



# Xylazine: What Clinicians Need to Know

## Key facts about xylazine:

- **Xylazine is a potent central nervous system (CNS) depressant**, increasingly found as an adulterant in the illicit drug supply, that increases the risk of respiratory depression and fatal overdose.<sup>1</sup>
- **It is linked to overdose deaths.**<sup>2</sup> From 2015-2020, xylazine was involved in 25.8% of overdose deaths in Philadelphia, 19.3% in Maryland, and 10.2% in Connecticut.<sup>3</sup>
- **Administer naloxone for xylazine-involved overdoses** as it is often found with the opioid fentanyl. (Naloxone has no impact on xylazine alone.)
- **It can cause severe skin wounds** regardless of route of use.
- **Xylazine urine drug testing** is currently only available from reference laboratories (send-out, non-VA) at select facilities. Check with your local Pathology department.

## What is xylazine?

Xylazine is a non-opioid tranquilizer used in veterinary medicine.<sup>3-7</sup> It has no approved human use and is not listed as a controlled substance by the DEA (Drug Enforcement Agency). Called “zombie drug,” “tranq,” or “sleep cut,” xylazine is thought to enhance the euphoric effects of fentanyl and heroin.<sup>1</sup> Xylazine used in combination with fentanyl was designated as an emerging threat to the United States in April 2023.

The extent of xylazine’s presence in the drug supply is unknown,<sup>3</sup> and many people do not even realize they are taking it. The effects of xylazine can be rapid (within minutes) and last 8 hours or more, depending on the dose, route of administration, and if mixed with other substances.<sup>8</sup>

## What are the effects of xylazine in humans?<sup>9-12</sup>

### Acute physiologic effects

- Slowed breathing
- Bradycardia, hypotension
- Loss of consciousness and physical sensation
- Immobility leading to muscle and nerve damage
- Constricted pupils
- Amnesia

Little is known about the health effects of chronic xylazine exposure.

### Severe skin and tissue wounds<sup>13-15</sup>

- Can be ulcers, abscesses, or lesions
- Occur independently of injection site or route of administration
- Can worsen quickly and become severely infected
- May be slow to heal
- Look for/ask about skin lesions or abscesses. If found, refer promptly to medical services or wound care (*see pages 3-4*).

## Xylazine formulations and detection

Xylazine is typically a liquid for veterinary use; however, it can be dried into a powder that can be mixed with other powders and pressed into pills. Like fentanyl, this makes recognition difficult.<sup>1</sup> Routes of administration include intravenous, intramuscular, intranasal, and oral.<sup>6</sup>

