#362 Migraine Headaches, Acute Hypoxemia: A rapid review (TFTC)

[intro]

Matt: Welcome back to the Curbsiders, I'm Dr. Matthew Watto, here with my great friend, maybe my best friend, certainly one of my best friends.

Paul: Holy smokes, ah.

Matt: Dr. Paul Nelson Williams. Paul, how do you feel about all that?

Paul: Watto, this is a revelation. I don't know if I can keep going. [Matt laughs] I finally graduated. I've been waiting for years for this. This is really exciting for me, so thanks for that. I'm good, Matt. How are you?

Matt: Good. Of course, Paul, today, this is a tales from the Curbsiders episode. We're going to be talking about two fantastic Curbsiders episodes. I think you said we're not allowed to say "Peabody award winning" anymore.

Paul: Who's going to stop us? The Peabody people? I don't think so.

Matt: Okay, all right, we're going to recap episodes on headaches. Specifically, we're going to focus on migraine headaches, go back through some of the newer medications, and some tips and tricks we got from a great guest. And then, we're going to talk about and recap our acute hypoxemia episode, which is part of our Rapid Response series.

So, Paul with that, we should remind the audience that most of our episodes are available for CME through VCU Health at *curbsiders.vcuhealth.org.* This specific episode gives me and Paul a break from CME and our team a break from CME but the individual episodes we're talking about are available, so you can go back and claim CME Credit for those at *curbsiders.vcuhealth.org*.

Now, Paul, CME can be a headache, but we did an episode [Paul laughs] on headache. I'll give that a C+ for the transition.

[laughter]

Paul: Yeah, it's great, it was really good.

Matt: This was number 341 featuring Dr. Kevin Weber of Ohio State University. This was produced by Chris "The Chiu Man" Chiu and Isabel Valdez and, of course, Paul fantastic graphics by Edison "Eddie" Jiang. Who else, Paul, who else? Yeah. Now, Paul, maybe you've accused yourself of being a little bit of a curmudgeon. And speaking of curmudgeons, the brain, when it comes to migraines, Paul, our guest described the brain as being a little bit of a curmudgeon. So, to quote him, he said, "I like to tell my patients to think about a migraine like it's an irritable old miser set in its ways." Your brain, it just doesn't like a lot of changes. So, lack of sleep, being hungry, being thirsty, changes in the weather, Paul, these things all can set the brain off and I think that's helpful in counseling a patient with migraines. I'm not sure if you have a spiel, but I've been using that one.

Paul: Yeah, same. I think we've talked before. Sometimes, we get so excited to talk about medications and interventions, we kind of forget about just the basic supportive stuff that actually prevents

migraines, and I think just to remember just the usual stuff that everyone gets mad at you for saying, drink a glass of water, make sure you get enough sleep. Easier said than done in a lot of circumstances, but also really helpful for your migraineurs.

Matt: You made the point, Paul, you asked him, you said, "When I think of headaches, I just think of migraines, tension type, and then everything else," He gave you the blessing for that, Paul. He said I actually think that's a good way to think about headaches because in primary care, pretty much those two types, migraines and tension type, those are in our wheelhouse. I think if you think someone has one of these other types of headaches, certainly you're well within your rights to refer them to neurology. So, I think that's a good framework to have. The red flags, Paul, what do you think about mnemonics, Paul? We talked about the SNOOP 10 mnemonic. Have you started to use that?

Paul: I have not, and it's no one's fault but mine, I don't do well with mnemonics because I can't remember what the mnemonics actually stand for. I think the SNOOP's 10, it seems like a good one but I would have to look it up to know all the 10 things that is part of the 10 that I'm supposed to remember so well. I think, for the most part, it's really a guide to make you think of other secondary causes of headaches that are not just bread-and-butter migraine. Is that-

Matt: Exactly, yeah.

Paul: -kind of your understanding of things?

Matt: That's exactly right. If you have a teenager or a kid or a young adult that's presenting with classic migraines, they've had them for a while, you don't necessarily need to get any CNS imaging, which usually is going to be an MRI of the brain. But if someone, let's say, especially if they have malignancy or you suspect malignancy, or if they have their first and worst headache, if they're immunocompromised, those are some things that might point you in the direction. But the SNOOP 10, you can look it up. That's a whole list of things that might make you think about getting imaging to look for a secondary cause of a headache. But I am with you, Paul, I remember the mnemonic but I don't remember what goes with each letter, and then it's not helping me.

