



Xylazine: What Clinicians Need to Know

What is Xylazine:

- Xylazine is a non-opioid used as a sedative, anesthetic, muscle relaxant, and analgesic for animals, but it is not FDA-approved for use in humans.ⁱ It was not approved for human use due to severe CNS depressant effects.
- Xylazine is a strong synthetic alpha2-adrenergic agonist, synthesized in 1962 as an analgesic, hypnotic, and anesthetic.ⁱⁱ It has chemical properties similar to other drugs like clonidine and may have similar clinical effects.
- Xylazine has increasingly been found in the illicit drug supply, frequently mixed with fentanyl.ⁱⁱⁱ
- It may be referred to as “tranq,” or “tranq dope” when combined with heroin or fentanyl.

Xylazine Source and Preparation and Route of Administration:

- Xylazine comes as a liquid solution for injection in 20 mg/mL, 100 mg/mL, and 300 mg/mL strengths for veterinary use. The liquid solution can be salted or dried into a powder. In the illicit drug supply, it can appear as a white or brown powder. Because it can be mixed into other powders or pressed into pills, it can be difficult to identify based on appearance.
- The routes of administration include intravenous, intramuscular, intranasal, and oral; there is currently no information on vaping or smoking.
- It has rapid onset within minutes and can last 8 hours or longer depending upon the dose, the way it was taken, and whether it was mixed with an opioid or other drug(s).^{iv}

Xylazine Trends:

- Xylazine has long been noted in the street opioid supply of Puerto Rico. In the late 2000s, it emerged in Philadelphia and has been found more recently in many regions, including New York State (NYS).
- While the full national scope of overdose deaths involving xylazine is unknown, research and testing have shown that overdose deaths involving xylazine rose nearly 20 fold between 2015 and 2020 in all major US regions where xylazine testing was being conducted.
- The highest xylazine prevalence in autopsies has been observed in Philadelphia (involved in 25.8% of deaths), followed by Maryland (19.3%), and Connecticut (10.2%). Illicitly manufactured fentanyl (IMF) was present in 98.4% of overdose deaths involving xylazine.^v
- In 2021, 91% of samples of purported heroin or fentanyl from Philadelphia also contained xylazine, making it the most common adulterant in the local drug supply.^{vi}
- Data are forthcoming from NYS, but there are reports of the presence of xylazine in the local drug supplies in various parts of the state, including NYC, Onondaga County, Monroe County, and Long Island. It is thought to be an increasing presence.

Xylazine Effects:

- Xylazine is a central nervous system depressant that can cause drowsiness, amnesia, and slow breathing, heart rate, and blood pressure at dangerously low levels.
- At very high doses, or with other central nervous system depressants, xylazine can cause:
 - Loss of physical sensation,
 - Loss of consciousness,
 - Intensification of the effects of other drugs, which can complicate overdose presentation and treatment.

Why Do People Use Xylazine with Fentanyl:

- The “high” from fentanyl lasts for a very short time compared to the effects of heroin and other opioids. Xylazine may be added, at least in part, to extend the effects of fentanyl. However, not everyone who uses fentanyl is intentionally seeking out xylazine. In many cases, people are not aware that xylazine is in the drugs they are buying and using.

Why Should Clinicians be Concerned:

- Use may cause skin and soft tissue wounds, including ulcerations. In Puerto Rico, people using xylazine had a higher prevalence of skin ulcers compared to those who did not use xylazine (38.5% vs. 6.8%).^{vii} Reports from Ohio note necrotic tissue damage and severe abscesses after injecting and/or snorting xylazine that appear to be independent of injection sites.^{viii}
- These wounds are presenting atypically, tending to be on legs and arms (sometimes away from the site of injection), and appear to worsen more quickly than other skin wounds.

Xylazine Diagnostic Testing Challenges:

- Xylazine is not included in routine immunoassay toxicology screens and therefore may be under-detected. Additional analytical techniques are required to detect xylazine in biological specimens such as blood and urine.
- Even with appropriate testing, xylazine may not be detected due to xylazine’s rapid elimination from the body, with a half-life of 23-50 minutes.^{ix}
- Xylazine test strips have been developed, but as yet there is a dearth of information on their accuracy.

Presentation and Management of Xylazine-Involved Overdose

- Opioid overdose also involving xylazine presents similarly to uncomplicated opioid overdose. Xylazine can potentiate the effects of other depressants, such as fentanyl and heroin.
- While xylazine alone does not cause the severe respiratory depression observed with opioid intoxication, the profound mental status depression may cause airway compromise leading to suffocation.
- Naloxone should be administered for respiratory depression because xylazine and fentanyl are typically found together.
- People may find that naloxone will appear to be ineffective in some overdoses, as xylazine intoxication is not reversed by naloxone. Patients should be educated about this to avoid incorrectly attributing these incidents to “naloxone-resistant fentanyl” or “naloxone-resistant opioids.”
- Be aware that the person may breathe normally after receiving naloxone, but still be sedated from the xylazine. More naloxone may not be needed.
- There is no reversal agent for xylazine that is safe for use in humans; supportive care is recommended, including rescue breathing. Blood pressure may be unstable and in need of monitoring or intervention.

