

**ASAM**American Society of
Addiction Medicine

ASAM Practice Pearls Transcript

Understanding Medetomidine: *Emerging Challenges for Addiction Medicine*

Dr. Stephen Taylor: Welcome back to season 2 of ASAM Practice Pearls, where we turn clinical expertise into everyday addiction care, one conversation at a time.

Whether you're brand new to addiction medicine or a seasoned clinician, this season is designed to support your practice, improve patient care, and promote public health.

I'm Dr. Steven Taylor, ASAM's president and your host for season 2. First, thank you to everyone who shared feedback and topic suggestions after season one. We heard you, and we have some great episodes lined up for this season. We're also excited to announce that this season will offer continuing medical education credits, so make sure to check the show notes after each episode to learn how to claim your credit.

As a reminder, episodes will be released every other week from now through the end of August, so be sure to subscribe to never miss an episode. And now, without further ado, let's get started.

I want to begin season 2 by sharing a section of a recent New York Times article on a challenging new syndrome that has been causing a withdrawal crisis in Philadelphia, and in other parts of the country where it's starting to spread.

"A new drug has been saturating the fentanyl supply in Philadelphia and moving to other cities throughout the East and Midwestern United States. Medetomidine, a powerful veterinary sedative and, if not used every few hours, brings on life-threatening withdrawal symptoms. It has created a new type of drug crisis, one that is occasioned, not by overdosing on the drug, but by withdrawing from it."

"Medetomidine has been detected in the drug supply in Massachusetts, Maryland, North Carolina, Florida, Missouri, Colorado, Ohio, and increasingly in New Jersey and Delaware." So, for this reason, we have invited Dr. Jeanmarie Perrone back to speak more on the emerging challenges of Medetomidine. Dr. Perrone, welcome back to ASAM Practice Pearls.

Dr. Jeanmarie Perrone: Thank you for having me. I'm sorry that we're here under such extreme need-to-know circumstances for our patients, but it's important to disseminate what we are learning to our community.

Dr. Stephen Taylor: Last season, we did an episode on emerging illicit substances where we discussed medetomidine as an emerging adulterant in the illicit opioid drug supply. And for listeners who are new, or who need a refresher, can you briefly

explain what medetomidine is? How it differs pharmacologically from xylazine, and then provide us some insights on what have we learned since that last episode.

Dr. Jeanmarie Perrone: Those are great questions, and pharmacology is fundamental to understanding what's been happening.

So last April, at ASAM, we were really reporting on the experience we had from September 2024 to about that time, March-April 2025, when we gradually saw an increase in medetomidine in our drug checking results, a decrease in xylazine in our drug checking results, and various other adulterants in drug checking, including BTMPS and some caine anesthetics.

So, when we first started seeing patients with this unusual syndrome, they would tell us that this is withdrawal that happens within just an hour or two of their last use, and that it becomes very severe, very quickly. It was very different to them than xylazine, which had also created a withdrawal syndrome. But it was a much more mild, more kind of anxious/anxiety-related, but less of prominent, vital sign abnormalities. Less vomiting than what we're seeing now.

So, the difference, pharmacologically, is that medetomidine and xylazine are both alpha-2 agonists, which means that they bind at the alpha-2 adrenal receptor and use feedback inhibition to decrease sympathetic outflow. When people are exposed to medetomidine or xylazine regularly, just like clonidine, another alpha-2 agonist, you can develop tolerance to the relative pharmacologic effects. But then, as you develop tolerance, when you don't have that medication or drug exposure, you develop withdrawal. And medetomidine is about 10 to a 100 times more potent than xylazine as an alpha-2 agonist, binding at that alpha-2 receptor.

So, what we're really seeing is a much more pronounced, much more severe withdrawal syndrome that has features of clonidine withdrawal, which might happen in patients receiving clonidine therapeutically for hypertension. And then it stops suddenly. People can get a lot of rebound hypertension.

But what we're seeing in this current medetomidine crisis is something that looks a lot like dexmedetomidine withdrawal syndrome. Dexmedetomidine is an alpha-2 agonist that we use in, generally, ICU settings in order to control agitation and to provide sedation without significant respiratory depression.

