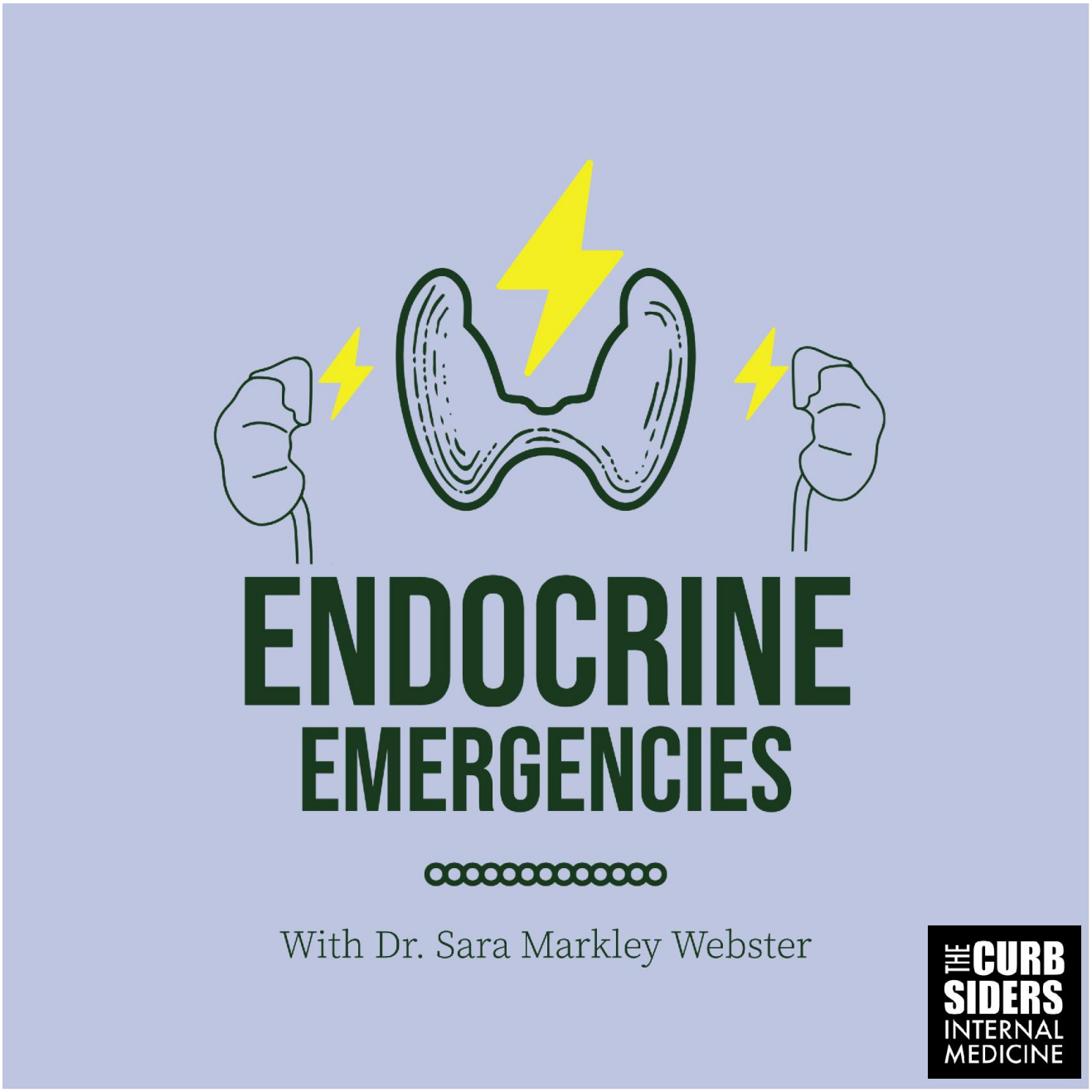
#372 Endocrine Emergencies featuring Dr. Sara Markley Webster



[The Curbsiders theme]

Dr. Monee: Welcome back to Curbsiders. I am not Dr. Matthew Frank Watto, as you can already tell. I'm Monee Amin. We're back with another inpatient episode, joined by my cohost, Dr. Meredith Trubitt. How are you this evening?

Dr. Meredith: I'm doing pretty well. How are you?

Dr. Monee: I'm pumped and they're about to find out why, but that's not relevant right now. What is relevant is on tonight's show, we discuss endocrine emergencies, a few that we haven't covered before. So, DKA and hypercalcemia episodes that we've already had. Tonight, we do adrenal crisis, myxedema coma, and thyroid storm with our guest, Dr. Sara Markley Webster. In just a minute, Meredith is going to tell you more. But first, will you please remind the good people in the audience what it is we do on this show.

Dr. Meredith: Sure, Monee. We are The Internal Medicine Podcast. We use expert interviews to bring you clinical pearls and practice changing knowledge. Tonight, we have a fantastic conversation with our guest, Dr. Markley Webster. She is an endocrinologist at the Atlanta VA, affiliated with Emory University. She's a mom of two small human wild things and one gigantic furry beast, aka her dog, who we talk about in the episode. Her main interest is in trainee education at all levels, and she particularly likes to work with the internal medicine residents to teach the endocrine topics they need to know for the boards and also the ones they'll need to know for real life, which aren't always the same. She's a shy introvert, but it's excited to be on the podcast. Like Monee talked about, we're going to talk about thyroid storm and adrenal insufficiency and myxedema coma. Without further ado, let's get to it.

Dr. Monee: Hey, Sara, thanks for coming on the show. We're going to start with some rapid-fire questions. To start, can you give us your one liner?

Dr. Sara: Yeah. So, 35-year-old mom of two small petri dishes and one extremely large beast of a dog that keep me busy and chronically exhausted.

Dr. Monee: [laughs] What kind of dog?

Dr. Sara: Great Pyrenees and she's beautiful and she knows it and she gets into all kind of trouble because she knows she's beautiful.

Dr. Meredith: Oh, nice. I'm the dog person. Monee can't handle the big dogs.

Dr. Monee: No, I cannot.

Dr. Sara: That means she would be your best friend, if you came over and she would never leave your side, ever.

Dr. Monee: I prefer Meredith's dog, Wrigley, who stays away with-- She just stays away with a ten-foot pole. It's fantastic.

Dr. Sara: [laughs]

Dr. Meredith: Yeah, she has antisocial personality. It's fine.

Dr. Sara: That's why we picked.

Dr. Meredith: All right, so I think we'll move through some of the openings questions quickly, but I think the one that Monee and I really wanted to know from you, Sara, was tell us a little bit of an example of good advice or feedback that you've gotten throughout your career during your training.

Dr. Sara: Yeah. I think the best was when one of my attendees-- I was really struggling with a patient and I felt we weren't connecting and we weren't getting through and we weren't hearing each other, and the attendee was just like, "You know, Sara, not everybody's going to like you and not everybody's going to want to listen to you. And that's okay. Maybe sometimes we need to say, 'Do we need to get a new doctor or do we need to get somebody else in here? Or, do we need to just take a step back and realize that you're not going to be able to fix everything for everybody?'" I think that really helped me put some perspective in that my patients have a lot going on, and I have a lot going on, and we're not always going to be on the same page, and that's okay. Maybe next time it will better or maybe next time it will be worse, but that's not a reflection of me personally. So, I think that really helped, because I was always like, "What am I doing wrong? Why can't I get across or get through to this person?" It really helped me take a step back from that.

Dr. Meredith: I think that's really good advice. I think, especially, physicians really are often people pleasing. Ans so, it makes sense that we often feel like that is a breakdown on our end, when in reality, it's just life. I think that's one we haven't heard of when we've done these shows so far, and that's really good advice. Monee, do you want to jump into our pick of the week?

Dr. Monee: This is a shared one just because it's very, very ridiculously exciting. So, friends, a couple of weeks ago, I found this bright orange flyer on my door saying that there was this-- It looked really sketch, I'm not going to lie. It said that Netflix was making a show and that they wanted to potentially use my house for the show. Punchline, no, they did not use it, but they're using my neighbor's house. The reason this is very exciting is who's involved with the project. So, they are filming a series adaptation, miniseries of the book, *A Man in Full*, directed by Regina King, starring Jeff Daniels, Diane Lane and Lucy Liu and William Harper Jackson, which is from my favorite show, *The Good Place*. So, very exciting. Today is happens to be filming day. So, if you hear some weird noises, it's probably related to that. The best part is I've had Regina King's sightings today. It's very exciting. I spoke to her.

