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# XYLAZINE: WHAT CLINICIANS NEED TO KNOW

Joseph L. D’Orazio, MD, FAAEM, FACMT, FASAM, FCPP

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## **Xylazine: What Clinicians Need to Know** **[video transcript]**

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Dr. Joseph D'Orazio is an emergency physician, medical toxicologist and Addiction Medicine Specialist at the Lewis Katz School of Medicine at Temple University in Philadelphia. He cares for temple patients in a variety of settings, including the emergency department, and inpatient consultants service for addiction medicine and toxicology, the trust clinic, which is an office based Opioid Treatment Program, and begin the turn temples low barrier access street medicine program, Dr. Drew Asiel, also served as a medical toxicologist for the poison control center at Children's Hospital of Philadelphia, and is regarded as a regional experts around substance use and substance use disorder treatment in Philadelphia. Over to you, Dr. Gracia.

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Thank you very much. And so we'll get started here about xylazine just want to point out that I have no financial relationships to disclose our learning objectives. And so we're going to learn everything that I know about xylazine. And so trends over time, what is what is happening at the, from an epidemiologic standpoint, the physiologic and toxicological effects of xylazine. We're talking about the wounds associated with xylazine, which I think was really hot topic. And then managing overdose and withdrawals are what we know and what we can do to help manage this. And then we'll wrap up with some harm reduction strategies that are relevant to substance use, including fentanyl and xylazine. So this topic has really taken an upswing as of late and certainly maybe back in 2018, we just first started discussing this, if he started as a problem in Philadelphia, and sort of the news as like continued to spread throughout our nation. And more and more stories sort of pop up, and especially with just yesterday, the Oakland DCP making this an emerging threat xylazine an emerging threat the United States. And so this is a major topic here. And so but how did it start? You know, I think most people here would know a little bit about xylazine. If your topic on this conversation, it's a veterinary medication that's used for procedural sedation. It's used in small and large animals. It's not a controlled substance as of yet, in the United States. And veterinarians typically use this in combination with opioids to do procedures sort of hit the market, the illicit market, mostly in Puerto Rico's our first sort of, you know, account of this in the 2000s, known as Anastasia de cabeza. And this is a drug xylazine was used in combination with cocaine or opioids, or even sometimes alone. And then it sort of migrated to the mainland us. And we first started seeing reports of xylazine news in 2006, and Philadelphia, but really didn't see a big uptick in it until 2018. But mostly find it in bags of heroin, fentanyl, in Philadelphia. And while there are more recent reports that it's found in other substances, including like pills, counterfeit pills, we're mostly seeing it in the glassine bags. And the reports that we've received is that it's always been an added supply locally, so it's not coming in, added prior to making it into United States. Now,

some of their more recent reports are saying that it is coming in in prepackaged counterfeit tablets. But up until now, we've mostly been dealing with this as a as a drug that's been added locally. And so you can see here, there are two different supplies that we sort of know about. The first one that's sort of been the major one that I've been sort of highlighting over the last couple of years is the veterinary pharmaceutical supply. And so this is diverted medication. I mean, there were literally finding bottles of xylazine at bagging sites at stash houses. When the DEA, you know, raids places, they'll find these bottles, but as of late, we've been seeing a lot more of a non pharma powder supply. So, you know, if you do a quick search online, you can see for xylazine powder, you can, you know, buy it very easily by the kilo here. And so, I think this is a cheaper, much more easily obtainable supply. And I think it is going to shift from the pharmaceutical supply to this, you know, illicit outer supply that's being imported through the typical trade routes. And so this is not a problem that's going away. I think it's only going to get worse in the next couple of years. I want to say thanks to jewel Johnson, she was sort of, for me, the first person to put this out there and some sort of journal that sort of alerted everybody and things took off from there. This is her article from 2021, as sort of highlighting how in 2018, these overdose deaths are, grew rapidly that involving xylazine. And nationally, you can see here that it's mostly in mid atlantic northeast states that we're seeing xyzyzy the most, but with some more more recent reports, that is really spreading, but it really has been concentrated in the Northeast. For some reason, Philadelphia seems to be the center of all this. And this is from a report from last year from the Philadelphia Department of Public Health, that 91% of samples that were obtained through drug checking, add xylazine in them. And you can see here that these numbers, the numbers of xylazine, associated overdose deaths has risen in the last few years. And you can see here in 2021 36%, of opioid overdose deaths were associated with xylazine. And if anyone follows is follows some drug checking and understanding what's in the supply, I think this is these people are doing really good work CFSR II, they're located outside of Philadelphia, and they work nationally, they work very closely with the Philadelphia public park, department public health, and have gotten us a lot of information about what's in our supply. And I think this is a great service. And I think everyone sort of needs to tap into this. You can see here that they have quarterly quarterly reports that put out information about what's in the supply. And you can see here from some summary slides that you know, most of the heroin supplies, samples have contained fentanyl, and xylazine. And they also go through what else is found in a spy. So you can see here they have cocaine samples, counterfeit appraisal, and tablets, so on so forth, and this could be really helpful resource for everyone to look into. The DEA put out a report in October of 2022, putting out xylazine as an emerging threat. You can see here from the data, they point out that the northeast, over the last few years has really had the most in xylazine, identified in samples and then percent in overdose deaths. But what's sort of surprising to me is this is something that I only recently found out when this report came out that the number of identified samples is rising rapidly in the south and also deaths. And so maybe south, the southern regions are the areas that are