And when patients are on dexmedetomidine in ICU for two or three days, they're at risk for having a withdrawal syndrome if the dexmedetomidine is stopped suddenly. And that withdrawal syndrome includes high blood pressure, tachycardia, vomiting. And that syndrome is actually a little bit worse if they're also weaning opioids at the same time.

So, all of that really mimics and creates biologic plausibility for us to have determined that medetomidine withdrawal is what we were seeing. We ultimately were able to get some confirmation of medetomidine exposure in our patients who were coming in with withdrawal. But it had taken a lot of effort in order to do that since testing is not available routinely,

Dr. Stephen Taylor: Given what you have described regarding the increased severity of the withdrawal syndrome that we're seeing, there are a lot of folks that are ending up in the intensive care units of various hospitals, as was actually mentioned in the New York Times article. Can you explain a little bit why that is, and what is the recovery from, first of all, the acute syndrome, and then ongoing recovery from medetomidine? What does that look like?

Dr. Jeanmarie Perrone: So, our patients generally present to the emergency department complaining of withdrawal, and many people know that opioid withdrawal is generally managed in outpatient settings with either buprenorphine or engagement in a methadone or OTP.

What's different now is that the patients don't want to go to detox settings or outpatient settings because they know they're going to get really sick. And what they're enduring is episodes of vomiting, these altered mental states, I'll say, patients describe hallucinations. I haven't really seen that. I've seen more of an encephalopathy where their eyes are open, and they can't really answer questions.

But all of that happening outside of the hospital prompts people to come to the hospital, and they generally look okay when they first get there, and within about an hour or two, they develop vomiting and then spikes in blood pressure, 220/120, associated with vomiting, and then usually tachycardia. So, heart rates in the 110-150 or 160 range. So, really prominent vital sign abnormalities, along with the vomiting.

At that point, what we've learned is that if we aggressively treat both their opioid withdrawal and their medetomidine withdrawal with clonidine and full opioid agonists, that sometimes we can stop the vomiting enough to get more clonidine into them, to prevent them from escalating to the full syndrome.

But about one-third of our patients currently still need dexmedetomidine in the ICU, maybe even more than that. Maybe a third to 40% at times. And varies by month. But a lot of patients are presenting to the hospital specifically with the intention of being admitted for this complex opioid withdrawal syndrome because they don't feel comfortable, and they know that other settings can't manage their withdrawal.

Dr. Stephen Taylor: And that's an important point because the settings in which patients do land, need to be, not only prepared to manage the withdrawal medically, but also understand that this still is a part of a substance use disorder syndrome. And then, once stabilizing that person, then providing ongoing treatment, that is going to be helpful.

Can you talk to us about how clinicians should respond, in terms of ongoing treatment of patients, with not only opioid use, but medetomidine use, particularly on an ongoing basis?

Dr. Jeanmarie Perrone: Yes, it's become very challenging. We are seeing some patients who are on the long-acting injectable buprenorphine, or high doses of methadone, who still have some use on top of that. And even that little bit of use leads to medetomidine withdrawal.

At first, we thought that patients were doing pretty well. They're on long-acting injectable buprenorphine, using less than they were using before. But even that exposure of 6 to 10 bags a day, or 2 to 10 bags a day, we're still seeing those patients develop the same syndrome. So, when you think about long-acting injectables as the strategy, that really creates the best safety net for our patients in some cases. Patients are still going back out with, I don't want to say cravings, it really hasn't been officially labeled that. But what we're seeing is patients are leaving the hospital, using again, coming back again. So, we don't really have a way to prevent people from following that craving.

We do discharge a lot of people on clonidine, and clonidine is being tapered as an outpatient. But it seems like, at least in the doses that we're using, it can control some of the vital sign abnormalities but doesn't seem as effective universally in preventing people from going back and using fentanyl with medetomidine in it.

Dr. Stephen Taylor: You've hit on an important point, though, that makes me think about another question that I have, and that is this whole issue of clinicians educating their patients and trying to keep them safe on the front end. How do we do that? How do clinicians keep our patients safe from the risks of medetomidine, and what are the harm reduction strategies that might be helpful?