Dr. Meredith: Do you want to tell everyone what you said to her?

Dr. Monee: Not really, Meredith, [chuckles] but I feel [Meredith laughs] you're just setting me up. So, what I had to tell Regina was, well, first I said, "Welcome to our humble abodes," plural. I just told her, "It was very exciting." That was the end of the conversation. She continued to be a director of a multimillion dollar show on Netflix. I did. Meredith pointed out very kindly that I made it several hours before doing something so ridiculous.

Dr. Meredith: Yeah, Monee kept it together until she didn't.

Dr. Monee: Yep. Honestly, I'm not going to lie. We're going to try to get through this, so that we can catch a glimpse of Jeff Daniels, because he is the star that will be in the scene that is being filmed at my neighbor's house. There's a very awesome group thread with my friends with pictures of us being creepy.

Dr. Meredith: So, should we jump in?

Dr. Monee: I think we're ready. I think we need to take it to our first case from Kashlak today.

Dr. Meredith: Today, we got Mr. Jerry first. He's a 68-year-old man with a past medical history of HFpEF, asthma, type 1 diabetes, hypoadrenalism. He presents the emergency department with one-day history of abdominal pain, nausea and vomiting. So, I'm going to be real honest here. The hypoadrenalism, I know is something important that I should know we should think about and do something about is probably relevant to this case, but I think we should start by just like maybe having a brief conversation on definitions of hypoadrenalism versus adrenal crisis and what those differences are and how that might reframe how you're thinking about these patients.

Dr. Sara: Yeah. Hypoadrenalism or adrenal insufficiency, depending on who you're talking to is just the person doesn't have the ability to make cortisol. Whether it's a pituitary problem or an adrenal problem, their body is not functioning the way it should. Typically, for a lot of people, it's more of a chronic issue, so they're taking hydrocortisone or something like that as an outpatient. When they come into the hospital, we get really concerned about adrenal crisis, which is where they could start having organ failure. They usually have hypotension and they're pretty sick and it has a high mortality. Some studies state up to 40%, if we don't treat or identify adrenal crisis early.

Whenever you have somebody who has any kind of adrenal insufficiency coming into the hospital, you always have to keep in the back of your mind, "Well, could this be adrenal crisis that's going on? Do I need to give them these high doses of steroids or do I need to treat this or is this something different? Is this an infection? Is this sepsis? Is this something else?" But anybody coming in with a history of adrenal insufficiency or hypoadrenalism, you should have it in the back of your mind that maybe this is adrenal crisis.

Dr. Meredith: Thinking about kind of that definition is all that's important for us to know just that is the lack of cortisol in the system or is there more to the pathophys that matters when you're thinking about that spectrum at all?

Dr. Sara: It matters a lot at the outpatient setting when I'm evaluating somebody for adrenal insufficiency, because I'm also looking at their mineralocorticoids and is this primary versus secondary? Because primary is much more likely to have a mineralocorticoid deficiency, where they're going to be hyponatremic and hyperkalemic. And secondary, not so much. When they're coming into the hospital though, it's kind of moot, because if they're coming into the hospital, they're going to need to be treated for the adrenal insufficiency. Usually, the doses of medications we use in the hospital cover both my glucocorticoids and my mineralocorticoids. It doesn't really matter that they don't have one or both or what have you, because I'm going to be end up treating them either way.

Dr. Monee: I think that you actually covered a couple of the points that I think we're trying to get to next, but we're going to take it back to Mr. Jerry for a second and hit on the things that you did maybe in a little bit more formal way. So, on further history, he's worsening fatigue over the last week in conjunction with that angio vomiting and abdominal pain. His initial vitals are significant for a temp of 35, heart rate 95, BP of 95 over 55, and he's saturating well on room air. His exam is notable for abdominal tenderness, but otherwise reassuring. His labs are notable for he's mildly hyponatremic, sodium of 130, K of 5.9, calcium 11, glucose 75, and his CBC is notable for a white blood cell count of 10.7. You mentioned previously about we're thinking about infection, sepsis, adrenal insufficiency, and in a way, I guess I'm asking the threshold, because I know I'm going to be pumping him full of fluids, full of antibiotics because I'm just going to cover that base. What should my threshold for these high dose steroids be?

Dr. Sara: Pretty low. When I have patients with adrenal insufficiency, what I tell them at home is if you have a mild illness, like you have a sore throat, you have a runny nose,

something like that, I want you to double up on your dose. If you have a fever above 38 Celsius, I want you to triple up your dose. If you have nausea or vomiting where you can't keep down your pills, I want you to come out into the hospital, so that I can give you IV hydrocortisone. When I have somebody coming into the hospital, that's a pretty big stressor in and of itself, not even including whatever the precipitate is that's bringing them into the hospital, the infection or the lack of glucocorticoids. And so, when I have somebody coming into the hospital, I have a low threshold to at least triple their dose. If I'm seeing things like hypotension, I'm seeing the nausea, I'm seeing vomiting, even though it might be sepsis, maybe they ate some bad chicken or something the other day, I still have a low threshold, because the risk of not treating them is so much higher than the risk of giving them that 100 milligrams of IV hydrocortisone and I really don't want to miss that person who's going to be in adrenal crisis and end up not treating them and have them be in the ICU for a couple of days, when they would have had a much faster turnaround if I had just given them the high dose steroids.

Dr. Monee: I think I missed it. How much did you say you usually do?

Dr. Sara: Typically, load somebody up. We'll give them 100 of IV hydrocortisone, and then you can do something like 50 milligrams IV every 6 hours. And depending on the response, it depends on how long you keep going with this. If they turn it around in a day, well, then I'm going to start tapering fast and we'll go to 50 Q8, then 50 Q12, and we'll drop it down fast. If they're not really turning around, I'm going to keep going with that 50 Q6, while we're trying to figure out what else is going on. Do they have some underlying infection? Is there an ammonia here that's contributing to this? But what else is happening?

With doses that high, if I give more than 50 milligrams of hydrocortisone in a day, I'm hitting both their glucocorticoid receptors and their mineralocorticoid receptors. This is why we don't have to worry about things like fludrocortisone in the hospital, because I'm typically giving more than that 50 milligrams of hydrocortisone per day. Even if they had primary adrenal insufficiency, I'd be covering their mineralocorticoids, anyway. We don't have stress dose fludrocortisone or anything like that. It's just the Hydrocort that we go with. That's why we prefer hydrocortisone for stress dose steroids, because it has the glucocorticoid and the mineralocorticoid. Something like dexamethasone, it doesn't have that. You want to stay away from something like dex. The high doses there are usually used for like brain edema and things like that, but not so much for adrenal insufficiency.

Dr. Monee: That's helpful. I'm not sure I ever remember that. So, I'm glad that you said that out loud, so hopefully it'll stick auditorily for me, the part about mineralocorticoids and glucocorticoids, being in cortisone and then remembering that dexamethasone doesn't have that, I think is something that I probably don't think enough about when I'm thinking about steroids. And stepping back just for a second, with sepsis, adrenal crisis, those things, I think kind of fit, is there anything else that you think about outside of those two when you see this in someone that has a known history of hypoadrenalism?

Dr. Sara: Really, it could be something just as mild as they've been chronically underdosed and they've had a mild stressor, something that we wouldn't even think twice about. Like they got into a fight with a family member or they had a bad day at work. People who have been borderline or marginal with their adrenal insufficiency and haven't been dosed well, it can actually tip into adrenal crisis with just minor stressors. So, it doesn't even have to be something big like sepsis. It's what we always worry about. But sometimes, we really don't find much because it was a pretty mild stressor. We look, but that doesn't necessarily mean we're always going to get the answer, which is really frustrating when you're like, "I need to know what caused this, so that I can tell you not to do it again, so that this doesn't happen again."

Dr. Meredith: Is there a set like dose that someone is typically getting in the outpatient setting or when you say, underdose, is that because everyone's on different doses?

