Rounding@IOWA: When to Suspect Atypical Recreational Substances

Transcript

[Upbeat theme music plays]

Dr. Clancy

Welcome to Rounding@IOWA, a Continuing Medical Education podcast developed by and for the healthcare team. I'm your host, Dr. Clancy, Professor of Psychiatry and Emergency Medicine and Senior Associate Dean for External Affairs here at the University of Iowa's Carver College of Medicine. Today we will discuss guidance for clinicians to assess treat intoxications and manage withdrawal of a group of atypical, often unregulated recreational psychoactive substances. These drugs are often available online at convenience store checkout areas or on the streets. These substances often have packaging with unproven claims of health benefits and claims of being all natural and safe for use. Our specific objectives today include. First, we want our participants to recognize when these substances may be affecting a patient either with intoxication or withdrawal. 2nd, we want our participants to acknowledge how these substances get in the hands of our patients and where regulation and oversight is not working and 3rd see the role physicians can play in being guardians for our patients, assisting in the banning of these substances from such easy routes of access. Our experts today are Dr. Rachel Morland, Dr. Ben Miskel. And Dr. Daniel McKay. Dr. Moreland is an emergency psychiatrist and clinical assistant professor of psychiatry here at the University of Iowa. She helped staff the University of Iowa Hospitals and Clinics level 1 emergency and trauma center, as well as the emergency services for University Medical Center North Liberty and University Medical Center downtown. Dr. Moreland graduated from Lincoln Memorial University Medical School. She then completed psychiatry residency at West Virginia School of Medicine. She practiced at atrium behavioral health and Wake Forest University before coming to the University of Iowa Healthcare this past year. Dr. Daniel McCabe is a clinical associate professor of emergency medicine. Being board certified in emergency medicine, toxicology and addiction medicine. He is the director of the medical toxicology program here at the University of Iowa. In addition, he is the medical director of the Iowa Poison Control Center. He graduated from the University of Iowa Carver College of Medicine. He completed emergency medicine residency at Chicago's Cook County Hospital. He then completed a toxicology fellowship at Regents Hospital and the Minnesota Poison Control system. Dr.

Miskle is a PharmD at the University of Iowa and a clinical assistant professor of pharmacy practice and science, he also serves in the Department of Psychiatry on the Chemical Dependency service and the University of Iowa Addiction Recovery Collaborative. He graduated from the University of Missouri, Kansas City College of Pharmacy. To all three of you, welcome to Rounding@IOWA.

Dr. Moreland

Thank you so much. I'm so happy to be here.

Dr. McCabe

Thanks for having me.

Dr. Miskle

Thank you so much. It's great to be here.

Dr. Clancy

Well, this should be a very interesting podcast because this is something that is frankly emerging faster than really medicine can keep up. And so this is a really timely and important session. And to all three of you, thanks for joining us today. I just gave the listeners a quick overview of your official titles, but could you give us a sense of what a work week might look like for you? Ben, let's start with you.

Dr. Miskle

Yeah. So my work week, like Dr. Clancy said, I am an assistant professor here, so I do a lot of education, a lot of teaching, specifically around psychiatry and substance use disorder education. And I also work in clinics, so I work in our addiction medicine clinics, both in, you know, a typical clinic setting as well as an urgent care style walk in clinic. So I get to see patients in clinic and work with a full interdisciplinary team.

Dr. Clancy

And Rachel, how about you? I know you're new, and so you're just easing into this job. At least talk about what you will be doing as well as what you have been doing back in North Carolina.

Dr. Moreland

Yeah. OK, so like you said, at the time of this recording, I haven't started working yet at the University of Iowa, but I will be embedded in the emergency department as a psychiatrist picking up psychiatric patients with primarily psychiatric concerns coming into the

emergency department and taking care of them as the primary physician. At Atrium where I worked before in North Carolina, we had a standalone psychiatric emergency department. That was partnered with a medical emergency department, but it wasn't physically connected to it, and I think that's fairly uncommon. People would come in to the psychiatric behavioral health emergency department and we would see them as primary patients. They would come in as walk-ins. The ambulance would bring them in, and we would see them and treat them. And sometimes we would admit them to the. In patient psychiatric units that were attached to the emergency department sometimes. You would discharge them with follow up so it works just like a regular emergency department, but it's all psychiatry and behavioral health, so that's what I generally did in my previous job. But I can't wait to see what happens in this new one.

Dr. Clancy

Yep. Yep. Well, we're glad to have you, Dr. McCabe, one of the most varied professors we have on campus. Tell us what a work week looks like. For you.

Dr. McCabe

Every week looks a little different. Almost every day I assist with the care of poisoned patients and managing poison scenarios, whether that's through phone consultations with the Iowa Poison Control Center bedside consultations that UHC or the outpatient clinics that we have here at UHC. At my core, I'm an emergency medicine physician. So even with the other responsibilities. I continue to staff the emergency department whenever my schedule allows and typically this happens on evenings and weekends, but every week is a little different.

Dr. Clancy

Absolutely and thank for all three of you every hour. Is a little bit different as well. So you all have very interesting and varied work assignments. So could you give us a sense of what drew you to this work? How did you end up doing what you do? And Dan, we're going to start with you.

Dr. McCabe

Sure. I believe I just got lucky. I've always enjoyed managing the undifferentiated patient and working within a multidisciplinary team. So that emergency medicine really fit and being the safety net for patients even made emergency medicine a complete natural fit for me. And then when I went to residency, I knew I wanted to pursue a sub specialty training. I knew I was probably going to end up in an academic practice and we had a large number of toxicologists who were deeply committed to teaching and patient care and academic work.

And I was fortunate enough to interact with them quite frequently, and that exposure likely played a major role in guiding me towards medical toxicology.

Dr. Clancy

Ben, how about you very much not a typical Pharm D job that you have.