picking up the most. locally in the northeast, I have some here's some data from Connecticut, you can see here that 5.8% of unintentional drug overdose deaths and Connecticut in 2019, there was 5.8% or xylazine. Positive but and that rose to 11.4% in 2020 and 2020. And what was the over and over again, is that every time we see xylazine, we see an opioid with that. And so we see here that 99.3% were positive for fentanyl also, so if you are positive for xylazine, you're also positive for fentanyl. And I'm gonna I'm guessing here that that point 7% had either some other opioid like another fentanyl derivative or a non fentanyl opioid. And some more data from Kennedy, you can see here as the years goes on, the percent of overdose deaths is rising that are associated with xylazine. In New Jersey, another state bordering New York, we see here that the number of percent of bags that are tested, bags of heroin that are tested are positive for xylazine. And so in 2020 20 22% of those bags contain xylazine were as 67% in 2021. And this number just continues to rise. The data for New York is a little more difficult to find. And so this is from New York State Department of Health sort of report just from March is saying that some data will be forthcoming. And so we're all looking forward to that. And I know that the medical examiner data is out there, I think, almost ready to be reported. So we're looking forward to that. But some more data from New York City in 2021 19% of all opioid involve overdose deaths were positive for xylazine. However, while that's a rising number they do report that there was a difference, a change in the testing and so they employed a more sensitive test. So that may have something to do with some of the rise. And again, we see that all xylazine involve overdose deaths involve fentanyl. So let's get into the pharmacology of xylazine. xylazine is a sedative. That's It's overwhelming clinical effect. It's an alpha two adrenergic agonist that stimulates the brain central receptors. It doesn't really have an effect and respiratory rate. However, it does blunt the response to hypoxia. And so what happens is, if your airway is occluded, you do not necessarily wake up to clear your airway. And so while it doesn't slow your respiratory rate down like an opioid would, it can cause suffocation and hypoxia and death.

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You know, and I just want to point out that I oftentimes I'm seeing that reports are like data that saying or not data, but graphics that are showing that xylazine causes a decrease in respiratory rate, and that's not something we're really seeing. xylazine is a drug that's very similar to some other drugs that we're very comfortable with or have or have a lot of knowledge about, and those are the imidazoline compounds. So these are drugs like clonidine, dexmedetomidine, oxy, oxymetazoline, tetrahydrofolate, Xanthine, and fluoxetine, and new these are all FDA approved drugs that we have data about, and we understand, you know, the major clinical effect of those drugs is sedation when taking in overdose. They also cause hypotension and bradycardia. And I just want to point out that we're not really seeing that with xylazine. Sometimes I see people using reports from clonidine to just report about xylazine. And I just want to point out, there's some differences. The one major thing is xylazine is not a major,

it does not have major activity at the imidazoline receptor. And the MME imidazoline receptor is what's really at fault for the hypotension and bradycardia. The pharmacokinetics are sort of typical for some of the anesthetics that we see out there rapid onset of action last a few hours. And like again, this is a sedative drug. And so this is what it looks like, centrally how it works in the brain. So in normal physiology, the presynaptic neuron releases catecholamines, it attaches to an alpha one receptor centrally. And that controls alertness, your blood pressure, your heart rate, a lot of homeostasis. And if there are too much, there's too much catecholamine. And there's a feedback loop in the in the in the synapse, and that what that can do that negative feedback loop is it can decrease the amount of catecholamines that are released from the presynaptic neuron. So there's a good check in balance. The problem is with alpha two receptor agonist like xylazine, it overwhelms this alpha two receptor and so mostly causes this negative feedback loop and causes excessive sedation. So it's locks the catecholamine release the outflow, and you result in sedation. Here's a good article from clinical toxicology that sort of points out the significance of imidazoline receptors. Again, xylazine does not agonize the imidazoline receptor, it really works with the alpha two receptor, which causes sedation. The biggest question I hear is how we deal with overdose from xylazine. And why I want to point out that our local knowledge has been that the xylazine has not caused significant problems in overdose in the sense that it's causing overdose deaths. It's certainly contributing. And mostly supportive care has been helpful in managing people who have signs of xylazine toxicity. But I think everybody sort of focuses on do we have an antidote to reverse it and does Narcan work because Narcan has been so helpful in reversing opioid overdoses that we sort of pointed like that our candidate is going to be at the scene. Can we use that to reverse xylazine? The answer is no. But we'll talk a little bit about that. But the point a one point I really want to bring up here is that everywhere every time we see xylazine, we're also seeing an opioid and so you should be responding to opioid overdose per usual protocol. If someone is has a decreased respiratory rate. There, you're unable to arouse them giving providing them Narcan to reverse the opioid is the most important thing you can do. Because xylazine is always found in combination with fentanyl or some other opioid on what we oftentimes hear about are Narcan resistant overdoses. And so said xylazine is not an opioid, Naloxone being an opioid antagonist is not going to reverse xylazine. So sometimes people will give Narcan, reverse the respiratory depression, expect the person to wake up and start talking to you, and you can be interactive with them. But since the xylazine, has not reversed it, the sedation continues. And so people will be will think that, oh, I need to give them more Narcan because they didn't wake up. And so I just want to point out that it is very, it's going to be very common if you give Narcan that that patient will still be sedated afterwards. And so what we typically do in this scenario is recovery position. As you can see a picture here at the bottom right, and some airway support, is that patient makes it to the emergency department what what happens with the care in the emergency department is mostly airway control, providing oxygen, head of the bed airway control, and in very extreme situations, the patient's need to be intubated and put on a