Dr. Sara: Yeah. The dose for hydrocortisone is very much dependent on somebody's body surface area. Standard replacement doses are seven and a half milligrams to ten milligrams per meter squared. If you think about the average US male, he's going to have a BSA of about 1.9 to 2 meters squared. You would expect that he's going to need somewhere in the range of 15 to 20 milligrams of hydrocortisone per day because if you remember way back to physiology, we know that cortisol has diurnal variation. I get that giant spike in the morning and then I get a milder spike in the afternoon before supper. We'll usually split that dose up two thirds or three quarters in the morning and the rest around 4 o' clock. So, if we're going to give him 20 milligrams, I'd give 15 milligrams at breakfast and 5 milligrams in the evening and then see how they do. If they're still having orthostasis or they're having abdominal pain and nausea, we'll bump the dose up. And so, we'll try maybe 15 and 10 and see if that helps. Or, if they say it's wearing off early in the afternoon, we might do 10, 5 and 5 to try to get their symptoms under control.

Usually, they're having a lot of discussion with their endocrinologist about how are their symptoms doing and are their symptoms under good control? I just had somebody come in the other day and he was having nausea all the time and GI had done this million dollar work up on him and he just needed an extra five milligrams of hydrocortisone and his nausea was completely gone. And so, he'd been just mildly underdosed, but he would have been somebody who a small stressor could have tipped him into crisis and he would have ended up in the emergency department.

Dr. Monee: Along those lines about dosing in the outpatient setting just so that I hear it, is there a need for prophylaxis in the situation of physiologic levels of steroids? I know you're laughing because we, hospitalists just cannot seem to remember or keep it straight, so please help.

Dr. Sara: No, I actually really like that question, because I was giving a lecture on this the other day and somebody asked me, they go, "At what point do you need prophylaxis?" I was like, "Well, not my doses, usually. That's a great question for ID, because I'm always getting the steroids down and I don't want you on those high doses." When you're thinking about prophylaxis, you don't have to do it for the physiologic replacement doses of hydrocortisone. You're looking at those 15 to 20 milligrams. That's about what your body would make normally. And so, that's not immunosuppressing you. If you get up to higher doses and so, there's really good data that doses above 20 milligrams of prednisone, which five milligrams of prednisone is the equivalent of 20 of Hydrocort. So, we'd be talking about 80 of Hydrocort. Doses above 20 milligrams of prednisone for more than three weeks are sufficient to immunosuppress you and that's when you should be looking for PJP prophylaxis, and then glucocorticoid induced osteoporosis prophylaxis and things like that, but not usually at your physiologic doses for adrenal insufficiency.

Now, I'm pretty sure all endocrinologists have those few adrenal insufficiency patients who just make their own hydrocortisone doses and they're on these sky-high doses and we can't convince them to come down, but that shouldn't be the average person with adrenal insufficiency.

Dr. Meredith: So, now let's go back to Mr. Jerry. I think the way we framed this case so far was like, "Hey, Mr. Jerry is coming in. You know he has this history of hypoadrenalism. How do you deal with that initially?" Let's say, he doesn't have that known history, but comes in the same way. So, still coming in with nausea, vomiting, you're worried that this could be like sepsis. We talked earlier that the adrenal crisis should always be on your differential for these patients just in case it's happening, but what's your telltale sign? Are there things that

you're looking for on there like history, physical, or are there specific labs that might point you more into that direction as you watch their course go?

Dr. Sara: Yeah, some of it would be history dependent. So, if you also said Mr. Jerry had a history of rheumatoid arthritis or sarcoid and had been on prednisone for weeks and had recently tapered off, well, adrenal insufficiency would rise much higher in my differential. But if he just, like we said, heart failure, asthma, maybe not. Now, the type 1 diabetes puts you in a tricky spot, because he has autoimmune disease and autoimmune disease tend to flock together. And so, it's highly likely that he could also develop an autoimmune adrenalitis that ends up with adrenal insufficiency. If I have somebody who has autoimmune disease already and they're coming in nausea, vomiting, hypotensive, hyponatremic, hyperkalemic, you've got to have, could this be a new onset adrenal insufficiency? This is adrenal crisis and I need to treat this. So, there are some things in the history that I look for that make me think about adrenal insufficiency.

If I'm getting that hypotension, hyponatremia, hyperkalemia, nausea, vomiting, abdominal pain, it's always going to be in the back of our mind, because it's a can't miss diagnosis. The question I usually get is, how do I tell the difference? How do I diagnose this? Do I just hand out the steroids and put them on and you figure it out later or what do I do here? I think that's a little tricky, because it really depends on when you're looking at Mr. Jerry, how sick do you think he is. If you think you can wait an hour before giving steroids, well go ahead and run a stim test and give him that 250 micrograms of ACTH and get a cortisol 30 and 60 minutes later and seeking his adrenal's function. It's not a perfect test, but it gives you some idea. If he's looking pretty sick and you're worried, go ahead and give him the steroids.

We can always figure out if he has adrenal insufficiency down the road and two or three days of high dose steroids aren't going to cause him osteoporosis, or give him PJP, or anything like that. We can always come back and figure out if he has adrenal insufficiency. If it's on your differential and you've got a suspicion, go ahead and treat it and we can figure out later whether or not he's actually got it.

Dr. Monee: Because it didn't come up earlier with the patient with a known history of hypoadrenalism? I think I might know the answer, but I'm wondering this is the first time that you've mentioned the stim test. So, is this something that you don't even need to do in a patient with hypoadrenalism or just it might be a silly question?

Dr. Sara: Yeah. Typically, and somebody who has a known diagnosis of adrenal insufficiency, somebody has done some amount of work up. They've gotten either that morning cortisol that's so low that you don't have to do a stim test. That cut off varies for primary versus secondary or they've done the stim test and the patient didn't stim appropriately. Somebody with a known diagnosis, we've done that work up. We've probably challenged that work up a couple of times, because all endocrinologists doubt each other and no one believes what somebody else does. If I have somebody coming to me and they're like, "Yeah, I've had adrenal insufficiency for ten years." "Really? Have you? Let's double check that. Maybe you've had recovery."

Usually, we're doing stim tests, not infrequently on them anyways to see if they've had any recovery of their adrenal glands depending on the cost. It's mostly, if I have a new diagnosis or I think somebody might have been misdiagnosed that I'm going for that stim test and it doesn't always end up being needed. You can use in 08:00 AM cortisol and if that 08:00 AM cortisol is really low, you can avoid it sometimes, but for a lot of people, they're not coming in at 8 o' clock in the morning. My random cortisol level isn't particularly useful. I can only use it as a rule out test. So, that random cortisol above 18 is what the guidelines say, there's some new data that says maybe 14 could be okay. But we say standardly 18 says, "Yeah, you don't have adrenal insufficiency. You can make cortisol." If there's anything else, you're stuck

doing that stim test, so you might as well just start with the stim test, so that you're not wasting time.

Dr. Meredith: I assume that regardless of whether you know that this is adrenal insufficiency or not, the steroid dosing that we talked about before is like the same across the board.

Dr. Sara: Yeah, it's the same across the board. When in doubt, when you're worried for adrenal crisis, you're going with those high doses of surrogates just to cover your bases.

Dr. Meredith: In terms of treatments, are there any other treatments that are beneficial from a supportive standpoint that a hospitalist would feel really confident in giving?

Dr. Sara: Like Monee said already, the things that you'd already be doing, lots of fluids. These people tend to end up really volume down. And so, you're going to be giving a lot of fluids. You're going to be covering with antibiotics while you try to figure out if they have sepsis. Typically, a lot of the electrolyte abnormalities are going to resolve with the fluids and the glucocorticoids. Hypercalcemia is typically just going to go away when you treat the adrenal insufficiency and you give the glucocorticoids and with the fluids. It's not necessarily something you have to focus in on and be like, "Oh, man, I need to treat this calcium of eleven. It's going to get better with the treatment of the adrenal insufficiency." It's mostly the fluids, the antibiotics, giving the glucocorticoids and trying to figure out what precipitated this.

Dr. Meredith: How fast do you typically see that resolution of their electrolyte abnormalities? Like next day or does it take a few days?