Dr. Jeanmarie Perrone: We have worked really closely with the Philadelphia Department of Public Health, who convened all of the different emergency medicine physician groups at our three academic medical centers, and really had us work together to create protocols and share our experiences, because this has been really happening in some isolated communities like Philadelphia, like Pittsburgh, but not all over the country.

And so, for patients who are traveling a little bit outside of Philadelphia, but not so far that their drug supply isn't contaminated with medetomidine, when they end up at a suburban or community hospital, they may have a mouthful to say medetomidine, and the clinicians may not be familiar with what they're talking about, can't even look it up because they're not really sure what the patient's saying.

So the Philadelphia Department of Public Health created these palm cards, which are just little information pieces of paper on index cards that they pass out to patients so that patients are aware of what's going on, so that if they get sick, they understand it

a little bit better, and they can understand how to ask for help, and to even carry the card with them if they seek help outside of our immediate downtown hospitals that are fairly well versed in it from this standpoint.

We do have medetomidine test strips, so if there was an alternative drug supply, medetomidine test strips might be effective in steering people to a non-medetomidine drug supply. But in Philadelphia, because it's in about 80 plus percent of the bags that are being checked, it's hard to find an alternative. But if you go somewhere where it's 50/50, or even less, it would be easy to detect it with those test strips.

Dr. Stephen Taylor: Wow, that is valuable information. So there really is an important public health aspect to how we deal with this problem. And so, thank you for highlighting that.

You did talk about your role being in sort of the ground zero, where medetomidine is really prevalent, right in Philadelphia area. But the fact of the matter is, it's a major problem in some other places as well. In Delaware, in Maryland, and I quoted the New York Times article that also mentioned some other places where it's being seen. Why has it emerged so intensely in these specific regions, and what makes these areas particularly vulnerable? And then beyond that, how concerned should clinicians be in other areas?

Dr. Jeanmarie Perrone: Yes, those are all really good questions, some of which we're really grappling with. But I can't answer why, in Philadelphia, we have kind of been ground zero for xylazine first and now medetomidine. But the switch from xylazine to medetomidine does appear to be temporarily related to legislation that was passed in Pennsylvania to schedule xylazine.

Both are only used in veterinary animal work, so they never really fell into the DEA scheduling because they weren't available for use in humans. But despite that, Pennsylvania thought that it would be helpful to add xylazine to the scheduled substances, so there would be more tracking of it and accountability, which was well-intended.

But the unintended consequence seems to be that there's been a shift from xylazine to medetomidine. And medetomidine, again, being just so much more potent, it's having much more of an effect. The reason we think that alpha agonists are added to the drug supply anywhere, is that they are psychoactive, they're sedating. People report that fentanyl was very short-acting. But by adding something that's a longer-acting sedative to that same drug supply, you get a little bit more drug effect for the same amount of fentanyl. So that's why we think it was being added.

The switch from Xylazine to medetomidine is possibly affecting our area more than other areas. Philadelphia and Pittsburgh are about six hours apart, so it is surprising that we would have the same drug supply. But we are hearing a lot from people in the

middle of Pennsylvania as well that they are seeing cases of medetomidine withdrawal.

Now, interestingly, xylazine got a lot of attention because of the wounds, and I would get a lot of calls about education opportunities and wound care talks all around the country because people would find xylazine in their drug supply. They didn't see as many wounds because I think there's a certain amount of penetration in the drug supply and overall prevalence in order for that exposure to add up to wounds or medetomidine withdrawal.

Right now, we are seeing colleagues who are reaching out with cases that seem similar to ours in various parts of the country. But just like we had a lot of difficulty distinguishing our cases from alcohol withdrawal or benzodiazepine withdrawal, and the testing is so difficult to accomplish, that I would suspect that if it's being seen in places, it should be seen in numerous patients, because once it's there, prevalent enough to affect one person, it probably will be affecting a few people at a time. So hopefully we won't see it as widespread as you know, fentanyl has been, but we are on the lookout for it.

It's very difficult to confirm definitive exposure, or really a withdrawal syndrome, until we have a cluster of them, and the drug checking correlates as well.

Dr. Stephen Taylor: Wow. So important. Well, let me just get you to summarize for us. What are the main practice pearls or action items you want folks to take away from this episode?

