

Dr. Stephen Taylor: Hello and welcome back. This is ASAM Practice Pearls, a podcast series from the American Society of Addiction Medicine. I'm your host, Dr. Steven Taylor. I want to take a moment to consider an all too similar scenario. We have two patients; both drink heavily; both stop suddenly. One has mild anxiety and tremors that resolve with a few doses of medication that could safely be taken at home. The other rapidly progresses to seizures and respiratory failure, ending up intubated in the ICU. What makes the difference? How can we predict who will develop severe withdrawal before it's too late?

Today, we break down the critical decisions in alcohol withdrawal management, diving into the ever-changing and unpredictable nature of AWS, where no two scenarios are the same. Making risk stratification not just important but essential. That is why we are so fortunate to have with us today, Dr. Tessa Steele, who is an expert on alcohol withdrawal management, and I am really excited to have her so that I can pick her brain and we can all learn together from her expertise. Dr. Steele, thank you so much. Please say hello to our audience.

Dr. Tessa Steel: Thanks so much for having me. I've been excited about this conversation, in part selfishly, because I rarely get to sit down and discuss a topic I'm so passionate about with an expert like yourself. And I think this is exactly what we should be doing more of—interdisciplinary discussions about an issue that affects so many of our patients and that we all really need to have primary expertise in managing.

Dr. Stephen Taylor: So, let me just start right in with questions. How do you assess the severity of alcohol withdrawal, and what factors determine whether a patient requires inpatient care or can safely undergo withdrawal in an ambulatory setting?

Dr. Tessa Steel: This is the real question at the essence of managing this syndrome, and I think it's important to realize that what we're trying to do is really challenging. We're, in essence, trying to predict the neurobiology in the person's brain who we're caring for with incomplete information.

So even if we knew, for example, the number of drinks that they drink, and with what frequency, and over how many years, we still wouldn't have all the pieces to the puzzle because there's gonna be an interaction with that individual's unique biology. And so, we do the best that we can, using the information that we have, and probably the most important piece of information we can gather is historical in nature and specific to the individual. So, has this person ever experienced alcohol withdrawal in the past, and what did that look like? Because that is a manifestation of that person's experience and their biology and really what we're trying to do, you know. I don't attempt to get more granular

than mild risk for severe or complicated alcohol withdrawal. And severe risk—you know, high risk, low risk—high risk of a severe or complicated course, especially as an intensive care unit doctor, I'm very focused on preventing those severe manifestations. And so, yes, history is one key piece. And then we're gonna think about the objective data that we have access to.

And so, the number one question, has this happened before? And what did it look like? If there were ever any high-risk features like seizures, a history of delirium tremens, needing intensive care in the past, those are things to be concerned about and will put someone in the high risk for severe alcohol withdrawal bucket.

But I also think about any history of blackouts, a history of pursuing addiction treatment in the past, concurrent use of downer medications can complicate a withdrawal experience, and then just trying to get a sense for how much and for how long the individual has had alcohol exposure.

Dr. Stephen Taylor: First and foremost, I like the fact that you're bringing us back to the basics, right? From day one of medical school, what we're told is the history is the most important element of your evaluation of a patient. And then, of course, the second thing we're taught is figure out those things that can kill your patient and make sure you address those first and foremost. And I feel like that's what you're doing, you know, what's gonna put the person in the bucket of the more severe withdrawal possibilities versus less severe, knowing that the most severe could conceivably put the person at risk for a life-threatening withdrawal syndrome, DTS, et cetera. So, I think you're hitting it on the head. But I'm assuming, also, that you're suggesting it's those folks who are in that more severe bucket that are the ones you're not gonna be so willing to try and treat on an outpatient basis.

Dr. Tessa Steel: A hundred percent. It's really, you know, and I'll round it out a little bit beyond the history because not all of us have access to the history when we're meeting someone, you know. Our emergency department providers are sometimes encountering a patient with no historical context. And sometimes, people are critically ill with other issues that they can't provide history. We don't have a social contact.