ventilator. However, in my experience that's been very few and far between. So just to point out Naloxone, it's indication for use apnea cyanosis, decreased mental status, and if you are in a setting where you're using some devices to determine pulse oximetry, low pulse ox. And so the question is, you know, is an antidote required and what antidotes are available? Again, I want to point out that the opioid portion of this is way more important if concentrate on the xylazine not think that xylazine is causing the deaths here, it certainly can be contributing, but once the opioid is reverse xylazine is relatively easy to control by xylazine, toxicity, bias and supportive care. There is no antidotal therapy available recommended. Some people have talked about some antidotes, one being Yohimbe been which is kind of classic. It's alpha two antagonists the opposite effect of this but it is not recommended. And this really comes from our experience with clonidine, not a recommended reversal agent for other alpha two antagonists like clonidine. Another one is a tip of muzzle and that's not an FDA approved drug that is used in veterinary medicine for the reversal of this drug. And there has been some reports and I left one here on the side about emergency use of this drug in case someone did get into zoo or wildlife Anastasia, sort of point out, this is just like a letter to the editor, there is no data, this is not recommended. And in my opinion, it's not something that really needs to be used. For the majority of these cases can be managed with some supportive care if you're in the field, it's mostly recovery position. It's a jaw thrust, maybe and sort of just airway control, bringing them to the emergency department is this is something that emergency physicians are would be very comfortable managing. There has been some talk about using other alpha two agonists so far for partial alpha two agonist. And that's a little confusing, like why would I give a drug that works at the same receptor. And so this is a topic that comes up in Toxicology sometimes, that if we have a strong receptor agonist and use a partial agonist, Eric can display some and decrease the effect. Also, that is not recommended in this scenario. We do now have some data to help us understand a little bit about what xylazine overdose look like. And, hopefully, doctor, some of the doctors that actually wrote this report are online, Dr. Love, wrote this article that just came out within the last week or two. So this is a report that looked at opioid overdose deaths and compare the ones that are positive for xylazine and others that were negative for xylazine. And so she pointed out that most patients required multiple doses of naloxone, and it did not vary between xylazine group and then the absent xylazine. Absent group, there weren't a major difference in cardiovascular complications. And with these patients, coma was documented in both groups, and there really didn't seem to be much difference between the xylazine positive and xylazine negative patients looks like there was a significant portion of patients that were sedated for hours that persisted beyond four hours and no difference between the two. As you can see here, most patients were discharged from the emergency department whether you were xylazine, positive or negative. And so that just points out that this is actually once it makes it once a patient makes it to the emergency department level of care. It is relatively easily managed. I also want to point out some vital signs here I think because I think there's been missed some misinformation out there about the hypotension

bradycardia. And as you can see here, comparing the two groups, there was really no difference in their vital signs. Since blood pressure, heart rate, respiratory rate all seem to be similar. I'm not sure I understand. And then here's a report from an article Journal of analytical toxicology in 2022. And these are looking at the severe overdoses from xylazine. You know, these are very unlike the ones that we're seeing. These were major large overdoses, massive overdoses with xylazine, with levels that were sky high. And sort of the, there's a huge difference in these cases, these cases were fatal, massive overdose, what we're seeing our load, low concentration overdoses when we're seeing that combined with opioids. And again, we're not expecting major toxicity from the from this drug.

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Another question I get is, well, how can we do some testing, you know, testing is not readily available right now, there is no urine immuno assay, like we would test for opiates, benzos, cocaine and a urine drug screen. That's not readily available. So we're not seeing a lot of hospital testing, or outpatient office testing. You know, there are some more higher level complex tests that can be performed to to detect xylazine and serum and urine. But from my experience, most of these tests are not available at a at an office level or at a hospital, they're sent out to a forensic lab, that oftentimes takes a couple of days to return. And that can be very expensive to my biggest worry is there the false negatives from this, you know, this is a drug that's rapidly eliminated from the blood, I would expect it to be in the urine for a little bit longer. But I can imagine that someone who used xylazine, eight to 12 hours prior may have a negative test when they get when they eventually get their blood or urine tested, and then could be erroneously told that they were not exposed to xylazine. And so that can be confusing for people. So currently, we're it's not a test that's performed widely or and certainly is not rapidly performed for, you know, to effect bedside management of this drug. The next topic that sort has been coming up a lot lately is xylazine test strips, especially from a harm reduction standpoint. You know, currently, there are, you know, from the community, there are a lot of people that are asking for this, and they feel like this could really be beneficial. You know, I think at a community where all of the bags of fentanyl contain xylazine, I don't I'm not quite sure how helpful that would be, I think many most would, would be positive. And then I don't I'm not quite sure what you would do. But in communities that are seeing xylazine rarely, or are a little more infrequently, someone could definitely use the xylazine test strip to avoid use, or avoid exposure to xylazine. Or even testing their tablets, if they believe it's counterfeit, to see if there's xylazine in them. And there has been some reports that these btn X xylazine tech chips are out there, I certainly have not had access to them. I don't know a lot of people that have access to them. But I've seen some reports on social media that they do exist. And then CFSR II, the Center for forensic science research and education has done some testing on the strip's so to sort of show their efficacy and certainly it's able to identify xylazine readily. There is some concern for some false positive and the biggest one will be lidocaine which sometimes we see

