

Dr. Stephen Taylor: Welcome back, friends and colleagues. This is *ASAM Practice Pearls*, a podcast series from the American Society of Addiction Medicine. I'm your host, Dr. Stephen Taylor. Today's episode is part of a special four-part series featuring highlights from ASAM's 56th Annual Conference. In this episode, we're turning our attention to *Emerging Illicit Substances: What Clinicians Need to Know*, a session that drew significant interest at the conference. I'm excited to welcome our respected experts, Dr. Jeanmarie Perrone and Dr. Alaina Steck.

Dr. Alaina Steck: Hi, everyone. Thanks. It's good to be here.

Dr. Jeanmarie Perrone: Hello. Thanks for having us.

Dr. Stephen Taylor: Thank you both for being here. I'm really happy to have you to discuss this great topic. Let me start out with our first question.

Can you give us an overview of your session, the key topics you covered, and why this area is so important right now?

Dr. Alaina Steck: In our talk, we reviewed the pharmacology of a lot of the newer psychoactive substances that are on the market. We looked at recent trends in use, management of intoxication and withdrawal from these classes of substances and then testing for these different agents.

It's important because the landscape is evolving really rapidly, and so clinicians need to be facile with identifying and hunting down these different agents and have some flexibility in how they approach and manage use of these substances.

Dr. Jeanmarie Perrone: I would just say we also come to this from a lens as addiction medicine doctors, but also with a background in medical toxicology and emergency medicine, so it's a slightly different angle of acute care.

Dr. Stephen Taylor: Can you expound on that? What do you mean?

Dr. Jeanmarie Perrone: Sure. So, Alaina and I did emergency medicine residencies and then followed with a two-year medical toxicology fellowship, which is studying poisonings and overdose etiology and treatment. And so that was a natural progression into the work in addiction medicine.

Dr. Stephen Taylor: Absolutely. That's great. So, you are uniquely qualified to address this topic. So, what are the most important takeaways from your session that practitioners should know when it comes to emerging illicit substances?

Dr. Jeanmarie Perrone: I think it's hard to keep up. The landscape is changing constantly. And I think what we really want people to know is: Where are the resources to find what is happening? So, drug-checking services, local warnings from

public health departments. There's a program called the National Drug Early Warning System.

There's a laboratory called the Center for Forensic Science Research and Education that does really active surveillance of novel psychoactive agents. So, a lot of those resources can be readily accessed and can inform what's happening in your local environment.

Dr. Alaina Steck: Another important takeaway is that we often focus on our clinical response when we're talking about a single patient — what do you do with someone who's right in front of you? But our response is not just that immediate stabilization. A lot of what is important when we're talking about these agents are the coordinated efforts that come out.

Efforts to educate other clinicians, to reach out and work with your public health partners, and then to work with the patients themselves to help do things like conduct samples of the substances themselves or of biological samples.

Dr. Stephen Taylor: Do you have a favorite part of that?

Dr. Alaina Steck: I'm a big fan of the patient-level testing. I know Dr. Perrone does a lot with, you know, public health partners and broader approaches to these outbreaks.

Dr. Stephen Taylor: So, really, there are a number of different areas of this work that you can focus on depending on your particular interests.

Dr. Alaina Steck: Absolutely.

Dr. Stephen Taylor: That's awesome. Are there specific substances that are particularly concerning at the moment, and if so, why?

Dr. Jeanmarie Perrone: I practice in an emergency department in Philadelphia. And as I think most of our community knows, we've been really hard hit by very high doses of fentanyl, but also with xylazine as an adulterant. Xylazine has been around for about four years. I think everyone's familiar with the wounds and the problems associated with that.

But more recently, there was legislation in Pennsylvania that regulated xylazine as a veterinary sedative. And so, because of that, we've seen a shift to medetomidine, which is a new veterinary anesthetic that's emerged in the fentanyl supply that's really causing significant problems that we're going to talk about.