Dr. Miskle

Yeah, absolutely. You know, I always kind of joke that I kind of found my calling through things that I found challenging. So I typically didn't really like working with the brain. So I found myself going and pursuing A psychiatry residency program. I found substance use to be very interesting in the setting of why don't we have better treatments for this and why don't we do things differently and why don't we treat these like other disease states? And I really was drawn to those patients who are underserved and not getting good medical care that they should be. And so I kind of found myself just being pulled towards this situation and also being pulled towards an area that I may be able to help more. And so I really found myself in residency, I did a residency at the VA in Ohio and found myself kind of being pulled to substance use disorder treatment and wanting to really enhance that care and see how we can make it better.

Dr. Clancy

Great. Great. And Rachel, emergency psychiatry is not for everybody. Tell us what drew you to this work.

Dr. Moreland

Yeah, absolutely. I really love having variety in my work and I really enjoy every day being different. I think psychiatry in general, you can have a lot of. Breadth and depth and variety in your work, but especially emergency psychiatry. I get to see really a little bit of everything. I really enjoy working with acute psychiatric emergencies like psychosis, acute mania, things like substance use and addiction. You see a lot of, but also the kind of like Ben was talking about, the social issues and patients that really have a lot of trouble navigating these systems and having access to good psychiatric care. The emergency department is really the first place that they go and we're kind of the first line of people that have the opportunity to see them and treat them and really working as part of a multidisciplinary team with social work and pharmacists in the emergency department is huge. For me too, I don't know where I would be without social workers and pharmacists.

Dr. Clancy

I think we all like the team aspects.

Dr. Moreland

MHM.

Dr. Clancy

So today we're going to be learning about a group of recreational psychoactive drugs, for example, Kratom. Or Tianeptine, bath salts and Diamond Shruumz that fall through the regulatory cracks and are remarkably easy to get? See some of these at convenience store checkouts and wonder how did these get here? Who makes these? Who then sells these to the owner of the convenience? Store. From start to finish, how does this get in the hands of our patients? Who wants to take a stab at giving us some clues as to how these substances come about?

Dr. Miskle

I can kind of take a stab 1st and we'll go from there, but these kind of fall under the umbrella of designer drugs just in, in general, which are typically produced in these unregulated labs, if you will. And these unregulated labs really bypass those quality and control standards that we have set for other foods, medications and then they're typically shipped to the US repackaged. And sold to stores for resale.

Dr. Moreland

In the case of like tianeptine and phenibut, what's interesting is that they are medicines in other countries. So Tianeptine was called kind of an atypical tricyclic antidepressant, but it works. We can talk a little bit about tianeptine later, but tianeptine and phenibut they're used to treat things like depression and anxiety, but they're not approved here for. Used by the FDA as a medication. And sometimes that happens because they just aren't as good as other medications that we already have that can be prescribed or produced for less money. Sometimes it's because they have some sort of concerning component about them that we think maybe they're not as safe, but that's kind of where tianeptine come from.

Dr. Clancy

Dan, you know you interact with statewide organizations and the state ride services anything to add?

Dr. McCabe

Yeah, the regulation or unregulated in of these products is extremely nebulous. Most of them can be sold more as supplements rather than medications or they can be sold under the guise of being not for human consumption or for nebulous claims. And that essentially allows them to be unregulated. And this isn't a podcast discussing completely regulation,

so I'll try to stay out of all that. But essentially, if there are illegal substances in them. Then the DEA doesn't have jurisdiction, and if they're not being packaged or sold as a medication or food, the FDA doesn't have the jurisdiction. So essentially they fill this void of regulation and unless you can prove there's something that is illegal in them, you know there's essentially anything can be put in there.

Dr. Clancy

Wow. I know we are kind of moving into a world of medical freedom and so it's possible that even more of this stuff will fill the markets with stuff that's really unproven and untested. Do you have a sense of how easy these are to get, you know, you see them right in the convenience store checkout right next to tic Tacs. And if you want to find them, is it pretty easy to get?

Dr. Moreland

Yes, sure answer. They're pretty easy to get. You can really walk down to a smoke shop or a vape shop and you can purchase things like kratom. Sometimes Tianeptine is sold to look like little 5 hour energy drink concoctions. One time I was passing a smoke shop and they were doing like a Buy 2 get one free sale. Like if you got 2 delta 8 THC products they would give you a free sample of kratom. That was a couple of years ago, but it's just so incredibly easy to get these things in gas stations. Like you said, convenience stores.

Dr. Miskle

I'll just kind of add to that. I remember the first time I ever saw a sign advertising kratom. I was in Ohio and driving to my new residency site and I saw a sign that said kratom legal pain relief. And I thought that's kind of interesting. We never put legal coffee sold here, you know? And so it was just kind of interesting advertisement online accessible in stores. Many stores across the US and across varying states.

Dr. McCabe

The majority of the effort is just picking only one product, but you can get them anywhere.

Dr. Clancy

So my sense is it seems like they're becoming more and more available and they become more popular as well. What's your sense on the trends of as far as use and really the appetite of our society for these substances?

Dr. McCabe

Ben, you want to start considering that literally this is what you see all day long. I definitely have my thoughts, but.

Dr. Miskle

Yeah. I think trends with these are very interesting and some of these are being sold and being used for different things. And I think that's one of the big things to kind of note is that not everybody using a substance like this is intentionally using that substance to become euphoric or feel this quote UN quote high, right? Some of these are being marketed as things like they can be used for opioid withdrawal. Or they can be used for pain. I've had people tell me that they started on kratom, for example, because they told somebody that they didn't want to drink coffee, but they wanted something to pick them up a little bit and they were sold it at a tea shop. And so the use around these is kind of being marketed in a lot of different ways. But you can find many different reasons to use a lot of these substances just depends on kind of what. Questions you're asking and what your goal is with using the substance. It's not very dissimilar to what we do with, you know, over the counter products otherwise.