in cocaine, but they seem to be making their way to market and hopefully there'll be readily available in the near future. Onto the onto this report from the Journal of Addiction Medicine. This is reported about xylazine withdrawal in a patient that was hospitalized. You know, withdrawal is a really interesting topic. And we certainly have seen a lot of inpatients are noted often. But this case was a 29 year old who was admitted for wound care and you can see the picture of the wounds that was associated with this person's use. She was using 25 bags of heroin fentanyl IV per day for presenting symptoms of withdrawal were anxiety. She was tearful. She had she was restless, she had riders and dysphoria. They gave her multiple medications to help with what was presumed to be opioid withdrawal but the withdrawal was not responsive to her typical opioid treatments. And this is sort of typical, you know, certainly xylazine withdrawal is not a defined syndrome. I can't find it in a textbook anywhere. But we mostly have been learning about this through taking care of patients and so the major symptom that patients typically report are anxiety including restlessness and dysphoria. We have not seen significant vital sign abnormalities or seizures associated with this withdrawal. And this is to point out that the difference between this and a benzo withdrawal. So with with alprazolam Lorazepam, other benzodiazepines people who are using large amount of benzodiazepines, they stop and they end up with vital sign abnormalities, hypertension, tachycardia, diaphoresis, diaphoresis, altered mental status, and maybe even seizures. And we are not seeing that at all with xylazine withdrawal. It's relatively limited, but it can be so significant that it drives patients out of the hospital or out of an inpatient drug rehab, the anxiety the restlessness, the dysphoria can be pretty significant. And it typically lasts for a couple days, maybe up to a week. We have some corollary with other alpha two agonists like clonidine and dexmedetomidine, those drugs do have a withdrawal associated with them. So we're gonna assume that xylazine does too. However, with the alpha, these other imidazoline alpha two agonist, they there is some hypertension, tachycardia, but we're not seeing that with xylazine. And you can see here, you may have noticed that some of the symptoms that I've mentioned, have overlapping symptoms with opioid withdrawal or even benzodiazepine withdrawal. And here's a chart to just point that out. And, you know, some people, you know, not necessarily feel this is sort of controversial does is this a syndrome that really exists? Is it really just opioid withdrawal? That's just uncontrolled? Is it mixed is benzodiazepine withdrawal sort of confusing this situation? And I have the same sort of questions. Certainly my patients are reporting that xylazine withdrawal is something that's significant to them. And it's real. And I think we just really need to have more research to understand this. So what's the typical withdrawal treatment? Again, there is no data or evidence based recommendations on how to treat this withdrawal. This is mostly just from experience. And, again, we need more research to help us understand what the effective strategy would be to manage this withdrawal. We mostly treat it like sedative hypnotic withdrawal. So how we're treating benzodiazepine withdrawal or alcohol withdrawal firstline agents would be benzodiazepines, if you're in an ICU setting dexmedetomidine or fentanyl, Barbitals certainly phenol barbitals has been used outside of



ICU settings also and then some adjunctive medications, like clonidine to Zanna de la effects, a dean, Gabapentin and some anti-psychotics to they can all help with the anxiety. know some people point out boy clonidine is a alpha to center acting agonist and maybe you could backfill that could be sort of a maintenance drug, add some of that agonism to help with some of the withdrawal. And what I like to point out is that, in my experience, giving clonidine has been somewhat helpful, but it has not been does not resolve the symptoms. And I think that's mostly due to a dosing problem. You know, we're certainly seeing if you gave so much clonidine to sort of meet the needs from what people were using. And with xylazine, I think you would see a lot of hypotension and bradycardia. There's some other cutting edge things that people have been trying again, no data available for this, people talking about using ketamine or restless leg syndrome medications like repined overall. So it's sort of in summary, I think, you know, not every setting has as the same drugs available to them, like I can't expect an office based opioid treatment program to be using dexmedetomidine infusions. So just to point out that like inpatient drug rehabs, there are some limited medications that are available to them. I think benzodiazepines on an as needed basis for anxiety for a few days can be really beneficial. Fino bar papers can be also helpful and then adding medications on standard like clonidine effects, or lofexidine. And then adding on to Xana. D and Gabapentin and antipsychotics are super important. But people were really pointing out that you know, this is making it much more difficult to get patients inducted on buprenorphine. And I can completely see that, you know, we're seeing reversal or control of the opiate withdrawal symptoms, and with buprenorphine and leaving a patient, anxious, restless dysphoric. And they sort of feel like their withdrawal is not managed well. And so, you know, adding on a short course of benzodiazepines if you're able to and that appropriate setting I think can be really helpful. Adding on some of those adjunctive medications in an outpatient setting can be helpful and strategies and managing some of this as you're inducting patients on buprenorphine.