Dr. Stephen Taylor: Wow. Does the term "whack-a-mole" carry any significance for you?

Dr. Jeanmarie Perrone: I think that's really what we end up seeing. As soon as we get proficient at something, the landscape shifts, and we have to learn again.

Dr. Stephen Taylor: Yeah. But what that also does is it keeps you on your toes, and it keeps you learning. Absolutely. Is that right?

Dr. Jeanmarie Perrone: We have a job.

Dr. Stephen Taylor: That's right. That's right. What are the biggest challenges that you face when addressing these newer substances in practice?

Dr. Alaina Steck: Yeah. I think there are a couple of issues that we run up against. You know, the first is that with many of these new agents, the clinical picture isn't often clear-cut. I think in our training, we learn about substances in what we call toxidromes – so, toxic syndromes. Does this look like cocaine because it's a sympathomimetic? Does this look like an opioid with respiratory depression and miosis? But what we run into with a lot of these novel agents is that the clinical picture doesn't fit cleanly into one of those toxidromes.

And the other thing that ends up muddying our clinical picture is that people are frequently using multiple substances concurrently – whether they intend to or not.

Dr. Stephen Taylor: That last part of that phrase is the most complicating part of it – whether they intend to, whether they know about it or not. That makes it so much more difficult to deal with. Were there any surprising insights, controversies, or debates that emerged in your session?

Dr. Jeanmarie Perrone: Well, there were a lot of us that put the session together, and we are from geographic representation around the country. So, there are a lot of different local problems that people wanted to highlight. There's been a lot of concern about tianeptine, which is an opioid-like compound that's been problematic in the New Jersey/Northeast area. So, we talked about that. Ketamine analogs, some other new emerging problems in the Rhode Island area. So, I think we are all learning from each other.

Dr. Stephen Taylor: You know, I think that's interesting to hear you say that tianeptine is in New Jersey. I actually thought you were going to say Mississippi. Because I live in Alabama and in Georgia part of the time, and my awareness of tianeptine is as something that the Mississippi delegation of the AMA House of Delegates has been trying to get the AMA to pass resolutions to try to make tianeptine illegal or to do something to curb it. And yet here it is in New Jersey also, so that, to me, underscores the importance of us talking to each other from various parts of the country and really pooling together our information. So, are there any recent data trends or findings that stood out to you during your session?

Dr. Alaina Steck: So, Dr. Wightman, who's one of our colleagues presenting on this, put together a phenomenal resource database about places that you can go, including the National Drug Early Warning System and a lot of other places where people can look for recent trends. So, I think that that is probably the best place to go for any information from this session. And we've included that set of slides as one of our resources if you were to go and look up our session on the app.

Dr. Stephen Taylor: Excellent, that's great. If practitioners could implement just one key lesson from your session in their practice tomorrow, what would it be and why?

Dr. Jeanmarie Perrone: It's interesting. We see a lot of emerging substances. You know, some of the drug-checking results in our area include 10 or 20 substances per sample. And so, I think we try to teach that fentanyl is still the driver of nearly all opioid fatality. So, naloxone is still effective.

There may be people who use multiple substances at one time and don't fully, you know, wake up after getting naloxone in a fentanyl overdose. But still, that restored respiration — so the person is still going to survive the overdose. So, I think despite the breadth and diversity of substances, unfortunately, it's still fentanyl driving most of our problems, so naloxone is still an effective antidote. And naloxone in a regular dosing. We don't really need high-dose antagonists.

Dr. Stephen Taylor: That is so important. I'm so glad you said that because I think a lot of our listeners need to hear that, need to have that emphasized, because there's a lot of mythology around naloxone being ineffective in the setting of a fentanyl overdose. So, I'm glad you said that. Anything else that you would add to that?