Paul: You might have to help me with this and I might have the society wrong, but I believe he said that the International Headache Society actually came out with fairly clear guidelines for imaging, actually right before COVID happened. So, those guidelines may have gotten kind of washed away by other news, but there are pretty well-defined guidelines. That's probably what I would look up to-- and maybe with this SNOOP 10, but I would probably look at the guidelines too.

Matt: So, Paul, for a board of therapies for migraine-- because I do want to spend most of this recap talking about the therapies for migraine, the over-the-counter ones that most patients have tried and most clinicians are familiar with are things like you have your aspirin-acetaminophen-caffeine combination, which is branded as Excedrin, and that one, I know a lot of patients like to take that. And then, you have you're just run-of-the-mill acetaminophen and NSAIDs. But beyond that, there's a lot of new agents. Paul, has your practice changed with the triptans? He gave us some newer ones that I

hadn't really been using. Usually, I'm using sumatriptan but this is practice changing for me. I'm going to be trying these new ones out now.

Paul: Yeah, my practice has been the same. I leaned really heavily into sumatriptan. Your first love is the one that's kind of hard to forget. But Dr. Weber talked about rizatriptan, so there's rizatriptan and naratriptan specifically, as newer triptans that seem to have fewer side effects and are better tolerated. Matt, if memory serves, rizatriptan has a little bit of a quicker onset of action, but the naratriptan tends to last a little bit longer, if that helps make the differentiation. And then, as we're talking about the triptans, every time I order one for my patients, I don't know about you, I get about 27 different scary pop-ups from electronic health record [crosstalk] [Matt laughs] the patient, serotonin toxicity, and then, I have to sign a legal waiver saying that it's okay.

But Dr. Weber made the point really that it's just mostly a theoretical concern. It's not been borne out in observational studies. So, you can prescribe the triptans with a fair amount of confidence for patients who are on other psychiatric medications and not have to worry about sending them screaming into serotonin toxicity.

Matt: Yeah, and the main one that he said he doesn't mess with is patients with known cardiovascular or cerebrovascular disease. There's not a ton of evidence. It's theoretical because they cause vasoconstriction. I think people with uncontrolled hypertension is the other group. So, a lot of your younger patients aren't going to have these problems. So, you can use them in the younger patients. But if they're middle aged or older and sicker, then you definitely think about these. And that's why, we're going to talk about in a second, the newer agents have really been great because they don't have any contraindication for patients with prior cardiovascular disease, which has really been helpful to a lot of people.

Paul: Matt, do you think it's worth mentioning-

Matt: Oh, yeah.

Paul: - one of the more common side effects is actually chest pressure. So, one more good reason to not prescribe that to a patient population that has possible atherosclerotic cardiovascular disease, because, first of all, [unintelligible 00:07:51] technology would certainly be scary, but just know when you're prescribing it even for patients who don't have those things, it's probably worth mentioning, "You might experience a little bit of chest pressure with this medication"-

Matt: Yeah.

Paul: -which is not something I had been doing routinely.

Matt: Same, I feel very guilty about that, but I am certainly talking about that now. One time people may want to still reach for sumatriptan is-- and I don't remember if we talked about this with Dr. Weber, or with a prior headache guest was just if patients have a lot of like nausea and difficulty keeping meds down or they're vomiting with their headaches, the sumatriptan has a nasal formulation or a

subcutaneous formulation and that can be good for patients who are having a lot of stomach upset with their migraine headaches. So, that is one of the reasons it sounded like he was still reaching for it because it just has a lot more options in delivery system. But the newer meds-- and Paul, I'm not sure I didn't ask you this yet. Have you prescribed any of the new CGRP agents or the ditans?

Paul: No, I wish I was so bold, but I have been leaving those in the hands of my capable neurology colleagues so far. What about you?