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But onto the other portion of this case that was Then in the Journal of Addiction Medicine are the wounds. And those are the things that really have been popping up as the major problem with this drug. We have seen in Philadelphia, a significant rise in soft tissue infections and wounds over the last few years. And that certainly has been highlighted in many articles. And it's sort of the shocking and most significant things that people will see. And so it's trigger warning for this next slide, it has some severe wounds on it. And so this is what some of these wounds will look like in they're sort of severe stage, they kind of start sometimes start very small. But as they continue to grow, or someone continues to inject in that area, they can continue to get larger and larger and larger, you know, patients will tell me that the a good portion of this wound will be insensate, they have no feeling there. And so it's much easier to inject into that wound, but it certainly will propagate that wound to get larger and larger. And it can be so severe that it gets down into the lower dermal layers down into with exposed

tendons or even exposed bones. And the question is, what is the pathology that is causing these islands and associated wounds, and I think we don't really understand that as of yet, I think there's a lot of conjecture about what potentially could be causing it. But clearly, more data and more research is needed to understand these wounds. In my experience, it is mostly almost entirely associated with injection drug use, sort of when we first started presenting this data, I would say we didn't really we thought that maybe it could be occurring with inhalational smoking or intra nasal use, but really has been concentrated in the injection drug use POP population. Some people will say that they have developed a wound in an area that they didn't inject in, which is kind of confusing. But we mostly see it with places that people have been injecting it. But you know, there's a long history of people developing wounds from injection directors, I think there's nothing new. But certainly there has been a progression that has been worse, as xylazine has made it into the population. But we don't typically see large wounds with cocaine or methamphetamine use, we certainly can. But nothing like what we're experiencing was I love seeing some potential causes of these wounds, you know, certainly with fentanyl, there is an increased frequency of injection behavior, people are using many more times per day. So that may lead into it. Something that could be a vasculitis or a rheumatologic. Cause that's associated with this, especially with the repetitive injection, I think there's a significant cytotoxic effect of this drug and that may be causing a portion of this skin picking behavior certainly well known with with stimulants like cocaine or more with methamphetamine and cocaine, but certainly with methamphetamine. And that may, it may come into play here because you know, a lot of patients that that I take care of will tell me that they are using more stimulants to combat the sedative effect of this drug. And so certainly, if you're trying to avoid the sedation from xylazine, you may use a stimulant and then maybe you have some more skips skin picking behavior. There's certainly some poor wound healing. I think a major one here is malnutrition. And so I see a lot of infographics pointing out to increase your protein intake. And I think that's really important. There certainly is an infectious component to this. I don't think it's the major portion. But I think when it's late, I see a lot of necrotic wounds, with large s scars, and certainly there's bacteria growing underneath. But I think there's lots of different potential reasons for this. And certainly more research is needed. People point out the the vascular effects of this drug, and maybe that there is some vasoconstriction that may play into it. I can't imagine that's the sole reason why people were developing these wounds. I mean, certainly there, there are many more other drugs out there that have caused more vasoconstriction and xylazine. We don't see major wounds with those drugs. So like cocaine or methamphetamine injection drug use, we we don't see like necrotic fingertips and toes with this unless it's a late stage problem. So certainly vasculature. The vasoconstriction is not a major portion of this. So how do we treat these wounds? And the major thing that I recommend for people a cessation of injection, which can be very difficult to do, you know, it's very difficult for someone who has been injecting to stop using that method of use and moving to snorting or smoking, but that's a major thing because if you can stop inject dig into that wound that allows that wound to start

healing. I gotta say there aren't some, there aren't some major, you know, groundbreaking ways to help manage these wounds, it takes a long time. And it's just local wound care mostly. So removing that removing that eschar, as you can see here, in this first picture, remove the eschar, which is not easy to do. I mean, many people think that this needs to be surgically removed. But in my experience, keeping that wound moist using some enzymatic topical medications can help break down the eschar, keeping it clean with soap and water or you know, some other substances that I have pointed out here, but then adding some anti microbial coverage, that is non add heat that can help with non adherence. So you don't want someone putting a cover on that wound and then removing it everyday and peeling off all of the skin that's on there. So using a non adherent dressing is really important. The problem is we see a lot of these on lower extremities, and there's a lot of drainage that comes out of them, especially if someone is walking a lot. And so using an absorptive dressing can be really helpful when we see a lot of like soiled socks as the train is coming out. So reserved addresses can be really helpful. But here's an example of someone who came into our hospital. And over a number of months, as we continue to care for this person. Wounds didn't improve. And this was only just from local care, but it takes months. There are some higher technique things that that can sometimes happen, that to help treat these wounds. However, they're not like the typical routine treatment. And we see a lot of deep wounds at my institution where the tendons are exposed, or bone is exposed. And as when someone is able to grow some granulation tissue on top of that they could get a BTM a biodegradable temporizing matrix that covers over it to allow some healing underneath. You know, there has been a lot of concern about a night is for infection underneath that matrix. But that can be helpful skin grafting, I think, the major problem what happens with skin grafting is we put those on too early and they fail, or maybe that patient does not have is malnourished or doesn't have good follow up to care for that wound very well, and the skin graft fails. So this is typically left for a later stage coverage. And unfortunately, we seeing a lot more amputations. And I think that really goes to point out that, you know, people do not have a lot of confidence in their xylazine withdrawal management. They've had a lot of bad experiences at hospitals or inpatient drug rehabs, a lack of knowledge that this drug even exist, and people perceive that there's a lack of treatment for this problem. And so what we see is a lot of avoidance of care, which means we see more late stage presentations with more severe wounds. And then that leads to more amputations. But that, you know, clearly there is a lot a lot of research that needs to be done to understand this drug understand the toxic effects of the drug, and then treatment for this addiction. So just to review some harm reduction things and sort of things that I've sort of mentioned throughout this xylazine test strips that can be helpful, but really how effective are they if the supply, you know, there's 90% of xylazine in the supply already, it's going to be more helpful in areas that there's less frequent xylazine exposure. And for people who are using to expect longer periods of sedation. And so the environment, environmental factors can be really important, if they're outside in the cold, and they're using this drug that can cause you know, frostbite and some