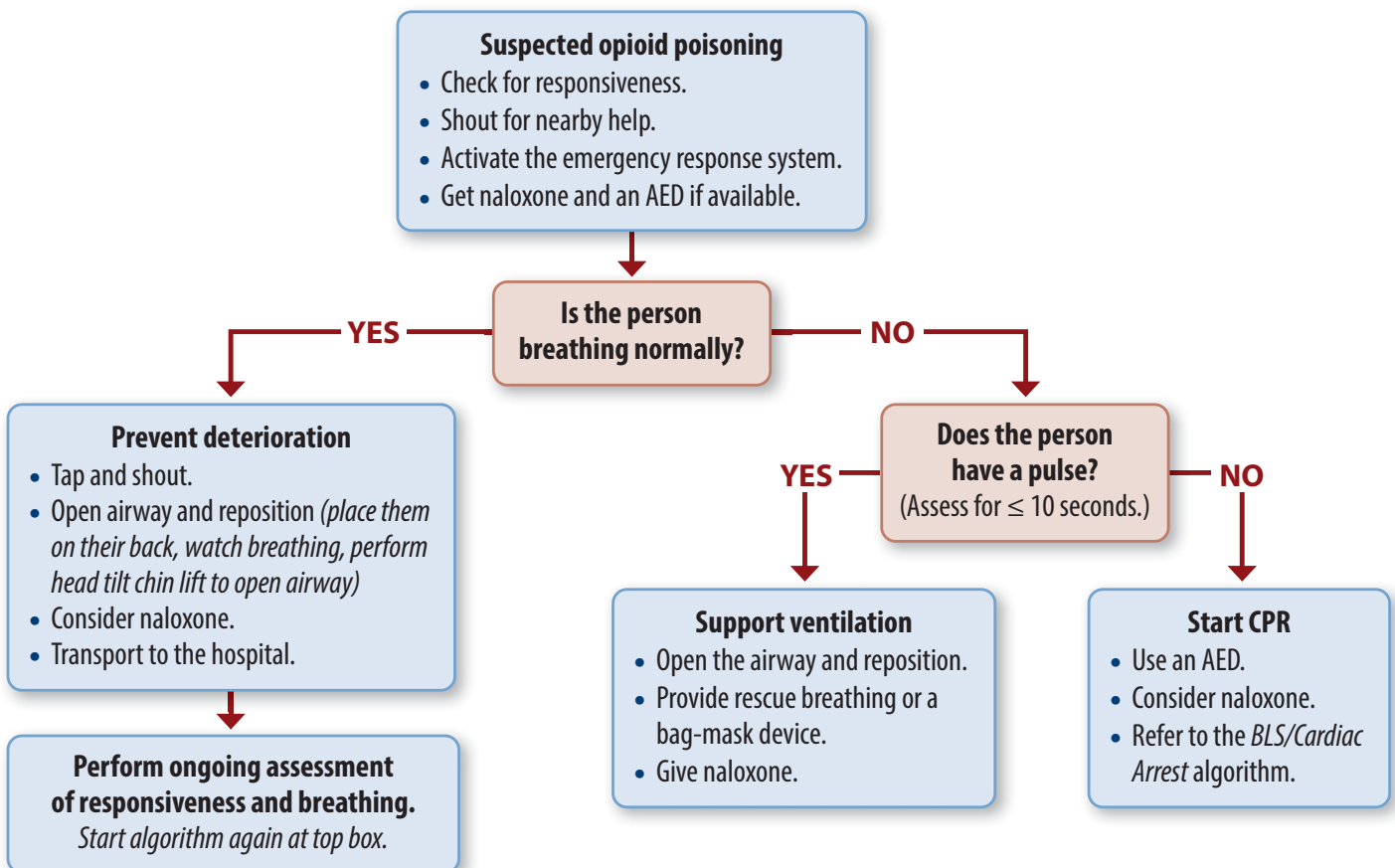
Veterans should be advised that they **cannot rely on how a substance looks, tastes, smells, or cooks to determine whether it contains xylazine**. Xylazine test strips for substance users to test their drug supply are under development, with at least two products available (*see page 4*).<sup>16</sup> These products are not 100% accurate, so safety measures should be taken even if a test is negative (*see pages 3-4*).

**Currently, VA toxicology screens do not include tests for xylazine.** Xylazine is rapidly eliminated from the body, with a short half-life of 23-50 minutes, making it difficult to detect.<sup>4</sup> Testing may be available through reference laboratories at some VA facilities. Consult your local Pathology department for availability.

## Xylazine overdose management

Xylazine overdoses present similarly to an opioid overdose with respiratory depression, hypotension, and altered consciousness. There is currently no agent for human use to reverse xylazine overdose. Xylazine-involved overdose deaths most commonly involve fentanyl. Although naloxone will not reverse the effects of xylazine, it will help with respiratory depression if opioids are present. Thus, clinicians should **administer naloxone for respiratory depression regardless of suspected xylazine involvement**.

### Opioid-associated emergency for healthcare providers algorithm\*



\*Based on American Heart Association algorithm, ©2020. [cpr.heart.org/-/media/CPR-Files/CPR-Guidelines-Files/Algorithms/AlgorithmOpioidHC\\_Provider\\_200615.pdf](http://cpr.heart.org/-/media/CPR-Files/CPR-Guidelines-Files/Algorithms/AlgorithmOpioidHC_Provider_200615.pdf)

In the ED, supportive care is recommended, including airway and blood pressure monitoring and other resuscitation efforts as needed.<sup>17</sup> **Clinicians should look for skin lesions or abscesses** requiring wound care. Xylazine-related wounds typically begin as red pinpoint blisters and can quickly develop into deeper and larger wounds if not treated early. (See below for more information.)

## Xylazine withdrawal management

Xylazine withdrawal symptoms may include anxiety, depression, nervousness/agitation, dizziness, shivering, nausea or vomiting, increased heart rate, and severe hypertension.