Matt: Usually, I have been referring patients to neurology and I will say part of-- we're going to talk about this a little more later, but I've had pretty good success with just the classic agents and using preventive therapies, the ones that are generic and older, which we'll talk about a little later. So, I haven't had too much cause for this. But now, I think the one or two patients I have in my panel that are having more difficult trouble with migraines, I would feel more comfortable prescribing these now. The newer agents, there's oral abortive therapies, the gepants, these are CGRP receptor antagonists, and they can be used for abortive therapy. There's ubrogepant and rimegepant, and they're both taken by mouth. Ubrogepant, you can take it to up to twice a day for abortive therapy and Rimegepant, you can take it once daily. It's longer acting. Actually, rimegepant can even be given as a preventive taken every other day.

These agents, they can be given right along with acetaminophen, NSAIDs, and the aspirin-acetaminophen-caffeine combination meds, so over-the-counter meds. He even mentioned he has some patients, if they are getting relief from triptans, but the triptan use is too frequent and he's worried about medication overuse headache, then this can sort of supplement that so they can alternate. Some days, they can take the gepants and some days, they can take the triptans. So, those are some of the newer abortive therapies.

And then, this lasmiditan, Paul, it's hard to say, have you seen this one in the wild? I haven't seen it in the wild yet.

Paul: Not yet, I'm looking forward to it. I'm also, by the way, just deeply grateful you're doing this section, not me. [Matt laughs] I'm so glad [crosstalk] have to say these names out loud.

Matt: The big challenge about this one, Paul, I just always think about some of the famous people who have gotten into trouble with the Z-drugs, and driving, or having these episodes where they don't remember, but lasmiditan has a warning on it that you basically need an eight-hour driving restriction if you take it. I see that as kind of a big impediment to taking this medicine. He says he's really limited it to taking it to people who mostly is home, not out driving because he'd worry about the sedative effect of the ditan, Lasmiditan. But this one too can be used in patients with vascular disease. So, it does have some upside to it and maybe future agents will be less sedating, but I don't know.

Paul: One practical tip that Dr. Weber gave about one of the newer agents is the rimegepant and, Matt, correct me if I'm wrong, but he talked about how, if you're using it as prophylaxis, so every other day, and you have a headache, you can then just take it as an abortive and then sort of reset your cycle. So, you can take it as an abortive and then start taking it every other day. For instance, if you usually take it

Monday, Wednesday, and Friday, and you have a headache on Tuesday, take it on Tuesday, and then you move everything to Tuesday, Thursday, Saturday instead. So, I felt at least empowered to kind of guide patients in that way, even though I may not be prescribing it as of yet. So, I thought that was a nice little point as well.

Matt: Agreed. Probably, the audience is thinking, "Well, how am I going to get these covered?" He did mention that sometimes, insurance companies want you to have tried, well, certainly other abortive medications and sometimes up to two triptan agents before you get to these. So again, this is helpful if you've tried some other things-- if you don't feel comfortable prescribing these yourself, at least try rizatriptan, naratriptan, or sumatriptan, something like that before you send the patient and try to get them these newer agents covered, but definitely want to try some things.

And then, the other medicines that are newer and these are more preventive therapy. There's two of the gepants. The rimegepant can be given every other day as preventive therapy. And then, there's another one atogepant, A-T-O-gepant, Paul. [Paul laughs] That's a daily therapy for prevention. It's not an abortive therapy, it's just for prevention. So, that's another option that you can give people. We'll talk about the traditional preventives in just a moment here but the other preventives that are CGRP agents, they're monoclonal antibodies, Paul. There's fremanezumab, erenumab, and [Paul laughs] galcanezumab and eptinezumab, Paul. Maybe I got some of those right.

Paul: No, that was stellar. Great stuff.

Matt: Essentially, these medications, he said, are well tolerated. Typically, again, you want to have tried a couple of other preventive therapies before you're going to get these covered. They're given either by injection or infusion, usually once a month or once every three months, so it depends on the agent. I've seen maybe a couple of patients on these. It probably just depends on your practice, and maybe that's just a sampling bias. But, Paul, I like to set you up for this point, because you're like everyone's favorite primary care doctor. Is there anything we can offer in primary care? I'm guessing no, but prove me wrong. [Paul laughs]

Paul: Matt, so much stuff. Yeah, I think we actually were fortunate to be trained that migraines are well within the purview of primary care doctors. I think you have a lot of tools in your armamentarium before you necessarily have to escalate to neurology. There are a lot of medications that we already have comfort with. I think the antihypertensives are probably the most obvious class of medications that we're already probably using. So, the beta-blockers specifically like nadolol or atenolol, I think we all know about.