Dr. Alaina Steck: I would just kind of reemphasize the point about naloxone — that it really drives home that perhaps in some of these cases where we're not seeing a very robust response to naloxone and we know that there was fentanyl involved, really underscores the point that there are probably other things mixed in. Some of the novel benzodiazepines, for example, can cause a very similar picture, but obviously won't respond to an opioid antagonist.

Dr. Stephen Taylor: Right. So that's good for people to be on guard. Thank you for that. Is there anything else that you want our listeners to know of a general nature or anything else specific, for that matter?

Dr. Jeanmarie Perrone: Thank you. I think that's a great opportunity for me to just share what we're seeing in Philadelphia because it's been pretty unique. As I mentioned, xylazine is less commonly found in our drug supply, and that's rapidly changed over the past year. In May of 2024, we saw a cluster of overdoses that were associated with low heart rates and persistent sedation despite naloxone. And we were able to rapidly test that cluster of overdoses, both local samples of drug

paraphernalia as well as biologic samples from those patients, and were able to determine that the patients were having overdoses from medetomidine.

Then, fast forward about six months later, medetomidine is even more present in our drug supply, meaning more people are getting exposed to it continuously. And we started seeing a very unique withdrawal syndrome starting in the fall, where patients were coming into the hospital describing, you know, their opioid withdrawal symptoms are worse than ever, and that they are using more frequently and having other problems. And so, they would come in for treatment, and within a few hours of getting some opioid withdrawal management like methadone, they'd be kind of quiescent for a couple of hours feeling better, and then very suddenly develop hypertension and tachycardia, a very significant tremor, diaphoresis, and get very, very sick — significantly needing very high dose opioids as well as other sedative agents and often requiring intubation and level of care in the ICU.

So, we collaborated with our Philadelphia Department of Public Health and two of the other health systems in Philadelphia to look at our ICU admissions over that period, and we found about 160 patients who fit this criteria of a unique withdrawal syndrome. We started treating them with dexmedetomidine on the premise that it was medetomidine withdrawal, and we were able to ultimately confirm that those patients had medetomidine in their urine through some elaborate testing at one of our hospitals.

So, we think we have a new withdrawal syndrome that we want to share our experiences with and also share our management strategies. And then you said resources — we did put a lot of this on our website. I direct a center at Penn called the Center for Addiction Medicine and Policy. We have a website called penncamp.org. And on that website, we have a webinar about medetomidine and all of the experiences that we've had so far, including the data that we presented at this meeting in a poster about medetomidine withdrawal.

Dr. Stephen Taylor: That is fascinating. So important and so useful information. Thank you so much for that. Let me ask you this: are there any other anecdotal stories that you can share with our audience that might sort of illustrate some of the concepts that you've been talking about?

Dr. Jeanmarie Perrone: Yeah, I think with the emerging drug supply, it's hard to know. You mentioned that tianeptine is in Mississippi, and I see it in New Jersey. We can't really figure out how drugs move across the country. And so, highlighting this opportunity to reach out and find resources through ASAM is really important. I mean, just today I was at one of the poster sessions and, on our medetomidine poster, a colleague from Vermont stopped by and said that they were also just starting to see less xylazine, less wounds, and now, suspicious that they're seeing medetomidine in Vermont as well.

So, Vermont and Pennsylvania are a few states apart, but, you know, obviously part of the Northeast. So, again, it's hard to predict which way drugs are going to move, and important to just be aware of what's out there.

Dr. Stephen Taylor: Absolutely. Dr. Steck, what are your thoughts?

Dr. Alaina Steck: I had a similar experience today at the poster session, passing by a poster about unprescribed ketamine use and a withdrawal syndrome there. I believe that was Doctors Brown and Terasaki. And, ketamine use is actually fairly infrequent or historically has been kind of on the order of about 1% of the population, but with some of these new ketamine analogs that we're seeing, people intend to get ketamine much of the time, but will end up with different clinical effects, or even now, yet another potential emerging withdrawal syndrome with many of these analogs, what the chemists are doing is adding an atom here, taking off a methyl group there. And that has some really unpredictable effects in things like onset of action, duration of action, intensity of the experience.