Managing Withdrawal:

- Xylazine withdrawal is not a well-defined syndrome. It includes anxiety, irritability, and restlessness. Severe hypertension is also possible.
- If admitted for inpatient care, clinicians must be prepared to manage xylazine withdrawal symptoms simultaneously with opioid withdrawal.
- Treat with benzodiazepines and/or alpha-2 adrenergic agonists, clonidine, dexmedetomidine, tizanidine, guanfacine.^x
- Opioid withdrawal should be treated early, with liberal use of medications for opioid use disorder or opioid pain management in order to mitigate any pain and discomfort that could further exacerbate the manifestations of xylazine withdrawal or lead to discharges against medical advice.

Wound Care:

- Avoid alcohol and hydrogen peroxide.
- Clean wounds with soap (if available) and bottled/tap water or saline.
- Cover with a non-adherent dressing (Xeroform®) covered by an absorbent one.
- Keep skin around the wound clean of drainage and moisturized (Vitamin A+D ointment).
- Goal for wound bed: keep moist (helps dead skin soften/fall on its own) OR debridement.
- Antibiotics may not be needed.
- Manage pain.

Harm Reduction Messages:

- Educate patients about xylazine in the illicit drug supply and ask about atypical wounds.
- Providers should be aware of the heightened risk of skin and soft tissue wounds among people who use drugs and provide both wound care treatment and harm reduction education (e.g., use sterile syringes, swab area with alcohol prior to injecting, rotate injection site, and avoid injecting into wounds) to reduce the risks of exacerbating local infections and acquiring communicable diseases.
- Educate patients to be aware of overdose risks no matter what drugs are used, and practice as much harm reduction as possible, as consistently as possible.

Basic Harm Reduction Messaging Providers Can Use with Patients:

- Go slow. Use less.
- Test your product if you can.
- Sniffing or smoking is probably safer than injecting.
- Try to avoid using alone. Because of the heavy sedation, be aware of your surroundings and your possessions, especially if you're somewhere that's not secure.
- If you are using alone, double down on other strategies. Have someone check on you. If you are using in a group, stagger your use so someone is always alert.
- Carry naloxone and know how to use it. Look out for each other.
- Call 911, be aware that a xylazine overdose may need more care than naloxone.
- Be sure the airway is open, as breathing may be blocked in slumped positions.

Resources

- [Xylazine Quick Guide for PWUDs \(Next Distro\)](#)
- [Xylazine in the drug supply \(Harm Reduction Coalition\)](#)
- [New York City Health Advisory](#)
- [2022 Public Health Alert Xylazine Update \(July 2022\)](#)
- [Philadelphia Dept of Public Health - Risks of Xylazine Use and Withdrawal in People Who Use Drugs in Philadelphia \(Mar 2022\)](#)
- [Substance Use Philly - Xylazine \(Tranq\)](#)

ⁱ FDA warns about the risk of xylazine exposure in humans. November 2, 2022. <https://www.fda.gov/media/162981/>.

ⁱⁱ Booze L. *ToxTidbits. Xylazine 2019*

ⁱⁱⁱ Mohr ALA, Browne T, Martin D, Logan BK. *Xylazine: A Toxic Adulterant Found in Illicit Street Drugs: U.S. Dept of State; 2020 [updated October 2020. Available from: <https://www.nvopioidresponse.org/wp-content/uploads/2020/10/u-public-alert-xylazine-003.pdf>*

^{iv} Michigan Poison Control Center, Wayne State University. *Fact Sheet: Xylazine. 2020.*

^v Friedman, J., Montero, F., Bourgois, P., Wahbi, R., Dye, D., Goodman-Meza, D., & Shover, C. (2022). Xylazine spreads across the US: A growing component of the increasingly synthetic and polysubstance overdose crisis. *Drug and alcohol dependence, 233*, 109380.

^{vi} *Risks of Xylazine Use and Withdrawal in People Who Use Drugs in Philadelphia March 16, 2022*

^{vii} Reyes JC, Negrón JL, Colón HM, et al. *The emerging of xylazine as a new drug of abuse and its health consequences among drug users in Puerto Rico. J Urban Health Bull N Y Acad Med. 2012;89(3).*

^{viii} Ohio Department of Mental Health and Addiction Services. *Drug trend reports. <https://mha.ohio.gov/Researchers-and-Media/Workgroups-and-Networks/Ohio-Substance-Abuse-Monitoring-Network/Drug-Trend-Reports>.*

^{ix} Kariisa M, Patel P, Smith H, Bitting J. *Notes from the Field: Xylazine Detection and Involvement in Drug Overdose Deaths — United States, 2019. MMWR Morb Mortal Wkly Rep 2021; 70:1300–1302.*

^x Ehrman-Dupre, R., Kaigh, C., Salzman, M., Haroz, R., Peterson, L. K., & Schmidt, R. (2022). *Management of Xylazine Withdrawal in a Hospitalized Patient: A Case Report. Journal of addiction medicine, 16(5), 595–598.*