One that was new for me and that Dr. Weber was particularly excited about was candesartan, the ARB, as migraine prophylaxis, which I had never heard of, and I'm excited to try. And then, the calcium channel blockers like verapamil are obviously a consideration as well. Matt, have you been using candesartan on occasion to start that as your prophylaxis yet?

Matt: I have not. But I have been using candesartan, Paul, because with our blood pressure episode we did relatively recently with Dr. Jordy Cohen, we talked about some of the longer acting because

Losartan, even though it's everyone's favorite generic, it's not as long acting but candesartan, telmisartan, olmesartan are longer acting. So, I have been using it for that. Which brings me to the next point is and you made this on the episode, Paul, that you don't think about dual purposing these medications because there's a lot of great options but maybe if someone has high blood pressure and migraines, you start with a blood pressure agent. If someone has obesity, they're trying to lose weight you can use topiramate. He mentioned topiramate is great medicine for migraine prevention as well. And I think you've made the point on prior shows about the TCAS, amitriptyline, nortriptyline for patients with all sorts of different problems, maybe depression or neuropathic pain. So, lots of--

Paul: Or even trouble sleeping, nortriptyline in particular is not a bad choice-- well, it's not a great choice for monotherapy for insomnia but if someone also has migraines, it's one to at least consider reaching for. I think a lot of people were a little bit scared of TCAS maybe because of the recent time doing rotations in the ICU, but they're well tolerated by a lot of patients. And there are indications for some.

The last one, sorry to cut you off, Matt, is the venlafaxine is not one that I had thought of as migraine prophylaxis, but certainly a medication I have plenty of comfort with, prescribed multiple times in the past. So, I might reach for that one a little bit more readily if there's, as you say, the dual-purpose indication of either chronic pain or depression, that might be one I might reach for a little bit more frequently now.

Matt: And we're a primary care, Paul. We are familiar with all of these meds, for the most part. Valproic acid is probably the only one on the list that not quite-- that's not one that I routinely prescribe without someone holding my hand. So, I think this is a great opportunity for you to really set the patient up for success, starting them on a preventive medicine if they're having frequent migraines. And then, we talked about a lot of the options for abortive therapy. On the episode, we did talk about some of the other alternative therapies. There are a lot of wearables, I guess you would say, or neuromodulators, Paul, like the one that looks like a tiara or a sticker that you put on your forehead, you can buy that over the counter. So, if I have the right patient, those seem relatively safe and those are something I really wasn't aware of. So, I'd encourage people to listen to the full episode because it's hard to do it full justice in just a short recap episode like this, but really great guests. Yeah, Paul, we've had some great headache episodes. I feel maybe that's why we feel comfortable with a lot of these meds, but I still feel like I could always learn more about headaches, and they're still scary to me.

Paul: Yes, I agree with all the above. Even though I speak with confidence, they still terrify me. So, it's like I'm always happy to learn more about them.

Matt: We had a new series, the Rapid Response series that is being helmed by Dr. Cyrus Askin everybody's favorite brand-new pulmonologist newly minted pulmonologist. And we had the guest, Dr. Nick Mark of ICU One Pager fame, and Twitter fame, Paul. He's also been on the show before. He was a great guest. The graphics for this episode were done by Edison "Eddie" Jiang. We talked about so much. This was more physiology than then we usually do, Paul, but it was very interesting. And Dr. Mark, Nick has a great-- I think he has a talent for talking about that sort of stuff and making it seem more approachable.

Paul: Yeah, He's clearly got very well-defined schemas as evidence. He does these ICU one-pagers that are just these schematics that outline all these complex physiologic concepts very, very straightforwardly. So yeah, a fantastic guest. But before we even got into the physiology, we talked a little bit about fundamentals and we defined our terms a little bit, Matt. Did you want to run us through it?

Matt: Yeah, I know, we have a lot of-- Paul, you and I are becoming less young by the moment. But we have a lot of younger people and I know they're still in training. They want to sound smart, and they're still being graded. So, when you're hanging around with a pulmonologist--

Paul: I'm sure where you are going with that, by the way [crosstalk].