Dr. Sara: It depends on how severe they are. Somebody with a sodium of 130, I expect I'd see pretty rapid recovery in that, maybe in 24 to 36 hours or so, but I expect that I'd see that normalized pretty quick. It also depends on if they've got something else going on. If they've got a pneumonia that precipitated this, well, there might actually be some underlying SIADH from that pneumonia that's contributing to the hyponatremia as well. Maybe it wouldn't recover quite as fast as I would expect. So, little bit of that depends on what else is going on. If it's just they were marginally dosed and they had some mild stressor that tipped them over, they usually turn around really fast.

Dr. Monee: Okay. Along those lines, I think about this in terms of discharge, because you're probably checking the meds more as you're discharging the patient. So, let's say Mr. Jerry is feeling better and he just wants to leave. Like, he just keeps pestering you. And he's overall improved. You mentioned that if they're getting better, you taper pretty quickly. What sort of things are you looking for to be like, "Okay, they're ready to transition, home," and then what does that look like?

Dr. Sara: Yeah. Usually, like you said, they're telling you, "I'm ready to go home. I'm feeling better. I'm feeling back to myself. I'm ready." It depends on how close I've gotten them back to their home dose because I did 50 Q6, then usually it's 50 Q8, 50 Q12. I might go to 25 Q12. My goal is trying to get back down to 15 and 5. And so, I might go 20 and 20, and then 15 and 15, and 15 and 10, and 15 and 5. So, it depends on where I am in this. If I at 20 and 20 and they're saying they're ready to go, I'm going to say, "All right, tomorrow you're going to take 15 and 15. The next day you're going to take 15 and 10, and the next day you're going to be back on your 15 and 5." We review the sick day dosing. I tell my patients, "This should be reviewed with you every healthcare contact you get, because it's so important." And it's any sore throat, any running nose, double up your dose. Any fever above 38 Celsius, triple up that dose. If you can't keep the pills down, please come in sooner rather than later. Don't wait.

The other thing I always check before discharge is, do they have a medical alert bracelet or dog tag? Because if they're in a car accident or they're ever found down, EMS needs to know that this person needs hydrocortisone, ASAP. And they often have it in the ambulance and they can give it enroute to the hospital. So, I always check that my patient has some identification on them that will tell emergency workers, "Hey, you've got to give this person hydrocortisone."

Dr. Monee: Great. I think you covered the counselling pretty well, actually. It seems like increasing the dose telling them when to increase the dose, and the setting of any stressor, and then making sure they have a medical bracelet. Are there any other things that you like to tell patients as they're heading out the door to help prevent them from having to come back with this?

Dr. Sara: Don't run out. That's often one of the big ones is. Don't wait until you have two days left to call me for a refill, because I don't know that it will get to you in time. I often also make sure that when I'm prescribing the tablets, I'm not prescribing just the number of tablets they need for maintenance. I'm usually throwing in an extra 50 or 70 tablets for a 90-day supply. So, that if they have those stressors, they have extra on hand and they don't have to worry about running out. And so, I usually want to make sure they've got more than what they need, because I'd always rather they take the tablet than not have the tablet and end up in the hospital.

Dr. Monee: I think this is intuitive, but I think we made this point a lot in the Onc Emergency, this episode too. As the hospitals, I'm not doing any of this alone, correct? These are not decisions I'm going to have to make.

Dr. Sara: No. Endocrine is always more than happy and would actually, probably be little bit irritated if you weren't calling us about these patients and saying, "Hey, I have somebody with adrenal insufficiency coming in sick." "Mm-hmm, yeah, I'm going to go see them right now, because I want to make sure that we're on top of all of the steroids and we've given the right amount of fluids and we've got the antibiotics." Most endocrinologists are pretty obsessive about things. And so, adrenal insufficiency is one of those things we like to stick our fingers in. Sometimes, you might just find us there, even if you haven't called us.

Dr. Monee: I was going to say, I'm not going to lie, I feel you guys have a bat signal or something when your patients come in and I'm very grateful every time.

Dr. Sara: Many of them have our direct cell phones or a way to send us a message to say, "I'm in the hospital," so that we can be like, "I am coming, I will see you, I will be there." So, definitely for my adrenal insufficiency patients, they know how to reach me and then I just insert myself regardless of whether I'm asked or not.

Dr. Meredith: [giggles] I appreciate the honesty. I think we can recap a little bit, because I think we've touched on a lot of really helpful information. I think to start broadly, we're talking about adrenal insufficiency and adrenal crisis, which is for us in the hospital really just significant for the lack of cortisol that these patients have. If you have any concern for this happening, whether it is they have a known history or enough clinical clues in the emergency department to trigger you to not hesitate and starting the high dose steroids, if the patient doesn't have a known history and you think that they can tolerate doing a test, go for it. Otherwise, if you have any doubts, just go ahead and start the steroids and figure it out on the back end. I think that's the high points that we hit. Monee, do you have anything else to add?

Dr. Monee: One of the things I liked that you mentioned, Sara, when we're getting ready to send people home is let the patient be the guide. There's no need to force the issue about

tapering them if they're already feeling better and their vitals and labs all look good. So, I think that's a good thing to keep in mind, because I think we all get a little cautious sometimes, and listening to the patient can be helpful, shocking. Anything you want to add to our recap?

Dr. Sara: No, I think you guys hit all of the big key points. I should mention that there is the option for stress dose steroids that you give continuously, because there's relatively new data that came out that said maybe stress dose steroids, maybe they have a period where their levels still fall below physiology. There is an option that you can give continuous hydrocortisone through an IV, and it's 200 milligrams over a 24 hours period, and it's just a stable dose. But none of the hospitals that I've worked at have been able to do that successfully. So, it's not something we typically reach for, because pharmacy is usually able to hand out that 150 of IV Hydrocort, no troubles. The delay in trying to have them figure out how to make the continuous hydrocortisone typically gives me of the heebie-jeebie sense, so I just go for the-- Yeah, just give the IV 100 right now and that way I know they've got something. But there is an option to do continuous hydrocortisone, if it's available at your institution.

Dr. Monee: Great. I think we are ready to go to our next case to Kashlak. Ms. Nancy, she's 78, has a history of hypothyroidism, HFrEF bipolar. She's been stable on her lithium for years and she recently got started on amiodarone for AFib. She was brought into the emergency department by her family. They said that she's been disoriented, confused. Her vitals initially are notable for hypothermia. Her temp is 35. Her heart rate is 49, blood pressure is 80 over 40, starting to panic, and her oxygen saturation is 91%. Her exam is notable for being lethargic. She's got some rails, bibasilarly, and she has decreased deep tendon reflexes. It's similar to our last case with the known history of hypothyroidism. I feel myxedema coma comes to the differential a lot faster in this situation. But one of the things I don't think I've ever fully appreciated is that there's a spectrum from hypothyroidism to myxedema coma. So, what helps you distinguish that from physical exam and that sort of stuff?

Dr. Sara: Yeah. So, not going to lie. I get called not infrequently and they'll be like, "Dr. Markley, this person's TSH is the highest I've ever seen. It is 200. I'm worried about myxedema coma." What I usually tell people is if you saw this patient in your office and you didn't have labs, would you be admitting them to the hospital or would you be sending them home? Because if you're going to send them home, they don't have myxedema coma. If you're looking at putting them in the hospital, well, they very well might. That's what my first cut point is. If they look clinically well, this is not myxedema coma, because myxedema coma is a clinical diagnosis. It's not a biochemical diagnosis, it's not a lab diagnosis, it's a clinical diagnosis. And so, your patient has altered mental status and you think this could be due to lack of thyroid hormone.

Yeah, oftentimes you'll see things like hypothermia, and bradycardia, and hypoventilation, hyponatremia. You'll have these other triggers that give you support. They also typically happen to be older females in the wintertime. And so, you'll have this supporting information that says, "Yeah, this could very well be myxedema coma." At the very least, there's no harm in treating it like it is, because, again, all of the endocrine emergencies, myxedema coma has a pretty high mortality rate, if we don't catch it and treat it. If it's crossing the back of your mind, it's worthwhile going down that path to see if it is and treating accordingly.

Dr. Monee: I think the take home point here is, coma is in the name, people.