Dr. McCabe

Yeah, I would say it's really hard to give an accurate estimate to the general question of psychoactive substances because there's so many out there and it's not really clear sometimes when we're having these general conversations about what all substances we're including in this conversation, like Ben just brought up, there are a lot of over the counter substances that are regulated by FDA that people misuse. For various effects, I mean, classic examples are Benadryl, our Robitussin, or any of our cough syrups. And so if it's hard unless we define exactly which ones we're talking. But most of these substances are technically legal and honestly, most healthcare providers really are unfamiliar with them. Besides, the people kind of in these rooms, most people don't even have a starting point to start a conversation in our in our provider field, some providers will try to compare the effects to other, more classic substances they learned about in school. Which can work, but most of the time doesn't really apply and. The thing that I always like to talk about, you know, as a poison expert, I have some bias in these conversations because we don't have data on people who use these substances and don't have any problems. People aren't calling their Dr.s or poison centers or other agencies when they're actually having a positive effect without any negative issues. That means that some of our numbers are going to be a little nebulous, a little understated about use versus harm. But based on my experience and conversations with toxicologists, other directors of Poison center are addiction medicine colleagues. The use of these overall is increasing.

Dr. Clancy

Rachel, anything to add there?

Dr. Moreland

Yeah, I think to go off a little bit of what Ben said, a lot of these products are being marketed in such a benign safe consumable looking way they look. Like supplements and vitamins, they're marketed as being nootropic or cognitive enhancer, is, and almost like a health and Wellness field type of product placement, they look like chocolate bars. So I think people get the sense of them as being more benign and safe than perhaps they are so. Kind of like what Dan said too. It's really difficult to gauge the level of. Use, especially if we as providers are not asking people about them and they aren't necessarily right now getting any sort of sense of harm from them. Then we really just have no idea and a lot of these substances are used together and with other substances as well. So it's hard to get a good. Finger to the pulse.

Dr. Clancy

The federal government has had, you know, significant limits on THC and even research on THC. And so most of the published literature on THC is retrospective looking at the harms of it, because that research can be done. But we don't know, you know, what THC can do going forward as far as benefits because the research has really never been done.

Dr. McCabe

Well, in the research it wasn't legal to have research being done on any benefits because you make something schedule one. That means that you can't do the research. And I'm certainly not saying that it's that it's good for you. I'm not certainly not saying it's the worst thing for you, but as you just brought up Gerry thing something like THC, it's just a classic example of. We don't have the data even though it's been around for a long, long time.

Dr. Clancy

So. You mentioned that you know it's really a lot of different reasons why someone may start into these, but is there a higher risk demographic group or set of demographic groups?

Dr. Miskle

I would say the hard part here is that you know, again we don't have great studies showing us or great data trend showing us who's using what of these substances and part of that problem is because we don't ask the questions as clinicians, hey, are you using this substance or that substance? You know, we focus on the key substances, but we don't get into a lot of these. I would say what I see more in the literature, though typically it revolves

around younger populations using some of these substances. But you know, in terms of having the data to support that we don't really have a ton of data around, you know the demographics using these sort of substances.

Dr. Clancy

Rachel in the emergency room. Any anymore common group that you see at least presenting with this?

Dr. Moreland

Not particularly the demographic that I see using kratom is actually. Younger males, who also have a history of a different type of substance, use disorder. And that's just what I see in the emergency department, and they're usually coming in for something else completely. Their primary concern isn't ohh, I'm withdrawing from kratom or I have a weird side effect to this phenibut or whatever. So it's hard to it's hard to get a good sense, but it usually is typically like maybe. 25 to 40 year olds.

Dr. Miskle

I think it's interesting in that space too. Specifically things like kratom and tianeptine we may tend to see follow kind of more trends that we see with opioid use disorder, more so in general kind of in that same time frame that Dr. Moreland said, as well as that, you know, we may see opioid use disorder more in kind of that time frame or at least more overdose deaths than that. Kind of general age range and so maybe there's some sort of correlation between that, but we don't know that for sure because we don't have the data to support it.

Dr. Clancy

So. Well, before we get into kind of more specifics on each. These let's talk a little bit about the ultimate dangerousness of these some of these. So I recall a morning in downtown Tulsa that when the emergency medical system was flooded with calls for ambulances because there were overdoses occurring all over the downtown with K2 and at one point there were 20 different individuals with delirium and seizures. On the sidewalks. So can we talk a little bit about the lethality associated with some of these substances? Every drug in excess can be a toxin, so, but let's talk a little bit about how bad it can be. And Dan, I'm going to start with you.

Dr. McCabe

Well, it's very difficult to accurately estimate the overall lethality of these substances, like any intoxicated agent, they certainly can increase the risk of traumatic injury. But we've also we've been involved in some unfortunate clinical outcomes where the substance

probably played a role, but in most cases, when you look at the medical examiner report. There are multiple substances and multiple clinical factors involved. From my experience, most of these deaths that are linked to these substances were reported to us only after the patient had been already been found or they had already been deceased. And then we're looking at post mortem levels, which are very different than alive biologic samples. And whether or not a provider could have been involved earlier and could change the outcome, that's really unclear at that point. But also, since most of these substance aren't included in standard post mortem testing, we're left with very limited data to make reliable estimates on the true lethality of any of these individually.

Dr. Clancy

You and I have talked. There's a lot of stuff out there that we have no ability to screen for as far as blood work. So let's start in with kratom, something that I am seeing more of in the emergency department. In fact, a few weeks ago had somebody come in with a large zip lock bag full of kratom. And we're going to go over several of these substances, but let's just have a general conversation about where did it come from? How long has it been? Around. What are some of the slang names? How does it work on? A molecular level. And what are the desired effects? And then we'll talk about how to undo it when it's too much. So who wants to start in on kratom. Rachel? You gave a great grand round with kratom as a big section, so let's have you start in on what we need to know about kratom.