So, what are the other tools that we have, you know, I think are important to think about here. I love finding patterns in laboratory data. That's the critical care nerd in me. And we can talk about some clues that you might look for and then comorbid conditions that could maybe take a less complicated withdrawal experience and make it more complicated. And so, I think before we think about setting, to round out a little bit more of objective data that we could use to put people in a lower risk versus a higher risk for severe withdrawal bucket.

Exam. We're thinking about fight or flight, manifestations, excess sympathetic tone, which is gonna look like tachycardia, hypertension, tachypnea. Yes, it's hard to know what people's baselines are sometimes. And so, sometimes relative tachycardia and hypertension are not obvious in this syndrome. But certainly, the general exam is critical. I think you can tell if someone is hyper-alert, anxious, agitated and those can be key manifestations of early withdrawal.

On labs, getting at that idea that the individual biology is interacting here with the alcohol exposure. I'm looking for things that show me that there's systemic vulnerability to this alcohol use, organ dysfunction, or metabolic derangement that suggests that the person may not be tolerating this alcohol exposure. So, I do look for classic AST > ALT transaminase elevation. Alcohol can be a potent bone marrow suppressor. And so, I'm looking for anemia and thrombocytopenia. Also an elevated MCV value on our CBC can be helpful.

And then, for metabolic derangements, I do look at the BUN, and I look to see if it's low. Often, we're looking for a high BUN and kidney dysfunction, but low BUN can be a marker of poor nutritional status that is available on any basic chem panel. And so, I teach my residents single digit BUN, you might think about alcohol use.

Electrolyte imbalances are very common. And I think about a pan-hypo electrolyte picture of low sodium and low potassium, low magnesium and phosphate. And then elevated anion gap. You know, if you look for it, you will find it, and it can be a clue for alcoholic ketosis or even shifting into lactic acidosis state.

So, on basic labs, you can get clues, and I frequently find them, and it makes me more or less concerned about an individual. And then the final thing, I think that really applies to people that were considering outpatient management, as well as wherein someone might be best served, is comorbid conditions.

In a clinic, if someone has severe heart failure at baseline, that could be exacerbated by sympathetic activity with alcohol withdrawal. That's a concern. In the hospital, I think about things that ignite the inflammatory response, like sepsis, trauma, burns, long bone fractures, brain injuries. And then alcoholic hepatitis or pancreatitis can really rev up the system that is already prone to being revved.

So, basically, any of those things get flagged, and in my mind, it becomes a higher risk situation where, why not have more monitoring? But I'm also excited about some of the newer studies that are coming out, really supporting home-based withdrawal management and the patient-centered aspect of that. And I think it is important to acknowledge that the majority of people are not

gonna have high-risk features that would prevent a home-based withdrawal management or clinic-based, outpatient-based with closed monitoring.

Dr. Stephen Taylor: That's great. What role do you feel like emergency departments should play in initiating alcohol withdrawal treatment? And how can they support the transition beyond withdrawal management and on towards ongoing care?

Dr. Tessa Steel: Emergency departments are a really pivotal environment for initial withdrawal management. They're also just a critical access point for many people that don't otherwise have access to care. And so, I think for many reasons, it's a prime setting for focusing efforts, and I think really expanding our efforts in delivering AUD care, not just withdrawal care, but transitioning to thinking about AUD management as well. But I also, working in a county hospital, know the limitations of that environment as currently structured. And I think that, at least as currently structured in many hospitals, as we think about the ED as a place of opportunity, I think we also have to think about the health system-wide approach and how could we support the ED basically becoming a setting where we can deliver more withdrawal management in AUD-focused care.

And so, I think that involves more support—support in the form of education and training but also staffing, and that could look innovative. And there's been exciting studies using peer support counselors in addition to social workers that have shown a lot of promise.

We have things like brief interventions that don't take a lot of time, but the more that we can support the staff in the ED to deliver this care, I think the better. And I think we have some more work to do there. And really, I think maybe a big emphasis needs to be in the education front on sharing the positive stories, the success of treatment when it is delivered, and getting people enthusiastic about engaging.

Dr. Stephen Taylor: Absolutely. So, during the second year of my fellowship—because I'm old enough that I did a fellowship that was a two-year fellowship in addiction psychiatry a long time ago—I had the opportunity to serve as the medical director of what was then called the Alcohol Detox Unit at Bellevue Hospital. I only did that for a year, and so it was obviously a very limited experience, but it was a very rewarding experience in part because of what you just described.