other environmental problems and then leading into the summer seasons. Two, that could be another problem with the heat, body position and airway control. So making sure that you're that you're in a comfortable position where if you were unconscious, you would continue to breathe. And when you are using using with a friend, and so someone can put you in a recovery position to allow you to recover from this use. And to point out that that naloxone is not going to reverse the sedation associated with this drug, not to withhold it. But to provide it for reversal of respiratory depression and expect the sedation continue pointed out that there's some some more survival use of stimulants to combat this. And that can cause some chaos, chaotic use. So people should be understanding that cocaine and methamphetamine is going to affect how you're using and the effects of the other drugs that you're using and mixing the two can be dangerous.

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How to Avoid wounds and so switching from IV use to intranasal or inhalational use is is the what have typically recommend, and if you are injecting to make sure to to be rotating injection sites, if you do have a wound to avoid injecting into that wound, and in especially, and then certainly not injecting into the, around the edges of the wound. So I hear people will say that I'm not injecting into the middle, I'm injecting right around the wound. And so the wound doesn't get worse. And actually, what that does is just allow that for that wound to expand further and further. Okay, that is all of the slides that I have for today. I certainly, I see some questions in the chat. And this is great. And I think I've got lots of time to open up to any questions about this topic. Wonderful.

40:47

I'm gonna start with Thank you getting a lot of love in the chat. So just wanted to kind of begin there, and then I'll try and take questions in the order in which they were received. So I know we had quite a few people asking about test strips, overdose reversal, you covered all of that. We have an attendee wondering if you know of any guidelines, or have guidance for supporting patients whose breathing is not suppressed, to the extent that they would require hospitalization, hospitalization, excuse me, or intubation. This person is thinking about community partners who patients and participants have expressed unwillingness to engage in emergency care, but who have capacity to provide breathing support.

41:29

Right, yeah, I think this is a community that that I engage with a lot in Philadelphia, we have a tight knit group of people who are helping each other out. And then there's a lot of field workers out there, too, that are doing reversals and asked me this question. I think one recommendation I've I've given is to use pulse oximeter, you know, there are certainly a lot of leftover pulse oximeters from COVID. And people have them laying around the house. And I

think they're really helpful, you reverse the opioid overdose, you put the person in in recovery position, as long as they're breathing, use a pulse oximeter to monitor their breathing. And then if you're in a setting where you can monitor them for an extended period of time, that's perfect, you know, certainly feel like there's some unsaid things that are kind of obvious, like taking them out of the an environment that is either dangerous or their environmental factors are involved. So avoiding like frostbite or hyperthermia. But certainly not things like splashing with water, I think he's mostly just supportive care monitoring them. So if their pulse ox, it continues to be low after reversal, providing more Naloxone may be helpful. And so maybe the opioid portion of that not completely reversed, or if their actual breathing rate is normal. So doing things like a jaw thrust or clearing their airway can be helpful. But that is not the case, then moving on to bring him to emergency department. And I completely understand someone who works on the street and also works in the emergency department, the some of the disinteresting coming into the merge score, and I get that and so there are some things that you can do in the field.

43:09

Thank you for that. I also want to say thanks for covering the harm reduction. And I have a kind of a follow up question to that last slide you presented. Do you have any specific recommendations for clinicians who are working with clients who have no intention or desire to stop using drugs, any other harm reduction strategies you would recommend there?

43:30

I think not. Maybe not more, no more things for xylazine specifically, but I think for people who are engaging with opioids, especially fentanyl, one with injection drug use, you know, I had there were some other things here. So clean technique, and everyone sort of focuses on not licking needles, I think the most important thing is making sure that people are cleaning their skin before injection, you know, the rate of endocarditis from Staph aureus is really high. And that's really linked to skin flora. And so making sure that people are cleaning their skin before injecting, using clean needles is like that's, you know, sort of typical stuff that we recommend. And sir, I'm not quite sure what the New York regulations are for needle exchange. But needle exchange is super helpful. Way to prevent communicable disease, not just Hepatitis C and HIV but also you know, bacteremia blood streaming infections, fixing with a friend so I'm using and you stay sober. Watch me and guard over me while I'm using and once I recover, then you use and I watch you use it, make sure we have Naloxone available. Mixing drugs, it can be much more it can be dangerous and making sure people understand tolerance and dependence. So you know, we lose a lot of people. overdose death we're coming out of it for First detox like incarceration, or maybe they're coming out of inpatient drug rehab or a hospitalization where they have lost their tolerance, return to use and overdose and die. And so we really need to make sure that people understand tolerance and dependence too.