You can also start to see some clinical effects that you wouldn't necessarily expect from a typical NMDA antagonist like ketamine. You can start seeing more serotonergic effects or more sympathomimetic effects depending on the specific drug that you end up with. So, it can, again, be an unclear and rapidly changing picture.

Dr. Stephen Taylor: Wow. So, basically, the landscape for the folks we take care of — people who use drugs — is really kind of like a *Forrest Gump* kind of landscape, right? “Life is like a box of chocolates. You never know what you're going to get.” And that is dangerous for our folks, to be honest.

And it also complicates our efforts to try to treat them, because you think you're dealing with a fentanyl overdose, but maybe it's fentanyl with xylazine, or maybe it's fentanyl with medetomidine, or maybe it's both, right?

Maybe it's ketamine. Or maybe it's some analog of ketamine that some imaginative chemist has found a way to play with, right? That really complicates our efforts, but it means that we really have to be intentional about our approach to our patients. So, that is really important. Thank you so much for that.

Dr. Steck, anything you would want to add?

Dr. Alaina Steck: I think I want to circle back to what Dr. Perrone had said about us all learning from each other. We don't have medetomidine at the moment in Atlanta, which is where I practice. Hearing about this and sharing our experiences has been really helpful, because now we are starting to see xylazine creeping more significantly into our drug supply in Atlanta. It is not out of the realm of possibility that medetomidine will closely follow that. So, as a practitioner, it's nice to be much more prepared.

And along those lines, if anyone sees an atypical case, I think the first thing to do is to reach out and talk to your colleagues — not only in the area you're practicing, but in other parts of the country.

And so, you can attempt confirmation with specimen testing. Your poison center is one of the resources that can help guide some of that testing. So, just a plug for the medical toxicology side of things.

Dr. Stephen Taylor: I will go ahead and mention that our incoming president-elect, Dr. Timothy Wiegand, is a medical toxicologist. And yes, he's taught me a great deal about the importance of medical toxicology to the work that we do, as both of you have as well. So, absolutely, and again, I can't underscore enough the importance of us staying in communication with each other, particularly from various parts of the country — which is why ASAM is so valuable. Because, with a quick phone call on speed dial, I can get in touch with folks from any part of the country. And when you have seen medetomidine in your part of the country in Philadelphia, and you haven't seen it yet in Atlanta, it's good for you to be able to pick up the phone and say, "Hey, Dr. Perrone, what is this? What am I dealing with? What do I do about this?" And that's something that we at ASAM bring people together to be able to do — so that is awesome.

Dr. Jeanmarie Perrone: One more comment. You know, I think about a third of the medical toxicologists in the country now practice addiction medicine. And many of us have shifted into this field, both because of the necessity and overlap, but also because of the leadership of Dr. Tim Wiegand, who got a lot of us involved in this work. So, it's great to see him leading this organization this year, but we owe a tremendous debt to our continued collaboration. I really appreciate this opportunity.

Dr. Stephen Taylor: Absolutely. Again, addiction medicine is where it's at. We are a big tent. We have medical toxicologists, we have psychiatrists, we have family medicine docs.

It is really important that we all understand that it's hard to practice medicine in any specialty these days and not know something about how to treat folks with addiction disorders. Thank you both so much for joining us on this podcast and sharing your wisdom. I'm going to say — I'm very biased — I think that *ASAM Practice Pearls* is a great place to come to get some information because we have experts like Dr. Jeanmarie Perrone, Dr. Alaina Steck, and they're sharing their insights from their session at our 56th Annual Conference, *Emerging Illicit Substances: What Clinicians Need to Know*. The full recording of their session will be available in ASAM's e-Learning Center starting May 26th.

Be sure to check it out. Don't forget to subscribe and share this episode with colleagues who may find this information helpful. Thanks for listening, and we'll see you next time on *ASAM Practice Pearls*.