Dr. Moreland

Sure. So kratom is, it's a plant that originated from Southeast Asia. It's been around for a very, very, very long time as a whole plant used for specific remedies in that part of the world. The genus species name is mitragyna speciosa and. Generally, we use it as the whole plant form. We don't take the active mitragynine, which is kind of more of the active ingredient for kratom like we do with like cannabis, right? So, it does as a whole plant, a lot of different things. It works on a lot of different receptors. Some of those receptors are the new opioid receptor does have some new opioid activity. It also has some serotonin effects, some dopamine effects. So, it can touch a lot of different receptors. People use it to get kind of euphoric, maybe similar to opioid effect, but some doses or strains of kratom people also use it as more of like a stimulant effect or like a kind of concentration and focus. Sort of effect. So it's a very it's a very interesting drug.

Dr. Clancy

Got it. What does intoxication look like when it's too much? How sick are they? What do we see when? When would you think, oh, this might be kratom?

Dr. Moreland

So they look generally kind of a little bit of altered mentation kind of drowsy. We don't actually see a whole lot of respiratory depression with kratom use even high levels of use. Maybe Dan can talk a little bit about that. I think it has something to do with it not activating beta arrestin pathway. So we don't see as much of that. But otherwise it looks a little bit like an opioid intoxication.

Dr. McCabe

I completely agree. Honestly, the last time I've heard beta arrestin pathway was when I was thinking about kratom probably a year or so ago. In cases of true toxicity, it most of the time mimics an opioid toxicity, but we need to recognize there's an entire spectrum when we think about toxicity, right? Are we talking about not feeling well? Are we are, you know, kind of subjective? Are we talking about having withdrawal states? We're talking about completely obtunded with respiratory depression. All those things can happen. And so, you know, the treatments for that are essentially in the toxicology. We're all we describe, those as supportive care. But that doesn't mean that we put up our hands and think we can't do anything. That means if we think they have respiratory depression, we would give them a loxone if they have any symptoms specifically or any abnormalities on in their labs you work through those, you treat them supportively with different medications for nausea if they're starting to withdraw and I say that because you know, if the patient comes in and I'm sure I don't want to step on anyone else's toes when I want to think about my addiction medicine colleagues and the work that they do, I tend to want these patients to kind of come out of their toxicity smoothly. And so we can have a good conversation with a meaningful conversation about their use. And maybe get them into the next steps of conversation rather than completely thrown them into a withdrawl. And we've kind of stopped the ability to have those next conversations.

Dr. Clancy

And Ben, that's often when you get called. Hopefully you get called that people recognize what Rachel said is you know, this is an opioid activation. And so there's an opioid reaction happening as well. Once the intoxication is over. So Ben, do you get called in to help with some of the withdrawal protocols we might use?

Dr. Miskle

Yeah, absolutely. We definitely treat patients from our clinic with kratom use that meet criteria for opioid use disorder. And sometimes they meet every criteria for opioid use disorder. And so we treat them as if they do have opioid use. Disorder. And so with that, there are a lot of studies out there that actually show that treatment with medications for

opioid use disorder, specifically buprenorphine is most often cited as being really effective in treating cravings and withdrawal for patients with kratom use.

Dr. Clancy

Rachel, how about you? You know, you gave a great presentation on yousef, buprenorphine. And I know you work in the emergency setting, so it's hard to look at the continuity aspect, but.

Dr. Moreland

There have been a couple of patients that I talked about, one in my grand rounds, actually a lady who had a very long, significant history of opioid use disorder had been sober for 10 years. She actually had been overusing her tramadol and she was bridging her prescriptions with kratom, and then she was visiting a friend and withdrawing from kratom. And so we talked a lot about transitioning her to buprenorphine naloxone. And people tend to have very good success with that. And you can use it to kind of taper down and. Reach stability that way and Wellness that way. Or you can maintain them on the MAT just like we do anyone who's sober from opioid use disorder and being maintained with their stability. On MAT, you can continue them on it to maintain stability. And people have had very good success. I think there was one paper that tried to kind of stratify like level of use in grams of kratom and what doses are helpful and effective with buprenorphine naloxone. But that's one paper. And I think usually you just treat the patient that's in front of you to see kind of the benefit with that.

Dr. Clancy

Yeah. And they come in with bags of kratom. It's hard to hard to know.

Dr. McCabe

And Gerry, when it's sold here in a powered form, so when it's entered the US market, that can remove the a reliable way to really assess potency and it's very common as a toxicologist that people want to hand us baggies of drugs and have us and don’t get me wrong sometimes. When we think it's a it's a credible threat. Our state hygienic lab. A will test it for us. We're very fortunate to have them in this region. Or if we think that there's an academic interest, we can, you know, find a specific. Like lab, but the reality is most of the time, even when those studies show things like grams, it's well based on what you know it, what's the product that we're starting with. And as this has been marketed as a natural pain reliever and then also as a recreational substance, it's a very interesting to me that Rachel just brought up. Some patients will use it to try to. Wean off of other opioids or to help with other opioid dependence, but I've certainly taken care of, and I'm sure we all have taken

care of patients where this is their first opioid they've used probably. Because. It's so easily available and so some patients, you know, every patient's a little different on why they started using it or why they're dependent upon it now.

Dr. Clancy

Great, Ben.

Dr. Miskle

Yeah, if I can just add one more thing here too. Is that a common theme that we'll talk about today as well is again remembering these are all unregulated products and so intoxication and withdrawal may present very different from one case to another depending on possible contaminants or you know what the actual substance actually is.

Dr. McCabe

Or what other medications they're on?

Dr. Clancy

Absolutely. We'll talk about that big umbrella of bath salts. So let's. Move over tianeptine. And kind of the same set of questions. What is this? Where did it come from and what are patients trying to get out of it? And when there is withdrawal issues, how do we treat it? Who wants to start on tianeptine?