The effort was always to get folks to not just complete their detox but to then go on and continue on in ongoing care for their alcohol use disorder. But what I do remember a lot of was how we took care of folks on the unit. And so, I'd love to

hear, you being the inpatient specialist and you doing this now almost three decades after I stopped doing it, please bring me up to date and bring our audience up to date on what is being done now in terms of the best medication strategies for managing alcohol withdrawal. The common challenges that you face taking care of folks who are going through withdrawal management in the inpatient setting.

Dr. Tessa Steel: You know, it's exciting to hear your prior work, though. I think that the Bellevue Hospital is a place where some innovative protocols have really come out of that hospital for managing withdrawal. And so, I've incorporated those investigations into kind of my own understanding and practice for sure.

I think it's very much paired with the earlier discussion about [the] risk profile of the patient, but how can we think about medication selection and dosing? And those are the two things that I am thinking about when I'm trying to decide how to tailor treatment to the patient in front of me.

And so, the prediction of the neurobiology is part of that, right? Because ideally, we'd be able to align pharmacology to the underlying neuropathology. And I think over the last several decades, we've learned a lot more about what is happening in the brains of people when they've been exposed to alcohol chronically.

And so, what are the issues that we're trying to correct with medication? And so, I'll talk a little bit about the neuropathology, in that we can think then about different medicines and what they offer and what they don't offer.

And so, alcohol is acting as a GABA, the main inhibitory neurotransmitter in the brain as an agonist of GABA signaling. And so, it causes sedation, and the brain, in its amazingness, is going to try to adapt to that to maintain a normal state of consciousness by downregulating GABA signaling as it's exposed to GABA with alcohol and then also trying to upregulate excitatory signaling. And the main neurotransmitter there is glutamate. But a lot of pathways become involved. So, on the one hand, when someone stops drinking, we know there is this GABA gap. The GABA agonism that was provided by the alcohol is gone.

And so, I think it's been very natural to think about benzodiazepines as an appropriate class of medicine for filling the GABA gap. Benzos are a pure class in that they really act specifically at the GABA-A receptor to augment GABA signaling. And we know that works for many people. We have many studies showing that these agents prevent seizures and progression to severe alcohol withdrawal. But there are increasing case series and case reports demonstrating that some individuals are what is now known as benzodiazepine refractory or

resistant. And so, it's prompted us to think more about do we need to hit glutamate with our medications? Do we need to antagonize the glutamate system?

And so, there are individuals where I'm very concerned right off the bat. They're already showing severe withdrawal physiology on presentation. So, we're already kind of behind the ball. We're not gonna prevent severe withdrawal in that situation, and we've given a few doses of benzodiazepines, and we're not seeing a great effect even as we escalate the dose. In those individuals, I think more proactively about hitting glutamate. And so, what agents do we have to antagonize glutamate?

Phenobarbital is the most commonly used in hospitals now, and it's had an escalating use nationally in hospital settings in the US over the past decade or so, especially. Though it's an old drug, and there are protocols in the southeast, for example, that were used in hospitals there since the eighties with success. Parts of Europe used barbitol or barbiturate therapy to treat withdrawal very commonly also. But it's a nice agent, and then it offers GABA agonism, as well as glutamate antagonism, and it has shown some effectiveness in these individuals that have benzodiazepine resistance.

I think, in terms of outpatient use, though we don't have a lot of experience or evidence in that space, we are starting to see studies published out of the emergency department with phenobarbital being given and then discharged from the ED to home. And so far, that strategy looks pretty safe as well.

It's an exciting time as we learn more about the neurobiology because I think it opens up other treatment options in the future that have not yet been as well studied, but other anti-epileptics that hit glutamate, you know, ketamine as an NMDA receptor antagonist could be an interesting agent as an adjuvant or primary agent for withdrawal. Gabapentin, which is recommended by guidelines for less severe alcohol withdrawal, also addresses neuronal excitation through calcium channels.

A takeaway from this might be that it is time maybe to step back and think open-mindedly, and maybe get familiar with a variety of agents because we're dealing with an individualized problem, you know, and to tailor to the individual. We can't be super prescriptive always with our agent or our dosing strategy.

