs on them they will have a Iph as they're breathing their Co. 2 down.
- All of this leads to a lot of problems with the neurologic access, because what the brain is sensing is that they that they are

- They're alkalotic and alkalosis tends to cause patients either trying to stop breathing. But then they don't want to do that, and also causes people to panic. So when people have panic attacks, they also tend to become alcoholic. It increases or excuse me, it decreases vagal tone overall. So your sympathetic drive goes up in these patients. And so for all intents and purposes, they look awful. You can diagnosis their.
- There are some diagnostic questionnaires you can get. I cannot pronounce the name. It starts with an N. The second letter is I, and then it is definitely a Japanese name, and I butchered every single time. So I'm not going to embarrass myself. Now, you could do C. Pets on these patients, and there are some predictable patterns on them. They will actually have an early cessation due to the fact that their Co. 2 will not climb because they are going to hyperventilate. But they're going to feel short of breath and then become tachycardic very early on. That's not universally true. The really cool thing about it, though, is it's treatable.
- It's critical because this is a pathologic problem of muscle control, muscle usage, or the skeletal system. The problem is, is, there are very few people in the State of Virginia training to treat it so. Dysfunctional breathing treatment is often managed by physical therapist. I see a couple of our physical therapists in the back. You don't need to look. Everybody's done yet but you need to find a physical therapist who's used to working with these patients. What many times happens to these patients, they get told they need to be on a graded exercise program. So they get sent out. And they say, just increase your exercise gradually over time. And what we know about patients with dysfunctional breathing syndrome. If you do that, they will fail because they're always going to fail at the same point, and then they get tired of failing, and they don't know what to do about it, so it actually requires you to treat the dysfunctional breathing syndrome first, st and then you can do the granted exercise training.
- But it is very treatable. And we've had some success with patients in there. Okay, so we're almost gonna wrap up. But we have a few few takeaways
- 1st without it's Bq. Mismatch, particularly if you're on rounds, and you're getting questioned by your attending. Always say Bq mismatch medical students, bq, mismatch every single day of the week. Oxygen therapy is not regulated by the FDA, but it still should be treated like a prescription.
- You should be thinking about what you're trying to do with it? Who is going to benefit? And you should be having your patients work for at least 15 h, and they're going to get a survival benefit from. I'm not going to tell you that if your patients don't meet those criteria you shouldn't prescribe it, but it probably doesn't help them that much.
- All people, every single one of you. If you go skiing in Colorado, you get hypoxic ignite, don't check it because it'll freak you out, and for sure, if you check it, don't send it to your friends, because they will also freak out on your behalf you don't need to wear oxygen when you go to altitude, if you're normal. But if you have patients who have Copd pulmonary hypertension, other hypoxic states, you should not discourage them from going to altitude. You just need to individualize their treatment.
- Really, bad Ards user requires a lot of things. And really, what we should know is that the 2 of us have way too much fun with AI generating all these images, all those images were generated from either copilot chat. Gpt. And I want to thank the chief residents who changed all the spelling mistakes that the AI created for them,

because without them you would have seen which I was really looking forward to pronouncing.

- We do have a lot of people we need to thank. 1st of all, before I get there. Really, John deserves all the credit for this lecture, as you can see. I didn't know which slides were coming next, though he had told me what I was supposed to talk about, which was good, and it was really fun to work with him, and also to see how high I could get his heart rate during round by not responding to his text messages. So we also want to thank y'all style of fallout.
- I really tried to get John to do the trump dance up here with me, but he said, we also want to thank Alex, who is here, but she's also covering John's pager because he's on a call in the Nicu right now.
- We I. This is the 3rd one is you. I did not. So apparently we're thanking the PCM fellows here. Thank you for showing up and listening to our Dorky rounds. And and also to Dr. For taking a chance on the 2 of us presenting the version of the series, because 2 things could happen. One my best slide. Yeah. Okay. One. We could have the best lecture. It really was the best lecture. All the best slides were used. All the best graphics were used to do a lecture like this one, or you will never see another one of these lectures again, because you're like, please, that did not work out well at all today, and we're not going to repeat that. And with that we will take time for about 5 min of questions.
- Can I answer every question that would be 2 mismatch?
- Alright?
- Alright, cool. Well, thank you, guys for both being here.
- My question is actually somewhat related to your last case. So you mentioned this dysfunctional breathing syndrome, which is kind of something that was new to me, and how Cpap of cases.
- I've yet to order a Cpap in my early career. That's fine. Most people have yet to order a Cpap. They take a little while to get done. So that's the common. Okay? Yeah. So my question was really, just like, what are in the pulmonary realm? Winter times, we should be thinking about that. And how do we actually order that have also active?
- Okay, well, that's a problem we need to talk about with your fellowship director. But so Cpap is really useful in a couple of situations. If you have a patient who has dyspia that can be explained by other causes easily. So you get an echo, and it's kind of abnormal. Maybe they've got some diastolic dysfunction. They have pfts that are a little bit abnormal, but they just seem to have problems with any sort of exercise Cpap can help you distinguish between cardiac limitations and pulmonary limitations. So you can key into them.
- I would say, a vast majority of our cpets end up coming back as they just haven't exercised, which is actually a really useful finding right? If someone's dyspic on exercise. They don't know why you get a seat. Bet it's like you're normal. But you're just out of shape. It can really drive people to actually get in shape. That happens for me a couple of times occasionally, if they will. Also, when you have those patients that are, there's a disproportionate exercise, intolerance and pfts will lead to another kind of cpap, which is an exercise Cpap, where we put a pulmonary catheter in them and do exercise testing, because then you can find people that develop right ventricular dysfunction, even though they don't have pulmonary hypertension at Baseline with exercise or they'll underfill their right ventricle during exercise, so as you load the right, as the right ventricle needs to load, it stops

loading, and that can be helpful diagnostically. So the times that I would order a cpet is when you have dyspnea that you can't otherwise explain.

- You don't need a cpap to diagnose dysfunctional breathing syndrome like I said, there are some questionnaires. If you just Google dysfunctional breathing disorder, you'll find the questionnaires pretty quickly. They've become pretty popular since Covid-nineteen came around. You can also see it people that are breathing primarily in their upper chest not using their diaphragm at all, probably have some component of a dysfunctional breathing disorder. Probably the easiest thing I usually diagnose it walking into the room and watching the person talk to me. They can't complete a fence unless they have really bad asthma or Copd with an fed one that's really reduced. They're probably a problem the other clue to it can be someone who suddenly says I was in a choir a year ago, and now I can't actually sing in the choir because I get on air too quickly that a lot of times is dysfunctional sort of so, Cpa, when and the way you order it is cpet, and the order should just that's that's it. And then it gets it goes into a queue. They do in the lab, and someone has to read it. Apparently that's gonna be gone.
- I want to know also that we did try to coordinate our clothes. John texted me last night. I said, What are you wearing? And he said, Are you wearing a tie? I said, What's a tie? And then he showed up with a tie on. I thought it was very clear. No ties no questions in the chat. Who knows?
- Thank you, guys, take care thing like that, are they at higher risk? All right, thank you.