Dr. McCabe

I mean I can start with tianeptine if we want. And my colleagues can obviously correct any misstatements that I make. But tianeptine is, like Rachel brought up earlier. There is a mu opioid receptor, agonism properties of it. But it's also some vague anxiolytic effects. A lot of them have been reported. Some of them haven't really been proven. It's been around since the 80's, the 1980s and at least in 24 countries that I'm aware of, it's classically kind of marketed more towards depression. It's never been brought to market here in the United States. So in the US it's been marketed as a nootropic. So essentially to help sleep aid kind of. Improve that kind of balance is kind of a nebulous term that will be used for things, but it's commonly called here in our in our country, in the United States as gas station heroin, there's also street names called Zaza Tianaa Red there's a few other ones, so it's also an unregulated product that is a recurring theme here. It's really kind of hard to determine how much use is too much before you get dependence, but it's believed that tolerance of tianeptine actually occurs really rapidly. And patients tend to use more to try to almost like, seek a recapture of the short lived euphoric effects and they take more and more and more. That's kind of what's classically described. Every patient's obviously a little different. Now

when we think about what signs or symptoms people have, agitation can actually be a presenting symptom of the withdrawal and then treatment for the withdrawal. Independence is really, really, really difficult because besides just treating them for an opioid use disorder, which they may have depending on the individual patient. Many times they also need to have adjuncts added to actually treat their anxiety, because you're taking away the anxiolytic apart. Part of this too.

Dr. Clancy

I certainly remember the basics of pharmacology that those substances that come on fast are the ones that can be very, very attractive and alprazolam is one of those. And heroin is one of those. Cocaine is one of those. And so now we have tianeptine as well, Ben and Rachel, anything you want to add about tianeptine being as far as? Intoxications and use before we get into withdrawal.

Dr. Moreland

Yeah. So people do seem to know or have an awareness. Sometimes that is used to treat depression and anxiety. So sometimes I have seen more uncommonly than using it as an opioid. But sometimes I have seen people say that they've been using it to kind of try to treat their own depression anxiety very similarly to how people have used kratom to try to self treat depression and anxiety. And then the half life is so short, it's 2 1/2 hours. A lot of the products that we see, they can be like anywhere from 5 to 200 times the amount of actual tianeptine as the medications over that are actually prescribed in Europe. So huge amounts of this substance in these products that people can just buy at a gas station. And the withdrawal is very much an opioid like withdrawal, but because it's also got some effects on, like dopamine, norepinephrine, there might be some. Increase like anxiety, agitation, tremulousness. Some people describe a little bit of a brain zap like you would see with an SNRI. So it's very interesting, but definitely mostly predominantly an opioid withdrawal type of picture.

Dr. McCabe

I would say as an emergency provider, when I see a patient that I think is dependent upon these, even though I'm relatively comfortable with managing patients with substance use disorders, I would reach out to my addiction medicine colleagues or my psychiatry colleagues for this withdrawal. Because a lot of times these aren't as quote simple as straight opioid like withdrawals. And you know, if they're continuing on down their anxiety, there might need to be an adjunct and that starts stepping outside of my role. So I know I commonly talk to our addiction medicine team about this and I try to get them into their clinic.

Dr. Clancy

Ben, what would you like to add?

Dr. Miskle

I'll just add, you know, both Dr. Moreland and Dr. McCabe presented this very well that there are some other things going on with this drug that we don't necessarily fully understand yet, very similar to kratom in a lot of ways too that we may see some of this kind of norepinephrine type withdrawal or serotonergic type withdrawal because again, we don't always fully know what's in these. And so, you know, I do think we need to be prepared for some other symptoms that maybe something like medications for opioid use disorder doesn't completely cover in terms of serotonin withdrawal or things like that.

Dr. Clancy

Rachel, I'm going to come back to you and Ben. Again, is it time? Is there enough opioid activation that is time for buprenorphine? For some of these patients?

Dr. Miskle

I would say absolutely yes.

Dr. Moreland

I would say yes. Sorry, Ben.

[laughter]

Dr. Miskle

I was gonna say absolutely.

Dr. Moreland

I agree. I agree. Definitely there are. There are some good studies to show that buprenorphine naloxone can be very, very helpful and effective in these patients. And some of these patients have co-occurring substance use disorders too. So we're always kind of like treating again, like I said before, we're treating the patient, we're seeing what would be the most helpful for them, but anytime. We have, in my opinion, my thought processes. Anytime we have a patient that has any sort of opioid dependence or addiction, then buprenorphine naloxone is an incredibly safe medication and it's shown a lot of benefit in maintaining sobriety and Wellness in these patients. And so there's a lot of reward compared to a pretty low risk for use.

Dr. Clancy

All right, let's move on to phenibut. Similarly, what's it doing and what's intoxication look like and what do we do to help the patient once they're ready for something better than where they are?

Dr. McCabe

I can go and start feel like I lost a few months of my life and fellowship related to phenibut, but we had some really very complicated cases, and then it was becoming very popular in the Midwest. Are my fellowship. And so we published a case series so. So I'll tell you my thoughts on phenibut overall it it's a very interesting substance. So it was reportedly invented by the Soviet Union as an Inotropic agent for their cosmonauts, it's been marketed to improve sleep or depression, but the data doesn't really show true clinical benefits in that realm. The mechanism of action. The more you dive into it, the mechanism action becomes extremely nebulous. It has gabapentinoid structure with GABA activity, probably more GABA B than GABA A and also inhibits because the gabapentinoid activity also inhibits voltage dependent calcium channels and it may inhibit endogenous. Phenethylamines. Well, so, So what does all that mean? Well, the clinical effects for intoxication are extremely broad. So an intoxication, sedation can happen. Delirium agitations or even seizures. So kind of the whole gamut can come from this. For an intoxication part for withdrawal can also be extremely broad. And the spectrum can be kind of all over the place. But it can. You can also come in with agitation, delirium or seizures, and those withdrawal can be extremely difficult to treat. So presumably we don't have the good data, but we presume it's probably the withdrawal are all so hard to treat because the GABA B effects to this very similar to Baclofen. And so due to this, sometimes extremely high doses of benzodiazepines, herb arbitrates are used in the inpatient setting to get patient through the life threatening withdrawal states, but then also sometimes Baclofen papers or similar can be used, but it's has to be tailored to the individual patient because we don't really have good guidelines to guide us on these.