Dr. Stephen Taylor: Absolutely. So, I'm curious. I've also read some things, and again, this is no longer an area that I focus on primarily, but I've read some papers on the use of valproate and some other agents, and I'd love to hear your thoughts on some of those.

Dr. Tessa Steel: Yeah. It's similar. Valproid is gonna have glutamate effects as well, and I think that a nice aspect of several anti-epileptics is that you give a loading dose initially, and then you have a maintenance dosing, and frequently, you can check serum drug levels to assess where you are. And so, that's true for Valproate. It's true for phenobarbital. Phenytoin doesn't look like it's maybe going to be as effective for alcohol withdrawal, but it is a similar kind of dosing strategy that people may have familiarity with in treating epilepsy.

But we're seeing that we can achieve control of alcohol withdrawal typically with lower doses of Phenobarbital and Valproate. And so, I think more research needs to be done in this space in terms of targeting serum drug levels, but there's a reassuring aspect to being able to know that you're not at toxic levels of these agents. And I think that's one of the downsides of benzodiazepines at times, is that we don't really know what an effective dose is, and we also don't know where we stand in terms of the patient and the effect and the toxicity.

Dr. Stephen Taylor: And then, of course, that becomes even more important, I would think, when you're talking about outpatient detox, which I know is not something you've done a lot of, and quite frankly, it's something that I have done, but certainly not to a tremendous degree, but that is always a concern of knowing where you are.

And as a result, when I've done outpatient alcohol withdrawal, I've always tried to get some person who could be the impromptu nurse, so to speak, for my patient. Who could keep an eye on them, and can gauge whether or not maybe they seem to be a little too sedated, and make those adjustments like we did in the inpatient setting when we had nurses abound, and could just keep an eye and see, oh gosh, he looks a little bit too sedated so we're gonna back off a little bit, or maybe there's more withdrawal than we expected at this dose so we can increase the dose a little bit. That kind of fine-tuning that we used to do again 30 years ago at Bellevue. I'd love to have the ability to have someone have that at home.

And that's why I always tried to get a loved one or somebody who was obviously not using and a person who wasn't experiencing a substance use disorder themselves and who could care for the person. But that isn't always easily available. And so, it is nice to have agents that can be a little less worrisome in terms of knowing where you are and not having to be concerned about overshooting the way you do with benzodiazepine. So, that's always helpful.

What else would you like for our audience to know about alcohol withdrawal management? What have we not talked about that's important from your perspective?

Dr. Tessa Steel: What are common pitfalls or challenges that we encounter in treating this condition? I think that we need to recognize that we're using sedating agents necessarily and that those agents have worrisome side effects, with the exception of maybe the off-label use of ketamine that doesn't suppress respiratory drive. As a pulmonologist, all of these medicines make me uncomfortable because they stop people from breathing. And so, I think one pitfall, though, is that we tend to develop our practice and our ways of doing things, and if we don't have a diversity of approaches that we feel comfortable with, we'll keep going with the same approach.

You know, we're comfortable with benzodiazepines, so we're gonna give benzodiazepines. It's not working in the patient. And as a field right now, we don't have a lot of guidance on how to change things up and a lot of experience doing that, but I think that would be where I'd love to see the field move, is in what are the adjuvant strategies that can be helpful and getting a little bit more specific about the scenarios in which we would use them. I don't think we have the data there yet, but even just gaining experience with using gabapentin to treat alcohol withdrawal as opposed to benzodiazepines and having that as a tool in your toolkit can be beneficial for certain patients that you're gonna encounter. And if you're on the inpatient side, trying phenobarbital at times as an addition or maybe as a monotherapy, dosing it more like you would for seizures, but lower doses. There's a lot of published protocols out there now.

Having more than one tool in your toolkit can be very helpful for the given patient in front of you. A big passion of mine is that we get very focused on treating alcohol withdrawal, it can be a life-threatening problem. It requires pharmacologic management, and so it captures a lot of attention, but then we don't make that transition into addressing the root cause— the AUD that needs our attention. And we're much better at that in certain settings than others.

