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Not Carfentanil—A Case of Unexpected Xylazine Detection.

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Guest: Dr. Nam Tran is a Professor and the Senior Director of Clinical Pathology at UC Davis Health, located in Sacramento, California.

Randye Kaye:

Hello and welcome to this edition of *JALM* Talk from *The Journal of Applied Laboratory Medicine*, a publication of the Association for Diagnostics & Laboratory Medicine. I’m your host, Randye Kaye.

Xylazine is an alpha-2 adrenergic receptor agonist used in veterinary medicine as an anesthetic and analgesic sedative in large animals. While not approved for use in humans, xylazine is increasingly found in the illegal drug trade and is emerging as an adulterant substance responsible for overdose deaths. Since 2006, xylazine has been identified in forensic toxicology samples in almost every state in the U.S. In July 2023, the White House released a national response plan to address the emerging threat of fentanyl mixed with xylazine.

The May 2024 issue of *JALM* features a special report describing the first documented case of xylazine at the University of California Davis Health. The patient’s presentation was not consistent with typical signs or symptoms of xylazine overdose and the case was identified only incidentally, as the laboratory was validating a new gas chromatography tandem mass spectrometry xylazine assay.

Today, we are joined by the article’s corresponding author, Dr. Nam Tran. Dr. Tran is a Professor and the Senior Director of Clinical Pathology at UC Davis Health, with specialization in clinical chemistry, toxicology, and point-of-care diagnostics. UC Davis Health is located in Sacramento, California and is considered as the largest Level I trauma center north of San Francisco. Welcome Dr. Tran. Let’s start with this. Why is xylazine such a health concern?

Nam Tran:

I think it’s an interesting drug that’s out there. It’s a health concern because it is often being attributed to... as an adulterant and additive to say fentanyl. We know that there’s a fentanyl epidemic going on right now and xylazine being added to this is both concerning, because patients don’t know that it’s in there number one. Some patients may desire it because they feel that it had an additive effect. And number three, some patients are using it and trying to avoid it because they feel that it alters the effects that they desire for these illicit drugs.

Xylazine itself, there's no real reversal agent for it if we are concerned about overdose. So, there's none that we know of, at least in the human world. A lot of this is study from the animal world so xylazine as a background was a veterinary drug. It still is, used quite often.

And excessive use can also lead to other complications such as wounds forming on your arms and legs from the vascular blood vessel damage and so forth. At the same time, having multiple compounds you're taking illicitly can also lead to other terrible drug effects that can lead to death and so forth. In fact, the numbers are rising astronomically in parts of the U.S. where xylazine is found, oftentimes with fentanyl.

Randye Kaye: Wow, that's frightening actually. So, the case study within your article mentioned that the patient noted daily carfentanil usage. So what's the significance of this compound?

Nam Tran: So carfentanil is something that we don't often detect. It's definitely made it into the news, a variety of these compounds. So carfentanil, a carfentanil in this case, is a super fentanyl if you want to call it that way and it's often used as a large animal tranquilizer.

So if you look at the potency of say heroin, and heroin is already very potent, and you compare it to fentanyl which is already a thousand times, many times more potent than heroin, carfentanil is even many more times potent. In some cases, just being exposed to skin can cause respiratory arrest and so forth, those complications like the other opioids.

And so carfentanil is a tranquilizer for large animals such as elephants and so forth. We're not the size of an elephant and therefore these people taking it, and sometimes these drugs finding their way as again, an additive into the drugs that they were thinking of as fentanyl, but in fact it's carfentanil, they're at higher risk for having an overdose of it. Some of these patients knowingly look for this because they know carfentanil is much more potent.

In our case, the patient noted that they were taking it. We did not detect it nor its metabolites but it was worth noting that patients are out there looking for this stuff too. And that's also a very dangerous compound that exists in the illegal drug trade.

Randye Kaye: All right, thank you. Wow, just keeps getting worse and worse, doesn't it? What are some challenges in bringing up your xylazine GCMS assay at UC Davis?

Nam Tran: So the challenge was one, the typical just can I bring out the assay? If we bring up any assay like any CLIA-certified or

accredited laboratory, we have to find samples that are naturally occurring.