Dr. Moreland

I think because we don't have very good guidelines, if I ever see a patient who has any substantial amount of phenibut use and like substance use disorder criteria met and they would like to detox from it or we're concerned from withdrawal, I would medically admit these patients because you're you may end up using. It looks like a severe. Alcohol or benzodiazepine withdrawal and that you can get an encephalopathy and delirium. You can get seizures and they usually need high levels of benzodiazepines, phenobarbital, and then like Dan said Baclofen and you can see. Higher than kind of usual doses of Baclofen when

you're treating these patients? So I definitely think they need to be closely monitored for sure.

Dr. Miskle

Yeah. I think one thing that's really interesting with this is if you actually look at the chemical structure of it, it's very similar to Baclofen. It's one chloride difference. And so that makes it kind of interesting. But then the other thing to really consider is exactly what they just summed up, which is we're looking at almost a very severe type alcohol withdrawal. And so doing this. Outpatient or in an ambulatory care setting is probably pretty risky, and I don't know of any data that would. Support it in any way, shape or form, but I think the other thing that's kind of interesting is you can almost use medications like we do for alcohol withdrawal in the setting of benzodiazepine or barbiturates or Baclofen to try to taper these off, but I really can't emphasize enough that if somebody is going to stop this, we need to treat them and taper them off of it in order to help reduce the risk of seizures and other. Other GABA type side effects.

Dr. Clancy

Just amazes me it's not illegal, just amazes me.

Dr. McCabe

I would say through the state, through the poison center. We manage a decent number of these and severe withdrawal states as in patients. And you know what? What was just brought up, the amount of benzos or the amount of different adjuncts that we have to add on to get these patients through is pretty impressive. And it's not that uncommon that we have to go to such extreme levels that patients end up in ICU's. I'm not saying every patient certainly does not need to go to ICU, but the individual patient, it really is a reassessment to safely get them to withdrawal.

Dr. Moreland

Yeah, certainly for the first couple of days, they should not be on a psychiatric inpatient unit where you can't do telemetry. You can't do drips. They need to be over there in medicine for sure.

Dr. Clancy

Excellent review. Let's move to a more vague category. Bath salts, Dan, you and I have casual conversations in the emergency room with mystery patients where we don't know what's going on. And every once in a while, the conclusion is maybe this is bath salt. So kind of what falls under the umbrella of. Bath salt.

Dr. McCabe

Just with that introductory question, I would say it's such a broad misleading term to describe something as a bath salt. Most of the time when we're talking about bath salts, we're thinking about synthetic cathinones. And cathinones in general, they're a chemical that's they are related to a naturally occurring substance found in the plant cot. The only pharmaceutical cathode you're likely to encounter is bupropion. And because that sometimes people will intertwine bath salts with bupropion a little too much because there's a big difference between them. But the it's a very broad there are hundreds, if not more, bath salts to lump them all together. It's very over generalized.

Dr. Clancy

Is it mostly ... It's just a hyperdynamic activating intoxication that we see with too much dopamine, too much, too much norepinephrine, too much serotonin.

Dr. McCabe

Yeah. For the most part, cathinones have a stimulant like effects patients might present with agitation, delirium, hallucinations, seizures, hyperthermia, dysrhythmias, rabdo, even coagulopathies, and also some patients on a different spectrum could just show up. And they have a little bit of mild anxiety. From having a little bit of a bad trip, so it is the spectrum. But when we think about cathinones and if we relate it back to the medication that we know about. Bupropion we know that that is it what we call NDRI, but it's also they're also serotonergic. So essentially dopamine, norepinephrine, serotonin so essentially are catecholamines. So you can think of it almost similar to a sympathomimetic but with some caveats there, but definitely stimulatory.

Dr. Clancy

Rachel, anything you use kind of in the acute setting when you see a bath salt intoxication in the emergency room?

Dr. Moreland

So if they come in with an acute, like altered mental status or agitation. I actually haven't seen it. Anecdotally, in real world practice too much, at least that I know of. Maybe a lot of people have been using bath salts and. Just haven't known, but we usually treat with benzodiazepines first and then sometimes with antipsychotics. But I my first go to is actually benzodiazepines.

Dr. Miskle

And I'll just, I'll just insert my ploy here as a psychiatric pharmacist, but again, always trying to treat patients orally first with some of those benzodiazepines or antipsychotics and then moving to the other things like I am if we need to.

Dr. Clancy

Absolutely.

Dr. McCabe

I guess if you're going to bring up bath salts in general, we should touch a little bit on what some of the street names are because some of our listeners might have heard, you know, there's national stories about these different things and there's so many different ones. But there are things like cloud 9 or Flocka or Bromo, dragonfly ivory Wave, vanilla sky, white lightening are very kind of classic ones, but the reality is that's only the tip of the iceberg. There's actually a really interesting book in the toxicology world called Fical, which is phenethylamines. I've known and loved by Alexander Shulgin, who actually he and his wife actually created, essentially our initial phenethyl means in our country. And they wrote a book about it. It's kind of a classic book in the toxicology world, and that was honestly in the United States, probably a step towards. creating hundreds of phenethylamines and cathinones, but recently there's a research group in California, Huffman's lab. I can't remember which. Which institution they're at in the California, but they actually are making it's whenever you see a JWH cathinone, that's actually one that they're making in the lab to try to create benefits of using these different things. So. The reality is, is there's hundreds, if not more of these. Some have been described of how they make them. Some are not. But a lot of times when you hear things like Bromo Dragon Fire Flocka, those are just classic examples of bad outbreaks in the area.

Dr. Miskle

The other thing we can kind of add just around regulation is a lot of these, the FDA or other groups DEA have tried to regulate bath salts, but all it takes is 1 chemical change in the structure to now make that legal air quotations around legal there in order to be sold again or rebranded or relabeled. And so these are these are really hard to even possibly think about removing. Completely.