And so, in the same way that when a patient comes in, in heart failure with a lot of volume overload, we wouldn't dream of discharging them without goal-directed medical therapies to improve the heart function that led to the volume overload. We're not just gonna treat them with diuretics. We don't have that same automatic response at this point, I think, as a community in medicine, you know, to alcohol withdrawal and immediately shifting to AUD treatment in all settings. And again, that's gonna take the support that we discussed, the education, the additional staff.

Bringing in the addiction consult teams to hospitals has been hugely beneficial. You know, I'm thinking about the work of Honora Englander and Sarah Wakeman at OHSU and MGH and many hospitals that have shown such promise in terms of improving patient outcomes. And they teach all of us how to care for addiction.

Dr. Stephen Taylor: I couldn't agree more. And I think, frankly, even if there isn't a formalized addiction medicine consult team, which thankfully is increasingly prevalent in hospitals, but just the fact that you, the person helping a patient through alcohol withdrawal, are an addiction specialist and you are focused on getting them safely through withdrawal. But I think it's imperative for all of us to communicate that from day one. And quite frankly, we used to do that even 30 years ago at Bellevue. From day one, folks would come in, and we started our campaign to convince them that the withdrawal management is just the beginning. If this is all you do, you are all but wasting your time. We would literally try all kinds of ways to make sure people understood this is just the beginning. You gotta go forward and continue with treatment and, again, having a dedicated consult team. Yeah, great. Perfect. That's the gold standard.

But even if they're not there, those of us who are actually helping the patient through withdrawal management, it seems to me it's our job if we don't have the other folks there to just emphasize that in no uncertain terms. And I think that can be very powerful.

So, I really couldn't agree more. Are there any other pearls that you want to share, especially as someone that's teaching the young minds coming up in our field what would you like our audience to know?

Dr. Tessa Steel: We need more research. We have a lot of medications that can help this condition, but we don't know which are best in which circumstance, and so what we really need is comparative effectiveness research. I think that's a really exciting field, and we need funding. And so, we should be pitching to our policymakers as well.

This is a common problem. When I studied this in the Veterans Health Administration, it was more common than heart attack, you know, and so, really, the resources that we are already spending on this problem, we should be focused on doing it better.

And I think that we can get there with additional research, and it embedded within that, how do we most effectively transition from withdrawal treatment, like you're saying, to long-term engagement in AUD treatment? So, it's a really exciting field because we know more about the neurobiology. We have medication options. We know medications help and, as someone who deals with a lot of brain dysfunction in the intensive care unit, encephalopathy, delirium that is usually multifactorial in its root cause, it's really an opportunity to fine-tune the management of a form of brain dysfunction that we know the singular cause of, we can develop and fine-tune our pharmacologic approach because it's a pretty uniform pathology relative to other syndromes.

And so, I think that makes it exciting for research as well. And so, I would just make a pitch to join the effort to advance this care. And it's an exciting place to work with great interdisciplinary colleagues, much like this conversation. It's exciting to get to chat with an esteemed psychiatrist like yourself, who's worked with adolescents, and here I'm coming at it from the vantage of an intensive care unit, you know, so that makes for fun work and important work.

Dr. Stephen Taylor: Absolutely. Well, there it is. I could not have said that better. I could not have taught people what you just did in terms of how to do alcohol withdrawal management the right way in the 2020s as opposed to the 1990s. Thank you so much, Dr. Tessa Steele, for sharing your wisdom with us.

This has been a really fun and informative conversation. I wanna thank our audience as well for listening to ASAM Practice Pearls and getting yet another opportunity to get some really valuable information.

For more learning on alcohol use disorder. Check out the provider's clinical support system, the PCSS MAUD education. It's free. This comprehensive program will provide expert training, guidance, mentoring on the prevention, diagnosis, and treatment of alcohol use disorder, including various resources related to alcohol withdrawal syndrome.

Also, don't forget to subscribe and share this episode with colleagues who may find this information helpful. We'd also love to hear your thoughts. What challenges have you faced in managing alcohol withdrawal? What solutions have worked for you? Be sure to check us out on social media and join the conversation. Thanks for listening, and we will see you again on our next ASAM practice pearls.