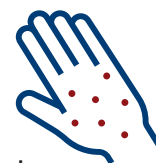
Given the prevalence of the combination of fentanyl and xylazine in the drug supply, **xylazine withdrawal may need to be managed simultaneously with opioid withdrawal.**<sup>18,19</sup> Higher doses of buprenorphine or methadone may be needed to adequately manage symptoms. Recommendations for treating xylazine withdrawal are evolving, but currently include treating with benzodiazepines and/or alpha-2 adrenergic agonists, clonidine, dexmedetomidine, tizanidine, or guanfacine.

**Treat withdrawal early** with opioid withdrawal management strategies. Strategies may need adjustment in the context of recent fentanyl use (e.g., 24-48 hours).

## Harm reduction messaging and approaches<sup>12,20</sup>

The following guidance for patients can help reduce the risks associated with substance use.

- **Educate about the presence of xylazine in the drug supply** and its effects on the body.
- **Counsel on overdose.** Encourage harm reduction practices, including:
  - **Have naloxone on hand**, and make sure you and family/friends know how to use it. (Provide overdose education and offer naloxone to all patients who use illicit substances.)
  - **Never take drugs alone and ensure you are safe.** Have at least one person who can check on you, call 911, or use naloxone. Call Never Use Alone (1-800-484-3731) if you plan to use alone.
  - **Xylazine test strips** can be found at harm reduction programs or purchased. A negative result does not guarantee the substance does not contain xylazine.
  - **If overdose is suspected, use rescue breaths.**<sup>17</sup>
- **Advise patients on xylazine sedation and unintended effects:**
  - Xylazine can cause you to sleep a long time. Make sure you and your things are in a safe place. Be in a comfortable position, not laying on top of your arms or legs, as this could stop blood flow to them.
  - If you use, take a **small amount** of drug first. Wait several minutes between doses.
- **Ask about atypical skin or tissue wounds, and look for them on examination.** Xylazine-related wounds typically begin as red pinpoint blisters and can worsen quickly to deeper, larger wounds. If left untreated, wounds may become infected, require amputation, or become life threatening.<sup>4</sup>
- **Counsel patients on how to care for and monitor xylazine-related wounds:**
  - Seek medical care for atypical skin or tissue wounds.
  - Do not inject any drug into wounds or areas around a wound.
  - Keep wounds clean, moist, and covered with non-adherent dressing and an absorbent pad. Avoid alcohol or hydrogen peroxide which can dry the wounds too much.



*Continued on next page >*

## Harm reduction messaging and approaches<sup>12,20</sup> (continued)

- Apply antibiotic ointment, petroleum jelly, or medical grade honey to the affected area.
- Do not scratch or pop the wounds.
- Seek emergency care if any of the following: any skin gets darker; any skin becomes hard or soft, or loses sensation; there are signs of infection (fever, chills, nausea, injection site feels hot or smells).
- **Consider pain management if appropriate**, specifically prior to dressing changes. Topical or local analgesics can be used but may have limited effect.<sup>21</sup>
- **Encourage substance use treatment or refer to Harm Reduction/Syringe Services Programs** (nasen.org/map). Harm reduction support may also be available at <https://nextdistro.org/>.
- **Educate on safer injection practices** (e.g., clean skin with alcohol swab and let air dry; use sterile needles and do not share or reuse them). If patients are not able to wait for a new/sterile needle, they can clean the needle with bleach and clean water using these instructions: <https://tinyurl.com/cdcccleansyr>
- **Discuss less risky routes of use** (snorting rather than injecting) for those not ready to stop.
- **Facilitate engagement in medical and mental health care as appropriate.**

## Resources

- VA Xylazine Patient Handout
- SAMHSA *Opioid Overdose Prevention Toolkit*
- Learn about Treatment: What's the Latest? Xylazine
- National Harm Reduction Coalition
- Xylazine and fentanyl test strips available from Lochness Medical Supplies Inc. and DanceSafe