Dr. Clancy

Sure. Just adding one chloride.

Dr. McCabe

And that makes it medically very difficult to manage something new to your area, because if one gets regulated and taken off the market, so to speak, well now you're introducing an entire new substance to the area and we can presume what may happen in that, but not always. Sometimes you get these outbreaks as something that are. Change in that chloride group change in that hydroxyl group has given you an entire different outcome that people weren't expecting I would make a plug towards in these situations where your area or you have a patient that's different than what you would normally expect. I'd strongly recommend calling your local poison center because a lot of times poison centers are the first to detect the patterns of these emerging substances in a region, and we actually have a surveillance system. In real time surveillance systems to public health. That a lot of times if your local region, you know your local ER clinic, anything like that, where you're seeing people having very different outcomes. Sometimes the poison center is the only way to actually have that be surveillance. So we've that's how these things start and you get regulation your you get law enforcement, you get public health agencies involved to try to figure out what's going on locally.

Dr. Clancy

Again, great reviews. I want to finish up with the story of Diamond shrooms and how the surveillance system can actually make a difference as far as improving safety out there for our society. So first of all, who wants to describe what diamond shrooms are and some of their dangers before we get into the impact and? The responsiveness of the system to try to make the environment safer. So let's do a quick overview of diamond shrooms.

Dr. Miskle

I think the brief quick overview here is diamond shrooms. They're really kind of synthetic psychedelics and they're related to siloe, Sibin and Silas and. But they have a number of reported concerns specifically to poison control centers and products have had other multiple contaminants in them, including things like per gallon or DMT or other psychedelics that were not expected to be in there. And so you know the risks really with it or that have been reported or seizures decreased. Consciousness, respiratory failure, multiple other things. But those are kind of the big concerns that have been reported.

Dr. Clancy

Rachel, I've not been exposed to these yet. I had. You've been exposed to those.

Dr. Moreland

I have not personally in my practice, been exposed to diamond Shroom, so it's exciting for me to be a listener and a learner as well, but for my findings it does seem like a lot of the issue that we have is that it's marketed as one thing and then we're finding a lot of adulterants or things that may have intentionally been just put in there and not disclose. As a different ingredient because I think Sila Sibin in its just general form wouldn't necessarily cause all of these like seizures and acute significant poisonings that we see. But there's a lot of different things that can be in these diamond shrooms that can be potentially pretty dangerous.

Dr. Clancy

So Dan, can you circle back around to this is an example of where you've been able to make the environment a little bit safer. So let's talk a little bit about point Control Center and what you did on a bigger system.

Dr. McCabe

Yeah, so diamond shrooms as they were brought to market, a company sold them with a variety of different products and very quickly there were cases reported nationally of effects that were besides just putting people in intensive care units that were just not coinciding with what you would expect from what should be. In there. So our bedside toxicology team and our poison center were actually some of the first identifiers of these nationally. And I'd like to shout out my colleague, Dr. Josh Trebach. He was on call and actually was the one that put it all together. So we had at least one patient that started at the university, one that got transferred to the university. And then at that same day. We had, I believe, two other cases in the state. Elsewhere. And he put it together of whoa, this is something new is happening. We immediately we're in contact with our state Health and Human services agencies. And the reality was they immediately put out the conversation to the national agencies. And thanks to these, to these established. Surveillance systems. The outbreak was quickly recognized as a public health emergency within days, and the CDC, the FDA, HHS, America's Poison Center, coordinate this rapid national response, and that included interviewing patients, literally driving to the hospital if a patient came in, and talking to the patient. Analyzing product samples, identifying retail stores and seeing what was on the shelves. And they were, and they actively worked to remove these things from the shelves as soon as possible as Ben brought up when the testing was done on some of these products, they found a wide variety of substances that were not listed that were not marketed to be in there and. Even when we get that list, even that list doesn't actually fully explain the wide clinical effects that we were seeing from these patients. So the success story though, is within a month of the initial reports of these and the bad clinical outcomes

we had this coordinated multi agency response led to a nationwide recall of the products and this was described by some of the individuals that we were working with the CDC on these big zoom meetings across the country, some of the officials. Should describe this as one of the fastest national public health interventions ever. Executed and so this was a powerful example of why bedside clinicians should report unusual or concerning exposures to a poison center or toxicology service as soon as possible. So as that individual provider may only see one case toxicologist or the surveillance system that we have may receive multiple reports and identify a broader pattern. In a region. And so that's gonna be the first step in a public health response. So this was a big success. The products that had these were taken off the shelves. So hopefully this is not going to happen again soon or ever, but very, very happy about that response.

Dr. Clancy 48:30

It's great, it's great. Just a few more closing questions. We touched on it, but these don't show up in our traditional drug screens here in drug screens. But and Dan, you and I have talked about kind of a higher level of screen that should be available at least at some of our. Medical centers is their ability to test for these substances when resources are unlimited.

Dr. McCabe

When resources are unlimited, sure, the vast majority of places there's only a few hospitals in the country that are going to do non targeted testing in real time. There are a few places that will do that, but very rare, but even then you need to have catalogs of what you're going to be looking for. So even those places, if it's not in the previous identified catalog, it's not going to come back as positive. But we do have really big reference laboratories across the country that you can send them panels. But it's. Not a it's not a panacea. You have to kind of tell them a little bit because they need a lot of sample to identify a lot of. Things. So I would come back to what I tell providers when I'm teaching, I guess, trainees. And most clinical conditions diagnosis is dependent upon a good clinical history and a physical exam, and then you support that with appropriate testing. So if there's a, there's rarely a single test, even urine, drug screens. I think most people recognize the limitations of those most. Tests do not provide a definitive answer without the clinical context behind it, so I stressed that clinicians should return to the fundamentals and feel comfortable reaching out for help when they have questions or concerns.