Dr. Sara: Yeah. Now, I've also had people tell me, "I don't think this person has myxedema coma, because they can talk to me. They're really slow and they're very confused, but they can talk to me." Well, the coma part is really just their mental status is not a baseline. You

can be lethargic, not answering questions well, not comatose and still have myxedema coma, but you're altered in some way. But, yeah, a lot of them are not really giving you much.

Dr. Monee: Okay. All right. I'll stop being snarky about that. The other piece to hypothyroidism or myxedema coma that I found to be interesting is, if I recall correctly, we maybe don't have the best understanding of the pathophys of this, or do we? Maybe I just don't.

[chuckles]

Dr. Sara: Well, TSH is the gas pedal of the body and thyroid hormone is the gas. You need it in order to maintain regular metabolic functions to be able to control heart-muscle contractions, regular muscle contractions, neuronal conduction, things like that. If I don't have any, well, nothing runs. That's why I get the brain of cardiac, because I don't have anything stimulating my heart to beat faster and I get hypothermic, because I'm shutting down my basal metabolic rate. I'm not metabolizing things to generate heat. And so, some of it makes sense. When I start shutting things down because I don't have enough thyroid hormone to run my body, that's when I start getting the organ failure. And the end organ damage in the organ failure is what I see as the hallmarks of myxedema coma. When I'm having my brain start to fail, that's why I start to get that altered mental status and heading towards coma. So, I don't have any gas in my body. Nothing is running, nothing is working, and everything's going to start shutting down. I need to fill up the gas tank for this patient again.

Dr. Meredith: I guess, keeping all of that in mind, so you're thinking about all this from how the thyroid is affecting the body. We've established that this is entirely like a clinical diagnosis. The thing that I think I struggle with is that when I think of altered mental status as such a key finding for it, I just feel like that's a huge differential that you're actually thinking through. Are there any scoring systems or any other clinical aids to guide you to say, "Yeah, this is more likely related to their hypothyroidism and this could be myxedema coma versus something else that they also have."

Dr. Sara: Yeah. I think there are some clinical findings that can really help point you in that direction. One is their speech changes and it's really hard to describe if you've never heard myxedema speech, but it's slow, thick, slurred speech. They've got a bunch of gumballs or something in their mouth and they're just not able to get the words out well. You can understand them with a lot of work, but it's work. They don't sound right. Their family members confirm this is not how they talk. Then you've got things like their reflexes, which might not just be hyporeflexia, but a lot of that is just delayed relaxation of the reflex. That usually is a pretty good, hmm, yeah, this is something going on with low thyroid levels here, because usually, we're not having that delay in the relaxation. It's fast up, fast down, and that can be pretty subtle sometimes. It's much more obvious when they're truly in myxedema. But sometimes, it's best elucidated when you actually put your finger over the biceps when you're tapping, so that you can feel the delay in the relaxation.

They've got typically the myxedema. They have edema that's nonpitting that you're seeing. They've got their vitals that are all wonky. They're hypothermic, they're bradycardic, they can be hypotensive, and their electrolytes are getting all wonky too with hyponatremia and things like that. It's kind of looking at the whole constellation of the patient because, yeah, there's a lot that could be altered mental status. It could be infection, encephalitis, other things. If it's on there, it's a fairly easy treat and they should start getting better pretty rapidly. Typically, people turn around within a day. I had somebody turn around within a couple of hours after he got his levothyroxine and he was like, "I feel like a new person." I believe it, man."

I feel a lot of endocrinologists might not even say, "This might not be myxedema, but there's no harm in giving them that extra dose of levothyroxine just to make sure and to get them bumped up to make sure that myxedema is not contributing to any of this." It's similar to adrenal insufficiency. It might be sepsis, but the risk of not treating adrenal insufficiency way outweighs the risk of just treating. And so, when I have myxedema coma popping on my radar, I think most endocrinologists will lean towards, "Let's just go ahead and give them a dose of the IV levothyroxine. Fill up the tank a little bit. Take this issue off the table."

Dr. Meredith: So, I think that's a good segue. Let's talk about the thyroid replacement and treatment. Where do you start?

Dr. Sara: Yeah. So, the guidelines say we should start with IV levothyroxine. The reason for IV is because these patients might have gut edema. The bioavailability of levothyroxine and the absorption are not great as it is. It's super finicky. If I also have gut edema compounding that, I want to avoid any absorption issues. We'll give IV levothyroxine and it's usually a loading dose of 200 to 400 micrograms. If my patient is younger, he doesn't have a lot of comorbidities, I'm going to err on the high side of that. If it's a little old lady or they've got some heart history, I'm going to err maybe on the lower side of that with a 200-microgram dose. I'm going to give them a loading dose right now and then what I'm going to end up doing is I'm going to be giving them every day after that 75% of their oral dose in IV form. And so, that's going to get their levels up. You can watch things to make sure this is working. You can get a free T4 level every three days or so, and you can see that their levels are coming up.

Typically, in myxedema, they've got lower undetectable free T4 levels. You can actually watch and say, "Yes, we are in fact getting these levels up. We're treating them appropriately." There is some consideration that you can maybe give liothyronine or T3 as well in addition to levothyroxine. Most of us are really comfortable with levothyroxine. We have a lot of patients who have hypothyroidism and we've given levothyroxine a lot, but liothyronine is not something we have as much experience with. And this is a pretty weak recommendation that the ATA gives. There's some concern that in myxedema coma, maybe you don't convert T4 to T3 as well in the periphery. And T3 is the active form. So, maybe we need to give of T3 upfront to get over the hump of the myxedema, get everything working again, and then we can let it go. There's some thought that you should be giving 50 to 20 of liothyronine in addition to the levothyroxine when you're first thinking about myxedema coma just to make sure that they have some T3 to get things started.

I was going to say the other thing for myxedema coma is you always have to think about, do they have concomitant adrenal issues? Lots of things in endocrine tend to go together. What you would hate to do is to have somebody who has myxedema coma and they also have adrenal insufficiency. They have autoimmune adrenal insufficiency and they had autoimmune hypothyroidism. I don't treat their adrenal insufficiency, because if I try to kickstart my metabolism and I don't have any glucocorticoids on board, I'm going to go into adrenal crisis.

We often recommend that you give people stress dose glucocorticoids as well to make sure you're not missing an adrenal insufficiency, even if they don't have a known history of AI. We can figure out later do they need to stay on the glucocorticoids or not. When you're treating for the myxedema, giving them that stress those glucocorticoids is kind of covering your bases to make sure you're not going to tip somebody into adrenal crisis right after they've been in myxedema coma.

Dr. Meredith: I think you already said this part too, but I guess, you can have variable lengths of improvement. Some people will improve pretty quickly and then some it might be slower depending on severity that they came in on.

Dr. Sara: Yeah. My little old lady, who's got a lot of other comorbidities and has a pneumonia that precipitated her myxedema coma, I expect she's going to take a little longer to turn around than my 40-year-old gentleman who just hasn't been taking his levothyroxine because he didn't think he needed it, and he got a cold, and I give him his levothyroxine, and he turns around in less than a day. It just depends on what else is going on with the patient and what's their baseline health for how rapidly they turn around. But usually, it's pretty quick.

Dr. Monee: Yeah, I think I remember in training at Kashlak that I had a patient. I think it was a communal patient. Everyone was trying to figure out what's going on with the patient. I remember there was like a eureka moment or something by one of my co-interns, and they went down the myxedema treatment pathway, and just like miraculous, the patient that had not been interactive for a while, a hot while, and it was incredible.

Dr. Sara: It's amazing how people can compensate too. We've got people walking around with TSH's of 200s feeling fine, and then you get them some levothyroxine, and they're like, "Oh, I'm a different person." And you're like, "Oh, yeah. Yeah, you are."

Dr. Monee: It's kind of that spectrum that we were talking about. Okay, so, I guess I'm curious now. You mentioned in the adrenal crisis part where you listen to the patient about when they're ready to go home. What does that transition look like for patients with myxedema coma in terms of their levothyroxine? Are you a little bit more conservative here or are you similar, like, listen to the patient?