45:17

Thank you moving right along. Is there a role for oral antibiotics at all and smaller or earlier wounds? Or is it mostly just topical care? And somewhat related? What types of bacteria are you seeing?

45:31

So it's mostly the typical skin Flora stuff. There's nothing in particular about this that different. Certainly, we we provide a lot of oral and parenteral antibiotics when people come into the hospital. I gotta say, though, I think it's oftentimes a little bit overkill, we do see some super infected wounds, but the vast majority of them are like superficial coverage. And so cleaning them soap and water and adding topical antibiotics for the majority of the cases is helpful. And then for the patients with deeper infections or of bacteremia or or, you know, more invasive infections, then moving on to antibiotics. I can see most of the wounds that we care for it's it's topical antibiotics, and and more rarely do we need oral antibiotics.

46:23

Another related question from the audience. What is the likelihood of saving limbs or I guess, the percentage of folks who end up actually requiring amputation?

46:35

Yeah, you know, the amputation is really a last resort and we see a lot of recovery. And, you know, making patient centered decisions, I think, is really important. I know, oftentimes, we need to we will, what we need to do as providers is avoid taking the easy route out of this, I think, sometimes people will see like, jeez, this person is really never going to recover from this and they sort of move to amputation. But people do recover from these wounds, they do heal, they may take a very long time to heal. And I think we just need to give a patient's you know, they need to be informed about the decisions, and that it can be very difficult for these wounds to heal and it can be a long road but they absolutely do heal. I think in certain sort of like, you know, extenuating circumstances where we have necrotic limbs like necrotic hand or necrotic toes that require amputation that is sometimes needed. But we you can salvage a lot of the a lot of limbs from your typical wounds.

47:48

Right, do you know has Thylacine been found in a significant number of people who are using cocaine or methamphetamine? Or is it or just with

47:57

fentanyl? Um, it's not exclusively with bags of fentanyl, like I said. And some of the DEA, we have seen some reports of cocaine contaminated with xylazine. That's really thought to be sort of cross contamination, it's being packaged in the same area. And it's just they're just not very clean about how they're packaging, and so some makes it into the other supply. I don't think that is a significant amount, but it does happen. But we've mostly been seeing it with a glassine bags of opioids.

48:36

Have you ever come across a person who is experiencing precipitated withdrawal from Naloxone while they are also sedated from silence with diluting? Excuse

48:45

me? That's a good question. I think that my biggest fear and sort of when I first got into this and sort of thinking about this a little more critically, like I have someone who I've given multiple doses of naloxone to because I thought they did, the first one didn't work. And now I've given too much Naloxone, and this person is vomiting, but they're sedate. And then now you you increase the risk for aspiration. And I gotta say, we have been seeing a lot more aspiration. Pneumonia is in the hospital. That's something that's significant. And I am not looking into that we have not been able to see the data or dive into this. But it's a question that comes up amongst our group all the time, is it because people are just getting more Naloxone, and they're vomiting more, but they're really sedate. And we're, and maybe they show up to the hospital a couple days later with this complication. And so it is a theoretical problem. I just haven't seen it much in from, you know, reversals or seeing people who are coming to the hospital after reversal. Haven't seen a lot of that. Typically, like if you're in withdrawal, it wakes you up enough that you're aware you're alert in my experience, but there's still this Part of the background of me that's like worry that we're seeing aspiration because of this exact scenario you have pointed out like you're reversing. You're you've gone overboard with the naloxone. Now they're in withdrawal, and they're sedate. And they're aspirating. So like, all I can say is, I confirm your concern, because that is also my concern. Great minds.

50:24

We have someone in the audience who has a patient who has been very successful on sublocade, but has recently relapsed, and they're wondering what impact xylazine potentially has on sublocade And whether it's causes sublocade to be less effective.

50:37

You know, I think this is a question that comes up a lot in addiction medicine groups, you know, like how to manage medication. Like buprenorphine through like the an injectable, like sublocade with someone who has returned to us and I think that's, we take xylazine out of the

picture, and it gets complicated. Supplementing with oral, or sublingual, buprenorphine, changing the dose of the injectable are things that we can manage, but I think I would go with the same approach when we're talking about xylazine. Now that person is coming off of this substance, whatever we do increase the dose of the buprenorphine injected add supplemental sublingual, buprenorphine, but adding these other adjunct medication, so adding a benzodiazepine for a short period of time as that person is starting to become abstinent from that substance. clonidine, gabapentin, NSAIDs as all adjunct medications and then adding an anti psychotic, so I'm really not doing much different when I'm thinking about xylazine. In that scenario.