Matt: When you're hanging around pulmonologists, you want to make sure you use the right terminology. Yeah, that was way too long of a walk. Sorry, audience. [Paul laughs] But hypoxemia, low oxygen in the blood, that's typically the number you're going to get from a pulse oximeter. So, that's hypoxemia. That's the pulse oximeter reading. Hypoxia is how much oxygen is there at the level of the tissues, and that's a different story. So having tissue hypoxia, Paul, that's bad. But it's--

Paul: So I've heard.

Matt: Just because somebody has hypoxemia, doesn't always mean they have hypoxia. It's just kind of differentiating those terms. And then, thinking about the oxygen content, that's how much oxygen is carried in the blood. So, somebody with hemoglobin of 7 is not carrying as much oxygen, as somebody with a hemoglobin of 14. Let's say they both have an oxygen saturation of 100%, the person with hemoglobin of 14, even with a sat of 100%, is carrying much less oxygen in the blood. And so, those were just some basic things we talked about, and then delivering that oxygen is dependent on your cardiac output. That's about as basic as we can get, Paul, to set things up.

Now, Paul, the pulse oximeter, I mentioned it. [Paul laughs] I think it's a flawless technological achievement with zero limitations. Is there anything about that statement wrong?

Paul: I think it's hard to argue. It is a technological achievement. So, I will give it that, but I think the other parts are probably less accurate, will say. So, you're setting me up to mention how the pulse ox works, and how we got the numbers in the first place. Actually, Dr. Mark was telling us that the way we derived the numbers from the pulse ox is we actually tested it on a bunch of servicemen back in the day, and these servicemen were almost exclusively white. And what we did is we gave them increasingly lower concentrations of oxygen, and then would map that out across-- sort of use that and then derive what the pulse ox was when using a pulse oximeter.

The limitations there are twofold. The first, and probably the most worrisome, I guess, is the fact that because they were almost exclusively white, there was no skin tone variation. As a result, pulse oximetry is less accurate in darker-pigmented, melanated skin. And we're talking percentages, like 3%, which, on the face of it doesn't sound like much, but 3% can be the difference between a lot of clinical

decision-making that we get. It can be the difference between whether someone gets supplemental oxygen supplied to them or not, or the decision to use steroids in COVID, I think was the other example that he used. 3% in pulse oximeter is actually a really big deal. So, knowing that you have that limitation in darker-pigmented patients is actually really important to know. And I think, Matt, you've made the point elsewhere, if the accuracy becomes important as opposed to the specificity, then probably your duty bound to get yourself an arterial blood gas, just to get a truly accurate number and make sure that you're actually doing your due diligence.

Matt: Yeah, because I imagine, hopefully, and I had seen at least some news stories on how far along this is. People are trying to write this by updating the technology to work on wider variety of skin pigmentation. So yeah, for now, you may be stuck, especially if you're going to base a very important decision on, try to just get a blood gas to get a more accurate measurement of the person's oxygen level. And then, Paul, did you make the point yet about-- now, when you put someone on supplemental oxygen, the pulse oximeter immediately registers that. If I don't see that oxygen jump up to 100% right away, I should be very worried because there's no chance it's going to get better.

Paul: Correct? Yeah, you failed and you intubate just immediately. [Paul laughs] The point that you're alluding to is that there is going to be a lag between your intervention and the change in the pulse ox reading. So, the pulse oximeter is not going to register things immediately, because it takes time to pump the blood from the heart to the periphery where the actual pulse ox is being measured. So, if someone has a low cardiac output, it might even take a little bit longer. But Dr. Mark gave us about at least 30 seconds before we're going to start to see the intervention change. So, do not panic if after you turn up the FiO2 or you apply non-invasive ventilation, if you don't see a change immediately, give the patient a chance to calibrate because it actually takes some time for the blood to go from the heart to the fingertip, where presumably the pulse oximeter is actually attached. So, just be a little bit patient [crosstalk]

Matt: This seems like one where people can slow their roll for like 30 seconds when they make a change, rather than be like, "Oh, no, it's not working. Let's go to the next thing," and you might not have given it enough time.

Paul: Right. Recognizing that in a rapid response, 30 seconds feels like two and a half hours. Yeah, it's one of the things where checking your own pulse for a second, just give your intervention a chance to work.