Dr. Sara: I actually think I'm probably less conservative here than I should be. When I was a fellow, I would get into some trouble for this, because I'd be like, "Ah, he's talking, he's eating, he looks better. Let's just go to PO. We're good." And my attending would be like, "What? No, I don't think so." I still think it's a lot based on the patient and how the patient is doing. If they're talking to you normally, they're feeling better, I don't see any reason to continue with IV levothyroxine. If they're not having any edema that you're seeing, it's fine to switch back to PO. The downside to PO in the hospital is timing. It is a huge pain, because nursing wants to give all of the medications at the same time, which is typically right around breakfast time. And levothyroxine likes none of those things. You're usually timing it to be given at four or five in the morning, and then the patient's mad, because they're getting woken up at 4 o' clock in the morning to take their levothyroxine, and then they can't fall back asleep.

I don't think there's really a right or wrong answer to how you transition. If it's easiest to keep on the levothyroxine IV, fine. I would say, if they've been in the hospital long enough that their free T4 levels have normalized, you definitely don't need to be on the IV anymore. But it is easier from a nursing and patient perspective to give the IV, because you don't have to worry about the absorption that you have to worry about with the oral.

Dr. Monee: In addition to telling them that you will be seeing them in clinic, what other anticipatory guidance do you give them in terms of avoiding it or all those sorts of things?

Dr. Sara: Yeah, so it's mostly, again, take your levothyroxine. One of the weird things about levothyroxine that doesn't hold true for a lot of our other medicines is, if you miss a dose, you can double up the next day. It's all about the number of tablets per week, because the half-life is so long. In fact, if you're really, poorly adherent with this medicine, I can have you walk into my clinic every Monday and do directly observe therapy of levothyroxine. I will hand you all seven tablets and you will take them in front of me and then I will get your TSH levels and show you that it really is just that you're not able to take the medication correctly. It's a lot of just take the medication. And if you missed it, you forgot it, double up your dose.

I do have some people who take the medicine all on Saturday. And they give me a little bit of palpitations because if they ever forget to take it on Saturday, they're going to be in much bigger trouble than if they miss one dose, which is why we tell people to take it every day. But it's all about getting in the correct dose per week, the correct number of tablets per week. That's what I usually talk to people about it. You've really got to get this in. If you have to put it on your bedside table, so it's the first thing you see when you wake up, put it on your bedside table, take it the moment you open your eyes, then go shower, get ready for the day, by that time, you can take your other medicines and you can eat your breakfast. And then you're not having to worry about the absorption issues that come if they're taking it with calcium or iron or dairy products, or you can take it right before you go to bed, as long as bedtime is two hours after your last meal.

Again, you can have it on your nightstand table, you're turning out the lights, you pop that super tiny pill of levothyroxine, it's itty-bitty and you just take it. But you have to take it. Do we need to set alarms in your phone? Sure. Do we need to have pill boxes where your family comes and helps you, if patients struggling with memory impairment? Sure. We've got to get it in and you've got to get it in consistently. That's the big thing that I really stress with patients and their families when they come in with myxedema is you really have to take this medication. You don't want to be back here again.

Dr. Monee: Just outside of taking medications, any other triggers they need to be aware of?

Dr. Sara: That's typically the big thing is, they haven't been taking it or they've been marginally adherent with it. Again, they're on that cusp of their able to hang in. They're compensating just barely, but any small thing tips them over. So, the biggest thing is just getting the medicine in and making sure that they're following up to make sure their doses are correct, because we definitely have people who are taking the same dose they were taking ten years ago and you're like, "That's not anywhere close to the right dose for you anymore. You've gained hundred pounds. We need to fix this."

Dr. Monee: Okay. I think we've covered a lot of ground here. So, I think it's probably we're due for another recap for this section. The first thing that comes to mind is the clinical diagnosis piece. I don't think I had realized that there's kind of a characteristic speech change that happens potentially as a part of the altered mental status. So, that was interesting. The other piece in terms of treatment, IV is done instead of oral, because there can be a fair amount of gut edema, so that sidesteps that part and gets the drug to the patient faster. Anything else, Meredith?

Dr. Meredith: No. I thought the other interesting part was just because we had just talked about adrenal insufficiency throwing on the steroids, because if you start, I think, as Sara said, increasing the gas in their body, they're going to need something to keep them going and everything like that with the cortisol.

Dr. Sara: You'll find with endocrine and endocrine emergencies, as long as it's not DKA. Almost universally, we are advocating for throwing steroids at people.

Dr. Monee: Yeah, it seems like autoimmune disease is running gangs almost [crosstalk] together.

Dr. Sara: They definitely do. Always, if somebody has any autoimmune disease, you're keeping thyroid, autoimmune thyroid, autoimmune adrenal in the back of your head. Autoimmune diabetes in the back of your head.

Dr. Meredith: Cool. So, Monee, you want us to jump to the next case?

Dr. Monee: Case number three.

Dr. Meredith: We got Ms. Eleanor. She's a 74-year-old woman with a history of hypertension and known hyperthyroidism. She's admitted to the orthopedic surgery service because she fell at home and fractured her hip. Ortho is planning on operating the next day for her, but they call medicine because they're like, "Hey, she's got other medical problems. Can you help us with that?" When we're thinking about Ms. Eleanor originally when we're writing this case, we're like, "Hey, surgery. Anesthesia. There's something with that with hyperthyroidism." That was the extent where Monee and I think stopped with our knowledge base. Can we talk through what are potential triggers we should think about for thyroid storm in patients with hyperthyroidism?

Dr. Sara: Yeah, surgery is one, definitely. Nobody wants to take a patient who has uncontrolled hyperthyroidism into the OR because the risk of thyroid storm is so high. We don't want to stress people who are already having something going wrong, like hyperthyroidism, where they could be having tachycardia, or AFib, or heading into heart failure, or things like that. Most surgeons appropriately will not take somebody who has uncontrolled hyperthyroidism into the OR. Unless it's an emergency. They're in thyroid storm and they're not responding to medical therapy and I have no choice but to get the thyroid out. Even then, they're not going to be thrilled about it. They're going to be talking to you about, "This is really high mortality. You know this, right? Are you sure you don't want to do this? Are you sure there's no other medications you can use your medicine?" Surely you have other medications

Most surgeons and anesthesiologists are really cognizant of, "Yeah, you have a history of thyroid disease or you're on methimazole? We want to make sure you're doing really well and that everything is stable before we take you anywhere close to an OR." Again, just like adrenal insufficiency or myxedema, it's any kind of stressor. These people are teetering on the edge, teetering on the edge, getting by just barely. Any kind of stressor or insult is going to could tip them over into storm. Again, storm like myxedema coma and adrenal crisis has really high mortality. And so, we'd like to avoid that, if possible.

Dr. Meredith: I'm assuming you can correct this if this is going to be completely wrong, but in the way we're just talking about myxedema coma, hypothyroidism essentially don't have enough thyroid hormone. Thyroid storm is going to be the exact opposite, I presume.

Dr. Sara: Yeah. You're going 75 in a 30 miles per hour zone. And so, everything's going too fast. You're tachycardic, maybe AFib, you're diaphoretic, you're hyperthermic, you maybe hypertensive. And so, everything is just going too fast. Your GI tract is going too fast, you're having diarrhea, you're losing weight even though you have a ravenous appetite and you're eating everything in sight. And so, that's hyperthyroidism. The thyroid storm is where you've been going so fast for so long, everything starts to give up. I'm getting my end organ damage, I'm getting liver failure, I'm getting heart failure. I have AFib with RVR. And so, I'm starting to have my end organ dysfunction that is signifying that this is a much bigger issue now and I need to treat this rapidly. I don't have time to wait anymore.

Dr. Monee: We're astute, we realized that this is a potential issue. This patient going into surgery. So, what do we do to get on top of it before anything bad happens?

Dr. Sara: Yeah. So, ideally, we're going to have some time and we're going to delay the surgery if we can. Maybe not for this lady with a hip fracture. We probably can't delay this for a very long time. I'm going to get started with some medications to try to shut off the thyroid production. Typically, that's a thionamide, methimazole, or propylthiouracil, commonly called PTU, because propylthiouracil is a pain to say. I'm going to get started with a thionamide. So,

you can't make thyroid hormone. If I really need to take this patient into the OR, well, I can actually transiently shut off their thyroid by giving them iodine. So, super saturated potassium iodine or something called Lugol's solution are both concentrated iodine. If I give iodine, I can turn off the thyroid for a short period of time, where I've saturated all the receptors, everything shuts down, it's not releasing any thyroid hormone.