Dr. Jeanmarie Perrone: I think we want to make sure that people are familiar with their local drug checking community and see what's being detected and how frequently medetomidine or xylazine or other adulterants are in your drug supply, including benzodiazepines, which are commonly added to fentanyl and puts people at risk for benzodiazepine withdrawal. And the patients themselves might not know that there's benzodiazepines in their fentanyl. So, we always need to know what's in the local drug supply to be more informed for ourselves and our patients, and in managing withdrawal syndromes.

Once you may be aware that medetomidine is in your area, we would say that withdrawal presents as something that looks like, perhaps similar to precipitated withdrawal: nausea, vomiting, retching, discomfort. There's really not as much myalgias and dysphoria as straight opioid withdrawal. It's really more prominently hypertension, tachycardia, vomiting. At some point after getting medications, there might be a little bit of a blank stare. I have not seen confirmed seizures. I have not seen confirmed hallucinations. But that is something that is discussed by patients, so that's also possible.

One of the hallmarks would be that giving a patient benzodiazepines or barbiturates to treat benzodiazepine or alcohol withdrawal, which may look somewhat similar on

the front end, doesn't really help and just adds to the altered mental status without really adding a therapeutic benefit. So, something that looks like alcohol or benzo withdrawal that doesn't respond, I would reach for Dexmedetomidine, and you assess the response to that. I think that's probably our best diagnostic confirmatory category at this point. And then, I would hope that your local health departments are interested in tracking this. You know, it's very difficult for any one physician to be able to follow more than what they're seeing, but perhaps a local reporting mechanism would be helpful.

And then, most importantly, I didn't mention this earlier when you mentioned harm reduction, but even though medetomidine is not an opioid, it really factors into the naloxone education that we're doing. We now want to adjust our naloxone education to say that intranasal naloxone absolutely works very well. All of these patients are taking fentanyl with their medetomidine. So, you still want to reverse the opioid, and naloxone is highly effective at that. But the endpoint is really increased respiratory effort and not wakefulness because the medetomidine will continue to have the person be sleepy in the setting of medetomidine-fentanyl exposure. But the respiratory rate will be resolved with naloxone. So, naloxone is still critical and important, but you want to time the endpoints to just the resolution of respiratory depression and not wakefulness.

Dr. Stephen Taylor: That is so important. Thank you for that. So, folks need to know that if they see what they think is alcohol or benzo withdrawal and treating it the way you normally would treat that doesn't get you the results you need, give it a shot with some dexmedetomidine. That's one.

Another is don't forget to report to local health departments, because they're the ones that are going to be able to track all of this, because this is, in fact, a public health concern. And local health departments need to be helpful.

And then of course, don't forget about naloxone. It is very important. People who are using medetomidine are often using fentanyl. Those are such important takeaways. What are the last things that you would want to say or to point our listeners to?

Dr. Jeanmarie Perrone: I would say there are 60% of our patients who are not going to the ICU, so there is a way to manage this with clonidine and OUD management. So, we are coming up with a lot of different regimens. We like olanzapine for the nausea and vomiting, you know, usual opioid related comfort meds. And then higher doses of clonidine 0.2 or 0.4, sometimes as often as Q2 hours to control some of this hypertension and tachycardia.

We also have a lot of information on our University of Pennsylvania Center for Addiction Medicine and Policy website, where we keep up to date on our medetomidine withdrawal protocols.

Along with visiting our website, you could also come see us at ASAM, where a panel of my colleagues and I are presenting on medetomidine withdrawal and alpha-agonist pharmacology.

Dr. Stephen Taylor: I want to thank our expert, Dr. Jeanmarie Perrone, for sharing her updated insights on the emerging challenges of medetomidine. Dr. Perrone, you have been so valuable and so helpful with this very useful information that I think very few people really understand and know, and really, yet so many of us need to know. So, thank you.

Don't forget to visit ASAM's e-Learning Center to claim your CME credits for this episode. There's been a lot of valuable information. Go ahead and get the credit for it now that we are able to offer that credit.

Also, make sure to subscribe and share this episode with colleagues who may find this information helpful.

We'd also love to hear from you. What topics are you interested in? Email us at education@asam.org.

Thanks for listening, and we'll see you next time on ASAM Practice Pearls, where we turn clinical expertise into everyday addiction care one conversation at a time.