51:52

There's a lot of questions about how common xylazine is in New York, how often it's being found. And I know, data is an issue for for our state. I'm wondering if you can speak to that at all, or if you know, when people can expect actual numbers on what's happening here in New York.

52:10

I don't know that last part. But I have been searching a lot for this recently, you know, leading up to this talk, I did find one reference to 25% of the New York supply being contaminated with xylazine. And that came from the New York Times article that came out just a couple of months ago, but it wasn't referenced and couldn't really find it. I know, we met with the medical examiner who said he had some data and we're hoping that it comes out pretty soon.

52:39

Something to look forward to for better or for worse. We put Unfortunately,

52:44

its medical examiner data. And so it's probably not going to be drug checking data. So they're probably not going to have that information. But really looking into the drug checking organizations out there. I imagine insight could be a really great resource for finding that information. Oh,

53:02

definitely. I have someone who is wondering if you have any specific protocols around the maintenance of xylazine involved withdrawal symptoms that you would be willing to share? And if the answer is yes, see, I would be happy to help distribute.

53:21



My answer is no. I think we're doing some pretty typical. We have like our own sort of rhythm of what we've been using in the hospitals. And these are all the medications that we mentioned here. And I think there are some organizations that are working on something like that to publish in the very near future. So look forward to that. I know Philadelphia, the public health department's looking to put out their sort of guidance to clinicians that should be coming out soon. And that's more than just one person like myself, it's going to be multiple, multiple providers putting their heads together to come up with the the protocol. I gotta say I lean more on to benzodiazepines as the first line agent. And I think other providers are sort of trying to stay away from benzodiazepines and lean more on to anti-psychoics, like olanzapine. And so it's just a difference in style. But all of there isn't one medication that's going to fix this problem. So adding multiple medications for supportive care is the way to go about this. Starting with point one or point two of clonidine three times a day, I think is a good start. For milligrams to Xanthine PRN 300 of Gabapentin 303 times a day and adding an anti psychotic whichever is the one you prefer like olanzapine or Cotai, a pain you know, up to three times a day for the retying and then for benzodiazepines what we've been doing is two milligrams you know, four to six times a day A soy two milligrams oral clonazepam PRN Q four Q six PRN anxiety. And that's sort of ineffective for us. And then tapering that off. But you know, only doing it for the first couple days as that person is going through a detox.

55:18

All right, two questions left here, we have someone asking about implicit bias and how that potentially impacts care. And wondering if you have any recommendations for how clinicians can pick their own implicit bias and improve the care that they provide to their clients.

55:37

Yeah, this is, you know, even despite knowing your bias, it's still difficult to stay away from this. And so, but you know, make sure you state what we know. And we don't know. And we don't know what, where the xylazine is all the time. And so making sure to listen to based on subjective feelings of withdrawal. Since there's no real objective finding for this, it can be very difficult. And so we're mostly concentrating on people who are using bags of fentanyl, because we know that they're, they're being exposed to it. So maybe checking your bias at the door, when someone is saying like, despite I know, I'm using pills, and I'm still having anxiety and dysphoria, maybe thinking about that their pills that they're using are contaminated with xylazine, I would love to have some objective information. That would be great if we had some rapid, rapidly available rapid testing for xylazine. So we can sort of check that at the door and not and sort of avoid the bias. But again, like I had stated during the talk, I'm just really fearful of the false negative in those tests, especially since xylazine, rapidly is going to be leaving the blood, he may end up having some some false negatives. And so you sort of like is going to have some providers ignore the symptoms that are patients, but really just listening to patients. I

think that's the biggest thing and not overlooking the complaints of anxiety and restlessness and dysphoria.

57:06

We had a question about information to share with folks, I put a link in the chat just now from the New York State Department of Health, their FAQ on xylazine. And we'll be sure to include that when we follow up with everybody this afternoon. Here we go. Since we can expect continued sedation after administering Narcan, how many doses would you recommend to reverse an overdose?

57:34

Well, the typical recommendation is that you give the four milligram intranasal Naloxone, and I think that's adequate for the vast majority of opioid overdoses. And then the recommendation is to repeat a dose if there is still respiratory depression after two to three minutes. And I don't I guess maybe the the question is, there's like a sub question to that like, because I know a lot of places are recommending eight milligrams or higher doses. And I really, I want to avoid that I think four milligrams is an adequate dose for the vast majority of overdoses and actually going to eight or 12 milligrams can just really complicate things and cause a lot more withdrawal symptoms. And I would avoid using these larger doses to start

58:21

to I know I said this already, but too late breaking final questions for you here. There have been reports of this medication being absorbed through the skin if and when handled or inhaled. What are your thoughts on this and how can this impact healthcare workers in the field when dealing with patients?

58:37

Um, you know, I haven't seen anything like that and I think I would stick with the, you know, without really looking into it. I'm not quite sure I have got a good answer for that. But certainly from with our information with fentanyl that you know, casual contact with an opioid like fentanyl does not cause significant opioid symptoms, it certainly should not cause an opioid overdose. And I would expect the same thing with xylazine. You know, this is not a drug that you expect to be aerosolized very easily in casual contact should not cause significant symptoms.

59:14

And I do want to get a final thank you out there for you Dr. D'Orazio for this wonderful presentation.

[End Transcript]