Now, two or three days after that, it's going to start making a whole bunch of thyroid hormones. I really need to make sure my methimazole is on board already. If this person really needs to go to the OR, I'm going to give some methimazole, I'm going to give some of this SSKI to shut off their thyroid. It also reduces the vascularity of the thyroid, if they're going for an emergent thyroidectomy or something. But those are going to be my best options to try to get this patient through their surgery safely.

Dr. Monee: Okay, so let's say that we don't know the patient has hyperthyroidism or we just maybe it slipped our mind that surgery hyperthyroid bad. What does that look like and then what do I do to fix that on the back end?

Dr. Sara: Oh, so it kind of depends. This patient may fly through really well. If it's a young Graves' patient, not Ms. Eleanor, who's 74 with a hip fracture, but if it's a young Graves' patient, they might come through surgery just fine. The older you are, the more comorbidities you are, the less you have the ability to compensate. The higher risk you are of something bad happening. There's not a great way to predict who, if they're going into surgery is going to end up in thyroid storm. I am not ever in the OR. So, I have never seen this happen. In talking to some of my ear, nose, and throat colleagues, they've said, "The surgery will be going fine, and then all of a sudden, the patient is crashing." It can happen early in the surgery, within the first 30 minutes or it can happen towards the end when they're getting ready to close up and they thought everything was fine.

The ENT surgeon I was talking to said, "Hyperthyroidism is one of the things that scares her the most because she doesn't have any way to predict, is this patient going to do fine or is this patient not going to do fine?" There was some data that said, "Thyroid storm happens equally often if the patient is hyperthyroid or euthyroid on their medications," which is terrifying from our perspective, because if it happens, even if they're euthyroid on medications, how exactly am I supposed to prevent this from happening and how am I supposed to best optimize them? And the answer is we don't really know. And so, they could fly through, they could do really poorly, and there's not a great way to predict which one they're going to do.

Dr. Monee: We've talked about treatment on the back end in a situation where a patient has had thyroid storm. I think this is a running theme and you addressed it in the last case, but can we talk again about steroids? I don't think I've ever talked about steroids so much, to be honest.

Dr. Sara: Yeah, I always find it a little bit ironic for somebody who is always trying to get people off of steroids, how much I talk about how we need to put them on for some people. All right, our patient has had this terribleness happen in the OR, they've gone into storm, they're having the signs of end organ damage, they're not doing well. We're giving them medications. We talked about methimazole and SSKI before to try to minimize risk. After, when we hit the fan, we're doing more often PTU now. And so, I'm going to give PTU. I'm going to keep going with my iodine and then I do have to give my glucocorticoids again. And again, we're going with my stress dosing glucocorticoids saying, again, storm hyperthyroidism, autoimmune disease, most commonly for many people, Graves' disease. And so, I'm worried that there could be a component of adrenal insufficiency going on here and I want to make sure I'm not going to precipitate an adrenal crisis. So, I'm going to give my IV hydrocortisone again.

It also gives me an extra benefit, because hydrocortisone inhibits T4s conversion to T3 in the periphery. It helps decrease the amount of active thyroid hormone I have floating around in the blood causing me problems. In that same vein, I'm also going to want to be giving a beta blocker. The recommendation is for esmolol or propranolol, propranolol is probably what's most commonly used in the US. I'm going to be giving propranolol to slow down the heart rate or help with the AFib and keep them rate controlled. It also inhibits peripheral conversion of T4 to T3. I'm reducing my active hormone with propranolol as well.

Endocrine has a garbage pneumonic for this called the five Bs, which is the worst pneumonic I've ever heard, because literally each one of the Bs is block. It doesn't help you in any way, shape, or form. It's block synthesis with your thionamides, block peripheral conversion with glucocorticoids, block peripheral conversion with beta blockade, block release with iodine, and maybe block hepatic circulation with cholestyramine, but that's not so much used anymore. But it's a terrible pneumonic. Whenever you talk to any endocrinologist, they will be like, "Oh, the 5 Bs," and you're like, "It's just block. They're all block."

[chuckles]

Dr. Sara: Yeah. I have a soapbox on that pneumonic. It drives me crazy. But, yeah, they're getting glucocorticoids too. And so, they're getting a stress dose just like we're giving for myxedema coma and adrenal crisis just to make sure that we're covering our bases.

Dr. Meredith: Is there any other supportive care to provide them? Because at least the beta blocker feels like that's definitely within my realm that I would feel more comfortable with. The others, I'm definitely just asking endo to help me with dosing and things like that. Are there in the way that there were fluids for like adrenal insufficiency or are there things like that we should think about?

Dr. Sara: If they're really hyperthermic, things like aggressive cooling can be used. Again, I'm not sure how much that would be you pulling that trigger versus me pulling that trigger versus us looking at each other and being like, "What do you think? Should we cool this guy?" "Ah, Sure, let's give it a try. It's not going to hurt anything." But that would be maybe the other thing that I would think about is depending on how hyperthermic they are, you might need to aggressively cool this person. You might end up giving your beta blocker as a drip. Instead of like a PO medication, just so that you can control it more readily and you can go up and down much more easily. As they're improving, you can start backing off faster. I think a lot of the time it's mostly endocrine sitting over there running the show saying, "No, yeah, we're going to keep going with this for a few more days" or "Oh, no, I think they're better." We can maybe talk about switching back or cutting back on our doses or weaning off. But, yeah, I think those are the big things.

Dr. Meredith: How long until you would see improvement in these? I'm assuming it's the same as the other cases.

Dr. Sara: This one's actually got some data behind it. So, they should approve within 24 to 48 hours. If they're not improving with our therapies at 48 hours, they need something better. Whether that's a thyroidectomy or plasmapheresis, but if these medications aren't working at 48 hours, you have to do something else, because they're now extremely high risk of mortality and you need to do something. The surgeons are going to want you to do plasmapheresis. You're going to be running down to talk with your colleagues about plasmapheresis and they're going to be like, "I've never plasmapheresed for thyroid storm," because most of us have never plasmapheresed for a thyroid storm. You're all going to be chewing your fingernails watching this patient very nervously while you figure out, is

plasmapheresis is going to work or are they going to have to go to the OR, because they're high risk of death without going and they're high risk of death with going, and I've got to do something.

Dr. Meredith: When you get to that 48 hours' time point, I would think that time is just the utmost importance also for the patient. Often when I think of plasmapheresis, I think of that as just usually little bit more logistics have to go into it than how I think of maybe the patient going to the OR. Does that play into the decision at all?

Dr. Sara: Honestly, this has not been a point that I've had to get to. Usually, if I'm hitting that 24-hour mark and I'm thinking about something, I've already got my ENT surgeon that I've talked to, and I've already gone down and talked with my nephrologist, who's going to be doing my plasmapheresis for me. And we've all sat there and been like, "Not me, not me, not me" because nobody wants to do any of these things because they're scary and really high risk.

Fortunately, our patients have always turned around by that 48-hour mark and we haven't had to go ahead with plasmapheresis. But I'd say it is something where you wanted to involve your consultants early to say, "Hey, I have this really sick patient, and they may very well end up needing plasmapheresis or a thyroidectomy. I'd rather you get on board sooner, so that if we need to pull the trigger on this, there's no delays." It's not a, "you're not in the hospital, you've never heard anything about this patient, you're going to come see them tomorrow," kind of situation. It's a "we've already talked about this and we've already got a plan for what we're going to do." So, I'm usually getting people involved sooner rather than later.

Dr. Meredith: Yeah, I think that's helpful, especially for this scenario where the time frame is so clear, helpful to know that even within 24 hours, if you're not seeing improvement to maybe start getting the ball rolling and expecting some of those things that might be logistically more challenging, I think that I don't know, at least as a hospitalist, I feel that's my one role is to make sure logistics happen in the hospital. That's I think really helpful to know.

Sticking with Ms. Eleanor, let's say she got better within her like 48 hours. How do you now start thinking about transitioning her out of that scary time into the rest of her hospital stay as well as to home?