We can certainly spike or pretty much contrive samples with xylazine, that's easy but there's no body to metabolize so that we can make sure we can detect any of the metabolites that form to further validate our test. So, without knowing the prevalence of xylazine in our area, so I'm in the Sacramento region of California, we weren't sure how much we were detecting. So once we brought up the assay, we're waiting away to find those natural samples and it took a while.

Fortunately for us, we already have high confidence in our assay. We have amazing laboratory scientists, and by the way, Happy Lab Week to people this week. But at the same time, we knew the assay, we're just waiting for those natural samples. For us, to make ourselves feel better, and this is not under our regular validation process nor would it count for our regular validation but it was just all so helpful, we are lucky to have the number one veterinary school in the nation and we have a vet hospital.

And of course, the veterinarians are using xylazine in many animals including horses, so we were able to get some horse samples to just test on initially just to make sure that other aspects were working okay until we found those natural samples, natural human samples that would count for our official validation.

We actually even share those samples with our sister schools too just so that they can start bringing up the assays as well. But on our case, it took a while but we finally found some samples as we were screening all these cases including the case that was reported in the *JALM* paper, and we were then able to successfully bring it up and we're one of the early facilities to bring it online on a mass spec-based platform.

Randye Kaye: All right, thank you. How does the prevalence of xylazine usage impact that assay development and are there other resources to help with it?

Nam Tran: I think that was the concern and as mentioned, we had almost nothing in our area at least. If you were in Maryland for example, I think if you're looking back at 2015, they had like 1% prevalence. In 2020, that jumped up to 80% and the number continues to go higher and higher. I think from the DEA, the Drug Enforcement Agency, they're showing over 190% increase over the last few years in the south of the United States already. The West is increasing but at a much slower rate.

So if you're working with those prevalence especially in places like California and perhaps in my area, it's a lot harder to pick

up. So, you need those numbers, as required by the federal government to validate, right? So you need certain amounts to make sure that your test is accurate, precise, and so on, and even run the appropriate stability assessments to make sure that if you were to transport the sample and whatnot, the stability of these target compounds are still viable.

So that's pretty much our take on how we got around that was we asked around for our sister schools, the ones that actually brought up the test, keep an eye out please for any xylazine, possibly share. Like I said, we did some benchwork, not for the CLIA work but working with our vet school because they have tons of xylazine samples that have been in their patients, and it was very good in that role. And then as we built out, we started helping other institutions too, so looking to other institutions that are seeing more xylazine seems to be a good way to accelerate validation of a new test.

Randye Kaye: Thank you. So finally, let's just talk a little bit more about your local community, since your institution has implemented the test. What have you seen? What have you observed in terms of the prevalence of xylazine in your community?

Nam Tran: Interestingly enough, we just talked about this the other week and our area specifically, the prevalence remains exceptionally low. I can count on one or two of my hands how many positives we've detected from screens. Now, with that said, I'll preface with, this also ties into how frequently doctors are ordering the screen test, right? We only know what we test for, that's other element but we have reached out to other areas of our groups, reference labs that test our area. They are also seeing low prevalence and again, they also state the same, this could be due to low testing volumes, people aren't ordering as much. But we also have other projects in the area with the federal government and they themselves also highlighted it's still very low in our part of the country.

So just like with many other drugs that have found their way into the U.S., there are various demographic, geographic variables at play. There could even be supply issues, like maybe it's difficult for drug manufacturers to get their hands on xylazine in our area compared to say in Maryland or Pennsylvania, which have increased their enforcement of this compound, right? The U.S. has not made this necessarily a controlled drug but in Pennsylvania for example, my understanding that they have also now making this a more controlled substance in their area. So they're trying to crack down but in California, we have not seen the prevalence that I would have expected compared to other places.

Randye Kaye: Wow. And the plot continues to thicken. Thank you so much for joining us today Dr. Tran.

Nam Tran: Thank you.

Randy Kaye: That was Dr. Nam Tran describing the *JALM* article “Not Carfentanil—A Case of Unexpected Xylazine Detection.” Thanks for tuning in to this episode of *JALM* Talk. See you next time and don’t forget to submit something for us to talk about.