Dr. Miskle

To piggyback off of that, just a minute to, you know, in our addiction medicine and colleagues and all of our resident learners that rotate through with us and our fellows. We always say if you just ask the patient, talk to the patient, they'll usually tell. You. And a urine

drug screen or drug screens in general, just don't come back to that patient interaction and don't really do much more if the patient already tells you. Yes, I've been using XY or Z. So talking to the patient is the most important aspect of this.

Dr. Moreland

I agree to also piggyback off of that. Getting a good history, especially like a non judgmental history asking specifically. About certain things. If you suspect something is key, sometimes I phrase my questions like using the words party, drugs, supplements, drugs off the street, but that may not even be specific enough questioning as what I'm learning there, I had a friend who was working on call for the Poison Control Center. And they got a call about a patient who was being started on naltrexone monthly long acting injectable for alcohol use disorder. And they went into a florid what seemed like opioid withdrawal. And it turns out they were using grams and grams of kratom. Four times a day and they hadn't disclosed it, possibly because we hadn't asked specifically enough if they had been using something like that. So good learning lesson for everyone involved.

Dr. Clancy

Yeah, very much so. Cannabis has become so ubiquitous now that when I ask patients about it, are you smoking any marijuana? Ohh yeah, lots.

Dr. Moreland

Yeah, people will tell you people will tell you if you ask.

Dr. Clancy

You 3 are very up to date. It's amazing your depth and knowledge on these very current things that continue to evolve. Any guidance to our listeners on how to stay current on this is there, is there a strategy that you use to stay current?

Dr. McCabe

I guess I can start. I personally I feel like it's extremely difficult and for some providers that this isn't their realm or their arena, almost impossible to stay fully up to date on this. Remember, you know we have a lot of people here that devote their life kind of to this part and we have a difficult time staying always up-to-date, same as our colleagues that don't do this for a living. Stay up to date on their part of medicine all day, every. Day. So for us in our arena for people here, we do take an ethical approach of trying to stay engaged. Locally and nationally, that means reviewing the literature. I'm trying to always stay up to date on the literature. Modern public health announcements, participating in committees nationally and regionally. Being on list serves national. And most important, listening to our

patients, because sometimes you'll actually get the biggest impact in your local area. I've thought well, a patient told me this 2 days ago and now I have another patient here today. And next thing you know, you start having more and you can feel the ebb and flow. So truly listening, but it's very, very, very difficult to stay up to date. I think anyone. And medicine to recognize it's hard to stay up to date on anyone specialty to ask anyone outside our world to be completely up to date would be very difficult. That's why I would just recommend reach out to the teams that do devote their time to this.

Dr. Miskle

And I would say I've been humbled by patients a few times in the setting of they tell me a product that they're using. And I say, what is that? Teach me about that. And then I get to go look it up as well and so don't be afraid to allow yourself to be, you know, humbled a little bit when you approach some of these new topics that you have no idea what you're even listening to.

Dr. McCabe

Our patients can be some of the best teachers. It is amazing that sometimes we get into this, this false sense that I have a doctorate. That means that I should know everything about this chemistry and then you have a patient that. As. A lot less education, or maybe minimal education, and they will come up with very complicated ways to actually get the substance that they want or to manipulate that substance in whatever way. And you talk to them and you actually realize, yeah, you might not have the bona fide degree, but you actually know how to use that chemistry. I completely agree that our patients, the more you listen to them, the more they'll teach yeah.

Dr. Clancy

Last question and it's for each of you what are some of the take home points you'd like to leave with our listeners. And Rachel, we'll start with you.

Dr. Moreland

Sure. So big take home point. I would like to really drive home. Is that just because something is sold at a gas station or looks like a candy bar or looks like vitamin doesn't mean it's benign, it doesn't mean it's safe and it doesn't mean that it's quality controlled even a little bit. Right. So we need to be careful what we're putting into our body. Allies and really just having a good awareness of what these things can actually do.

Dr. Clancy

Great. And how about you?

Dr. Miskle

Mine would be regulation and I don't necessarily mean making things illegal. What I mean is regulation around testing, regulation around quality control. This could really promote safer use as well as allow us to continue to research some of these substances. Too. And then whereas making these illegal would only further contamination risk as well as unsafe use, and potentially drive these underground. And so the biggest thing I want to say is we need increased regulation around quality control and testing more so than we do trying to make all of these drugs illegal because again if we try to make it illegal, it's going to be modified and there'll be a new product tomorrow.

Dr. Clancy

Dan, how about you?

Dr. McCabe

My take home points would be I think we all need to recognize that recreational substances are going to continue to be used by our patients and the specific substances and circulation will keep changing based on societal or personal factors of the of our individual patient. So I encourage anyone managing these patients to focus on the fundamentals. Take a thorough and nuanced history, perform a thorough exam, reassessed frequently if they're having clinical effects. And I also would say that just because of a provider has previously managed a patient that has been poisoned on any recreational substance or has helped with some kind of withdrawal state in the past doesn't mean the next case will have the same outcome unless they're, you know, they truly have a true expertise and what's kind of on the market now. If you're looking for a test to guide the care of the poison patient, I would say the test is a solid exam in history and then everything else should be dictated from that. And then after that. Up if you're uncomfortable, or if it's something new, just reach out to your experts. We're very fortunate here at the University of Iowa. We have so many people that devote their careers to this, that everyone is not just willing to help. Everyone wants to help. And so people like our addiction medicine colleagues are psychiatry colleagues. I feel like I pick their brains all the time. And I. I don't want to speak for them and put words in their mouth, but I would be shocked if any of our colleagues in that realm would not be really happy to help in these scenarios.

Dr. Clancy

Great job. Wow, what a great session. You guys, to our expert guests. Thank you for joining us on Rounding@IOWA. And thank you for the work you've done helping us all understand the always evolving market of atypical recreational psychoactive substances. For our

listeners, you can access instructions for CME and CEUs within our show notes, and as always, we hope you join us again on another session of Rounding@IOWA.