Dr. Sara: Yeah. That's usually a taper of the PTU and a switch over to methimazole and it's a pretty easy switch. Ten milligrams of methimazole is 100 of PTU. You're trying to get them over to methimazole for long term as outpatient, because it has much less risks than the PTU does with the PTU having risks of liver injury. And so, you're getting them switched over. You're trying to make sure that you have their heart rate down under 90 and then you're going to switch your beta blocker to some kind of XL beta blocker to try to improve adherence. Typically, they're going to go on the methimazole and the extended-release beta blocker and they're going to have rapid follow up because their levels are going to start dropping and I don't want to end up with somebody floridly overtreated who has a TSH of 200.

They're going to have rapid follow up in endocrine clinic, so that we can make sure we're backing off on their doses appropriately and that we're not over treating them and that we're not making them bradycardic and they're walking around with a heart rate of 40 and they needed their propranolol dose halved. And so, they're going to see me typically within four weeks after they leave.

Dr. Meredith: It would be the same time, because I always think of thyroid as like recheck it in four to six weeks is my reflex. So, it would be the same timeline almost. It's still that four to six weeks, I guess.

Dr. Sara: Typically, that's when I have them follow up is four to six weeks. I've been keeping an eye on the free T4 while they're in the hospital, so that I know that they're trending in the right direction. And usually, that's soon enough that I haven't tip somebody over into fluoride hypothyroidism, although I can't say that's never happened. Usually, that's a pretty good time frame to be able to see them back and keep tweaking their medications.

Dr. Meredith: Let's say they were seeing their primary care, they got follow up within a week. Is it worthwhile to check thyroid again that soon or would you almost always wait for four weeks to see?

Dr. Sara: They're going to freak out. It happens not infrequently. That happens at their post discharge visit, somebody get full TFTs and then they're calling me going, "You need to see this patient right now." And I'd say, "No, no, I know. Their levels don't normalize overnight. We have them on medication." "Are they having new symptoms?" "No." "Great." "Okay." They're just going to come back and they're going to see me and they have my number or my contact information to get in touch with me, if they start having symptoms again.

Right now, their levels haven't been shut down for long enough." We haven't blocked production with the thionamide for long enough. This is still the-- or the thyroxine they had in their system. It's going to take a minute for that to come down. And so, don't ever check the TFTs within a week of hospital discharge. That hospital discharge follow up, TFTs should be disallowed. They should not be allowed to be clicked because you're just going to freak out about them. Even if it was something like recovery from non-thyroidal illness, it's going to look wonky and then somebody's going to freak out about it. So, no TFTs at the hospital discharge follow up.

Dr. Meredith: What anticipatory guidance would you give?

Dr. Sara: So, that one's hard, because a lot of things that trigger thyroid storm, we don't have great information for who's going to get triggered or who's not. We know infection increases your risk, surgery increases are risk, but I don't have great ways to predict for this. A lot of the times, if I have somebody who's had thyroid storm, we're talking about definitive therapy because I'm not playing this game with you. We're not going to play around with methimazole and getting your levels knocked out. No, we're just going to definitively treat you, because you're not going into thyroid storm again. We'll talk about radioactive iodine versus a thyroidectomy when they're used by an outpatient. This is one of those times that I'm very clear that I'm not okay with continuing to prescribe methimazole long-term. You were really sick, you were critically ill, you could have died. We don't ever want this to happen again. And so, we're going to do definitive therapy to make sure that it doesn't happen.

For the most part, people are like, "Yeah, no, I never want to go through that either. I'm 100% on board with this plan. You do what you have to do." It works out well for the most part. Occasionally, you'll get somebody who's wanting to be very holistic and natural and doesn't like the idea of taking thyroid hormone replacement. That's just a conversation. If you're going to be taking something either way and hypothyroidism is much safer than hyperthyroidism. If we have to pick a poison, let's pick the one that's much safer and is less likely to kill you.

We didn't touch one thing for thyroid storm, maybe deliberately on my part, but that would be the Burch-Wartofsky score that I always get quoted when people call me for thyroid storm, and they'll be like, "Their Burch-Wartofsky score is 45." This is a scoring system that just

gives you points for different signs of thyroid storm. So, tachycardia and hyperthermia and altered mental status, AFib, any nausea or vomiting or abdominal pain. I tell people I meet criteria for thyroid storm when I walk up two flights of stairs at the hospital. And so, it's not specific. It doesn't tell you that, "Yes, this is 100% thyroid storm." It tells you, "This could maybe be a thyroid storm. It's not something to hang your hat on in the diagnosis. It's good for helping you think about the end organ damage that you're looking for with thyroid storm. Just because they have those things does not mean that they're in storm. Like I said, I meet those numbers by going upstairs. It's something to take and use with a grain of salt. If you're going to be using a scoring system for thyroid storm.

Dr. Monee: I actually think Meredith and I looked at that when we're reading and literally said the same thing, which is pretty easy to get those points and seems maybe not the best tool in really any situation.

Dr. Sara: Everybody, it's in the scoring systems that people look at when they search for thyroid storm. And so, everybody wants to calculate it, but it's just they keep in mind, it doesn't mean that they actually have thyroid storm. It just means it should be on your differential.

Dr. Meredith: Yeah, I think where it's valuable is making sure you're having it in your differential and thinking about it, because it's like a can't miss diagnosis, but, yeah, I think I was on service and looked at my list and I was like, "70% of my patients meet this criteria today." This isn't actually as helpful in that scenario.

Dr. Sara: I think they did a study that looked at scoring people with that score and found that it called thyroid storm in 20% too often. I was looking at that study and I was like, "I think your study is flawed because I'm pretty sure it calls it far more often than just 20% too often."

Dr. Meredith: All right. So, Monee, you want to jump into a recap of some thyroid storm?

Dr. Monee: To recap, when you think about patients with thyroid storm or have a history of hyperthyroidism, specifically in situations with surgery, it's really important to be on top of it ahead of time and generally done with PTU, methimazole, iodine. On the back end, if you happen to maybe not put all that together, it's really important to make sure that you're engaging all the appropriate consultants. Obviously, endocrinology and in the situation where a patient doesn't improve with treatment, within 48 hours they would potentially need something like a thyroidectomy or plasmapheresis, so getting all those folks on board.

One of the things that I also found interesting is, I think the running theme for all of these is that there's just clinical diagnosis, a whole heck of a lot more important than a scoring system, or a lab, or any of that. I feel that rang true all the way through capping it off with a Burch-Wartofsky score. Anything else, Meredith?

Dr. Meredith: No, I think you nailed it. Sara, do you want to go through some take home points that you want to make sure all the listeners got?

Dr. Sara: Yeah. I think the biggest thing is looking at your patient, because none of these you can hang your hat on lab diagnoses or biochemical findings. If your patient looks well, they probably don't have one of these. If your patient looks sick, they very well might and it's better to hedge your bet and say, let's treat them like they do rather than miss one of these diagnoses, because the mortality rate is so high. Again, patient looks well, I don't care that their TSH is 200. They're not in myxedema coma. But you could have somebody who went into myxedema coma with a TSH that's pretty close to normal. It just depends on their ability to compensate and what other comorbidities they have. It really depends on how your patient looks. If these are running through your brain, it's always safer to treat them not.

Dr. Meredith: This has been another episode of The Curbsiders, bringing you a little knowledge food for your brain hole.

Dr. Monee: Yummy.

Dr. Meredith: Get your show notes at *thecurbsiders.com* and sign up for our mailing list to get our weekly show notes in your inbox, plus twice each month you'll get our Curbsiders Digest recapping the latest practice changing articles, guidelines, and news in Internal Medicine.

Dr. Monee: We're committed to high value practice changing knowledge, and to do that, we need your feedback. So, please subscribe, rate, and review the show on Apple Podcast or Spotify or email us at *askcurbsiders@gmail.com*. A reminder that this and most episodes are available for free CME credit for all healthcare professionals through VCU Health at *curbsiders.vcuhealth.org*. Meredith and I really enjoyed putting this episode together with our whole team. The Curbsiders is produced and edited by the team at Pod Paste. Elizabeth Proto runs our social media, Stuart Brigham composed our theme music. I've been Monee Amin.

Dr. Meredith: And as always, I've been Dr. Meredith Elizabeth Trubitt. Thank you and goodnight.

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