### Overdose prevention



### HIV information for providers



### CDC xylazine information



### Safer injection practices



**REFERENCES:** 1. The Growing Threat of Xylazine and its Mixture with Illicit Drugs. (2022). <https://www.dea.gov/documents/2022/2022-12/2022-12-21/growing-threat-xylazine-and-its-mixture-illicit-drugs>. 2. Kariisa M, et al. Notes from the field: xylazine detection and involvement in drug overdose deaths—United States, 2019. *Morbidity and Mortality Weekly Report*. 2021;70(37):1300. 3. Friedman J, et al. Xylazine spreads across the US: A growing component of the increasingly synthetic and polysubstance overdose crisis. *Drug Alcohol Depend*. 2022 Apr 1;233:109380. 4. FDA alerts health care professionals of risks to patients exposed to xylazine in illicit drugs November 8, 2022. <https://www.fda.gov/drugs/drug-safety-and-availability/fda-alerts-health-care-professionals-risks-patients-exposed-xylazine-illicit-drugs>. 5. Press Release: Biden-Harris Administration Designates Fentanyl Combined with Xylazine as an Emerging Threat to the United States. April 12, 2023. Accessed May 9, 2023: <https://www.whitehouse.gov/ondcp/briefing-room/2023/04/12/biden-harris-administration-designates-fentanyl-combined-with-xylazine-as-an-emerging-threat-to-the-united-states>. 6. Ayub S, et al. Xylazine in the Opioid Epidemic: A Systematic Review of Case Reports and Clinical Implications. *Cureus*. 2023 Mar 29;15(3):e36864. 7. Holt AC, et al. Widespread Distribution of Xylazine Detected Throughout the United States in Healthcare Patient Samples. *J Addict Med*. 2023 Jan 6;17(4):468-470. Epub ahead of print. 8. Ruiz-Colón K et al. Xylazine intoxication in humans and its importance as an emerging adulterant in abused drugs: A comprehensive review of the literature. *Forensic Sci Int*. 2014 Jul;240:1-8. 9. Kacinko SL, et al. Xylazine: Pharmacology Review and Prevalence and Drug Combinations in Forensic Toxicology Casework. *J Anal Toxicol*. 2022 Oct 14;46(8):911-917. 10. Elejalde JJ, et al. Drug abuse with inhaled xylazine. *Eur J Emerg Med*. 2003 Sep;10(3):252-3. 11. Capraro AJ, et al. Severe intoxication from xylazine inhalation. *Pediatr Emerg Care*. 2001 Dec;17(6):447-8. 12. Alexander RS, et al. Xylazine and Overdoses: Trends, Concerns, and Recommendations. *Am J Public Health*. 2022 Aug;112(8):1212-1216. 13. Torruella, RA. Xylazine (veterinary sedative) use in Puerto Rico. *Subst Abuse Treat Prev Policy* 6, 7 (2011). 14. Reyes JC, 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*. 2012 Jun;89(3):519-26. 15. Bishnoi A, et al. Skin ulcerations caused by xylazine: A lesser-known entity. *J Am Acad Dermatol*. 2023 Aug;89(2):e99-e102. 16. Krotuiski AJ, et al. (2023) Evaluation of Xylazine Test Strips (BTNX) For Drug Checking Purposes, Center for Forensic Science Research and Education, United States. Accessed May 19, 2023. <https://www.cfsre.org/nps-discovery/drug-checking/evaluation-of-xylazine-test-strips-btnx-for-drug-checking-purposes>. 17. Substance Abuse and Mental Health Services Administration. SAMHSA Opioid Overdose Prevention Toolkit. HHS Publication No. (SMA) 18-4742PT2. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2018. Accessed May 19, 2023: <https://store.samhsa.gov/sites/default/files/d7/priv/five-essential-steps-for-first-responders.pdf>. 18. Ehrman-Dupre R, et al. Management of Xylazine Withdrawal in a Hospitalized Patient: A Case Report. *J Addict Med*. 2022 Sep-Oct 01;16(5):595-598. 19. Mulders P, et al. Xylazine Dependence and Detoxification: A Case Report. *Psychosomatics*. 2016 Sep-Oct;57(5):529-33. 20. Centers for Disease Control and Prevention. What you should know about xylazine. Accessed May 19, 2023: <https://www.cdc.gov/drugoverdose/deaths/other-drugs/xylazine/faq.html>. 21. Anekar AA, et al. WHO Analgesic Ladder. Available at: <https://www.ncbi.nlm.nih.gov/books/NBK554435>. Accessed Aug 1, 2023.