Matt: Now, Paul, since the hypothetical case we are going through throughout this episode was a rapid response where you're walking to the rapid response and talking about, what's the first thing you do when you get in the room? So, sick or not sick is going to be the first thing in your assessment and we talked about some of the things that are definitely bad signs or if the person has-- if their mental status is bad, if they're tripoding where they're like putting their arms behind them and leaning their head back, and putting their chest forward, that's always a bad sign. I usually don't see that end well. And then, lots of accessory muscle use, that's a sign someone's sick, someone's working very hard to breathe. Paul, you asked us the question about how do you recognize someone who's not protecting their airway, and do you remember what Dr. Mark's response was to that question?

Paul: He, in his defense, said not to be crass to qualify, but then said, it's this classic joke. It's like pornography, you know it when you see it [Matt laughs] which, I suppose, it's fair. For instance, if you see someone who has massive epistaxis, probably they're not protecting their airway, or they're actively throwing up, or if they don't have a gag upon suctioning. There's a fair number of obvious indicators, and sometimes it might be a little bit more subtle. But for the most part, at least according to Dr. Mark, you get a sense just by actually examining the patient, you'll see what's going on and recognize it when you see it, is reassuring to me.

Matt: Yeah. I was glad you asked that question, Paul, because that was one of those things where I would always hear people be like, "Oh, yeah, protecting their airway." And I sort of thought it was what he said, but it was good to hear him confirm that what I had been taking that to mean was actually pretty close to what it means and that it's not always super clear cut.

Paul: Yeah, exactly.

Matt: Anyway, I was glad that you were brave enough to ask that question, Paul, thank you. I'm sure the audience thanks you as well.

Paul: I'm always brave [crosstalk]. Sure.

Matt: Yeah. And then, we talked about this, Paul, the pulse oximeter, looking at that, make sure-- I mentioned I've been burned by this before. Sometimes, even if it's just like hanging by the side of the bed, it still can give you what looks like if it's swinging back and forth or something, it can still give you what looks like a tracing. So, just make sure it's actually on the patient and look at the waveform to see does it look like it's tracking with the heartbeat. And then, how low is the oxygen? That's going to tell you the level of severity. So, if it's very severe, like low 70s or less, that's worse, obviously, than if it's in the high 80s.

Paul: Well, it raises the other point about pulse oximetry, is that the low pulse oxes are theoretical, because again, because they were doing these on volunteers, they couldn't just lower their oxygen until they died. So, there was a cutoff. So, this is mostly a projected number. So, once you get below a certain threshold, I think Nick said 70%, it's almost kind of immaterial. If someone's pulse ox is in the 70s, it's bad. The degree of badness is almost academic at that point. Just recognize that the lower ends of the pulse ox, those numbers are neither specific nor accurate.

Matt: That was completely new information to me. I had never heard that before. And I think it's useful to know that clinically too. So, of course, you go into the room. In the old days, Paul, we'd have the paper chart in front of us, flipping through, trying to figure out what happened, what medicines were recently given. Nowadays, probably you're going to have someone on the computer telling you recent medicines that were administered and what's been going on in the hospital course.

But as you're doing that, if you happen to have-- of course, you're going to listen to the heart and lungs, do a physical exam looking for edema and such but if you have a point-of-care ultrasound, Dr. Mark

mentioned that that's something he finds helpful. He may look for B-lines in the lungs as a sign of pulmonary edema. He may look for lung sliding to see if the patient has pneumothorax and then looking for things like pleural effusions. And then, at the heart is the RV, does it look like the right side of the heart is large and overloaded with pressure or does it look like the EF is low? So, you can tell a lot from a point-of-care ultrasound if how to use it. And then, the testing is pretty basic chest x-ray, some blood work, maybe lactate and a blood gas. The blood gas is really what's going to inform our differential diagnosis.

And, Paul, there were quite a few causes of hypoxemia. But what did you think about this breakdown? Have you heard this before?

Paul: I have not heard it said in exactly this way, so I actually found this a really useful framework in terms of how to go through.

Matt: So, based on the A-a gradient, or what Dr. Mark likes to call the A-a difference, you can split things into, is it a normal A-a gradient, and there are a couple of things that cause that. So, the low inspired oxygen content is one of them, Paul, and that usually happens at altitude. So, most of the time, you can just knock that off your list depending on unless you're on like Everest or something evaluating this patient. And then, hypoventilation is something that can cause a normal A-a gradient, but low oxygen. And then, the final one was low mixed venous oxygen concentration.

But the most common one you're probably going to see in a rapid response and I think most probably, the pearl that people will be able to remember is V/Q Mismatch, so that's ventilation-perfusion mismatch. That could be something like a pulmonary embolism that would give you a high A-a gradient. It could just be obstructive lung disease or some filling process like pneumonia or pulmonary edema. Those are probably the most common causes. But the way you differentiate that from a shunt, which is another potential cause of an elevated A-a gradient, is when you slap oxygen on the person, does the oxygen level improve at all? Because oxygen that is not going to correct or is very difficult to correct with large amounts of supplemental oxygen, you've got to think about a shunt in that situation.

So, I think that's one of the most useful things. Like if you put the oxygen on, they don't get better, then, A, you haven't bought yourself time and B, you've got to think about, could this be a shunt? And Paul, he told us one iatrogenic cause of shunting, I'm going to let you talk about this one.

Paul: Yeah, he just [unintelligible 00:31:04] and I think he even framed it as when you're a pulmonology fellow, you'll get this concept at least once per week. And I'm like, "I have never thought of this ever in my life, and I am ashamed." But basically, you can actually cause iatrogenic shunt by administration of either nitrates or calcium channel blockers and impair-- The way he describes the lungs is very smart. And they just know to basal constrict to stay away from areas of hypoxia. But if you impair that, then you actually create this isogenic shunt, and one way to do that is to actually administer nitrates or calcium channel blockers, which will impair the lung's ability to vasoconstrict. Does that sound right, Matt?

Matt: That sounds right. And, Paul, I think we agreed on a different recording that if you make this diagnosis, you have to slam the pulse ox on the floor and moonwalk out of the room.

Paul: And the patient that you'd see this in is somebody who has already like a little bit underlying atelectasis or maybe a small pleural effusion. So, they have the capacity for things to go a little bit south already and then that's augmented as soon as you get one of these medications that impair the basal constriction. And then, you've apparently made the diagnosis in a way that I have never actually done. But yeah, that's right. You're a hero if you actually get to make this.

Matt: And, Paul, I think we forgot to say this, but if you're like me, and this was a long time ago now, my first night of residency was night float. And I went into the room of a patient with hypoxemia, Paul, and I called my senior. And he was like, "Did you sit the patient up?" And I was like, "No." And he's like, "Okay, sit the patient up. Did you put them on supplemental oxygen?" I was like, "No." And he's like, "Okay, do those things and I'll meet you at the bedside." So, simple thing and if they're already on oxygen, turn it up, sit them up, and then go from there. But those things go a long way and I think you made that point on the episode. So, supplemental-- I mentioned turning up the oxygen, Paul, you want to talk to us a little bit through oxygen delivery and anything here that stuck out to you the way that we talked about it? We went through in a stepwise fashion.

Paul: No, I think it was helpful. It is fundamental but I also think the fundamentals are important to know and often neglected. Everyone just kind of assumes that you know. So, I think to kind of go through them step by step was really helpful. Do you want to just kind of tick them off real quick?

Matt: Yeah, what about the nasal cannula? What percent increase in oxygen I should expect for each liter I give there? I feel that's a good pearl to have in your pocket. If you're taking care of patients.

Paul: You should expect, if memory serves and this figure is correct, a roughly 3% increase in FiO2 for every liter of oxygen increased delivery. The nasal cannula, the typical one that doesn't have the reservoir or anything else attached, just the two prongs that go into the nose, will give you between 1 to 6 liters of oxygen per minute, I think it's important to know.

Matt: So, if you're starting at 20% oxygen in ambient air, and if you ever want 6 liters, maybe you can get him up close to high 30s, close to 40% FiO2. And even though there's 100% oxygen coming out of those prongs, you're pulling in so much ambient air around it that it just dilutes the air and that's why you're not getting the same kind of thing as 100% oxygen. So, I thought that was an interesting-- I guess entrained air, Paul. That's a term I hadn't heard before, but I came across when researching this episode. Facemasks, Paul, what about those?

Paul: Yeah, it gives you a little bit more bang for your buck. And again, you still have this admixture of the ambient air. It's not perfect. That will give you between 10 to 12 liters per minute, which equates to about an average of FiO2 between 45 and 50%. So again, as we're ramping things up, certainly higher oxygen delivery, but it's not 100% oxygen because again there's still capacity to bring in some ambient air along with them. And then moving-- oh, go ahead.

Matt: Oh, yeah. I was going to say the-- let's [unintelligible 00:34:58] them off. The nonrebreather, that's the one with the bag on it. It has a facemask with a bag. The bag fills with oxygen. So, that's 100% oxygen. Probably, your lungs are bigger than the bag. Hopefully, your lungs are bigger than the bag, Paul. So, when you breathe that in, the bag is filled with 100% oxygen, but probably you're getting some entrained air as well plus that bag is not going to fill your lungs totally. But it's close to 100% oxygen that you're getting there. And then, if you really need the big gun, Paul, what are you going for next?

Paul: The step right below, we're talking positive pressure we support is the high flow nasal cannula, which is like I think it's like this mounted unit that just sort of blasts air. [laughs] It's humidified air, being the important thing where you can also control the flow rate as well. You can increase the FiO2 up to 100%. It also provides just a little bit of PEEP to keep those airways open before you actually bring in the fancier pants machines and you progress all the way to the noninvasive positive pressure support.

Matt: Yeah, and he mentioned and we had in our original show notes for this one that for patients with like pure hypoxemic respiratory failure, the high flow nasal cannula can be a good choice, even compared to the positive pressure, which we'll talk about positive pressure, noninvasive positive pressure, ventilation. That's like your BiPAP, your CPAP, or your bilevel, or your CPAP. With the CPAP, of course, you're setting a PEEP, positive end-expiratory pressure. Usually, you can set a FiO2 with that as well, how much oxygen you want to give along with it. With that, the main thing we talked about there is the patient has to be awake enough, Paul, that they can take the mask off if they're going to vomit. Probably not going to want to put it on somebody that is vomiting. So, people can't be in restraints either, because they need to be able to pull that mask off. So, there are some limitations there.

And he mentioned a good patient for this is if you've given a therapy-- let's say you've given a loop diuretic to somebody in heart failure exacerbation with troubled work of breathing, it's good to put them on maybe a bilevel or CPAP because it's expected to be a short time, like you think the person is going to get better with the treatment you're giving. I think it's hard for patients. I've seen it done, Paul. I've seen patients stay on this for a day or two but it looks horrendous. They're usually begging to come off by the end so they can eat and not have something like just flowing air in their face all the time. Any other thoughts about this, Paul, before we wrap things up here?

Paul: No, God, I feel like there was a point I was going to make and I lost it somewhere in there. I think that you hit all the high points, Matt. Yeah, I feel like we did a great job. We should be proud of ourselves.

Matt: Paul, I'm always proud of you, Paul.

[laughter]

Matt: America's primary care doctor.

Paul: Sure [crosstalk].

Matt: You think we can get that trending, Paul?

Paul: No, I don't.

Matt: I tried to do the national treasure thing trending for you. And now, my new push for you is *#americasprimarycaredoctor.*

Paul: I'll be selling supplements in no time [Matt laughs] Yeah, I think that's great [laughs].

[laughter]

Matt: I'll have to work on the hashtag. But, Paul, how about you take us to an outro?

Paul: Happy to do so.

This has been another episode of the Curbsiders bringing you a little knowledge food for your brain hole.

Matt: Yummy.

Paul: Great, classic stuff. Get your show notes at *thecurbsiders.com* and sign up for our mailing list to get your weekly show notes in your inbox. Plus, twice each month, you get our Curbsiders Digest which recaps the latest practice-changing articles, guidelines, and news in internal medicine.

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And a special thanks to my cohost for this episode, Dr. Paul Williams, America's primary care doctor [Paul laughs], and to our whole team. Pod Paste edits and produces the show. Elizabeth Proto runs our social media. Stuart Brigham composed our theme music. Until next time, I've been Dr. Matthew Frank Watto.

Paul: And as always, I remain Dr. Paul Nelson Williams. Thank you and goodbye.

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