

Xylazine: What Clinicians Need to Know

Key facts about xylazine:

- **Xylazine is an alpha-2 agonist medication used as a sedative/tranquilizer in veterinary medicine.**¹
- **Xylazine is being mixed with illegal drugs** such as fentanyl, cocaine, and heroin.
- **Xylazine can increase risk of sedation, respiratory depression, and fatal overdose** and has been linked to overdose deaths.^{2,3}
- Recent CDC data (2023) among 20 states and Washington D.C. indicates the monthly percentage of **deaths involving illegally made fentanyl with xylazine detected increased 276%** from January 2019 (2.9%) to June 2022 (10.9%).⁴
- **Administer naloxone for xylazine-involved overdoses** as it is often found mixed with opioids. Naloxone has no impact on xylazine alone but it may help with respiratory depression if opioids are present.
- **Xylazine 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 an alpha-2 adrenergic agonist used as a sedative/tranquilizer in veterinary medicine (not FDA-approved for use in humans).^{1,5-9} Xylazine is not currently listed as a controlled substance by the DEA (Drug Enforcement Agency). Sometimes known as “tranq,” or “sleep cut,” xylazine is thought to enhance the effects of fentanyl and heroin.² 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,⁵ and many people do not 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.¹⁰

What are the effects of xylazine in humans?¹¹⁻¹⁴

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 wounds¹⁵⁻¹⁷

- 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 present, refer promptly to medical services or wound care (*see pages 3-4*).

Xylazine formulations and detection

Xylazine is typically supplied as a liquid formulation for veterinary use; however, it can be dried into a powder that can then be mixed with other powders and pressed into pills.²

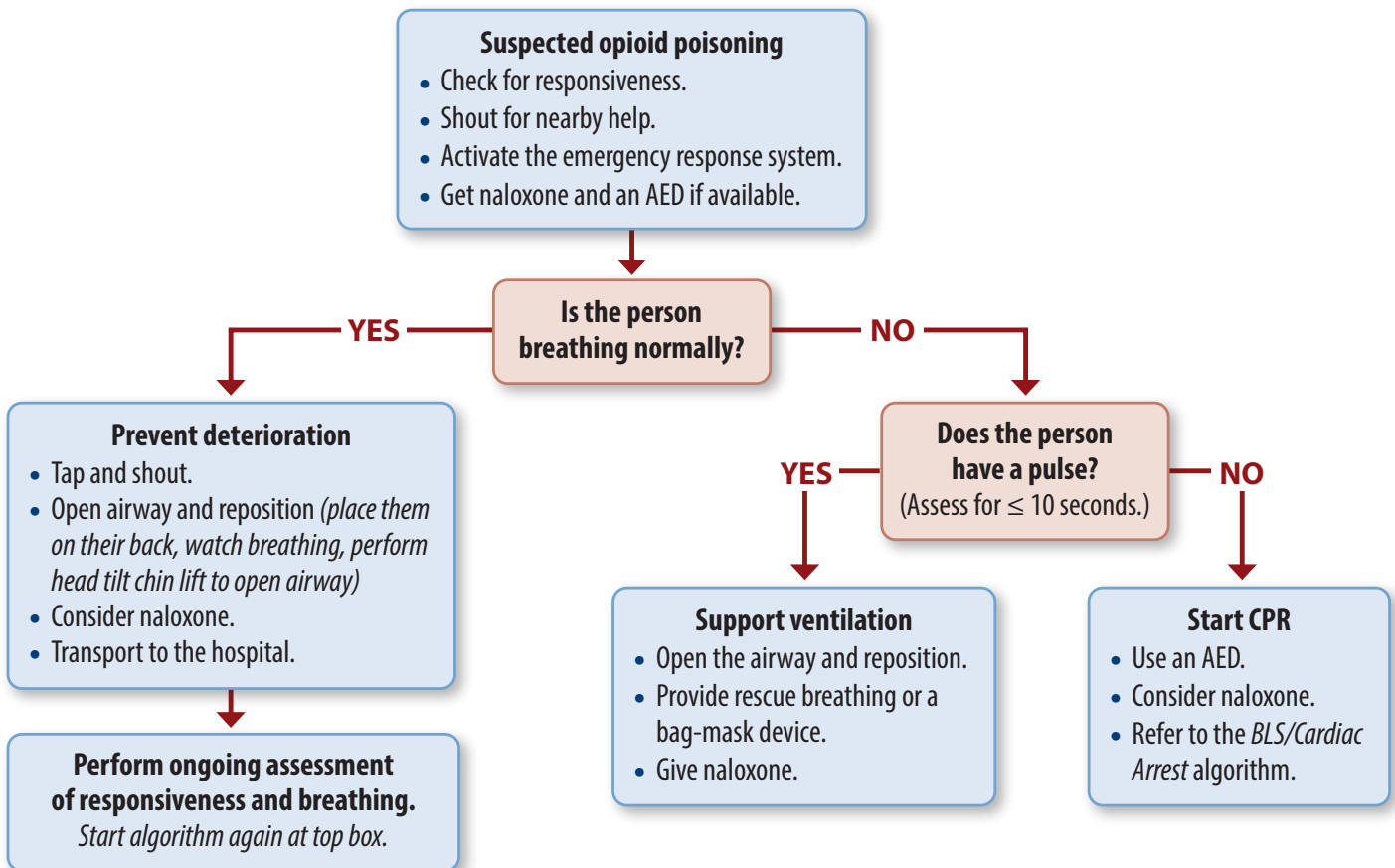
Veterans should be advised that they **cannot rely on how a substance looks, tastes, or smells to determine whether it contains xylazine**. Xylazine test strips are available commercially and can be used to detect the presence of xylazine in a sample of drugs.¹⁸ Xylazine test strips are not 100% accurate, so Veterans should be advised to consider safety measures even if a test is negative for xylazine (*see pages 3-4*).

Currently, routine VA toxicology screens do not test for xylazine. In addition, xylazine is rapidly eliminated from the body, with a short half-life of 23-50 minutes, making it difficult to detect.⁶ Specific testing may be available through reference laboratories at some VA facilities. Please 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 available for human use that will reverse the effects of a xylazine overdose. Xylazine-involved overdose deaths most commonly involve fentanyl. Although naloxone will not reverse xylazine, it may help with respiratory depression if opioids are present. Thus, **naloxone should be administered 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

Xylazine overdose management *(continued)*

In the Emergency Department (ED), supportive care is recommended, including airway and blood pressure monitoring and other resuscitation efforts as needed.¹⁹ Clinicians should look for skin lesions/abscesses requiring wound care. Xylazine-related wounds typically begin as dark purple blisters with irregular borders and can quickly develop into deeper and larger wounds if not treated early. *(See below for wound care information.)*

Xylazine withdrawal management

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

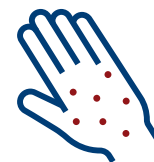


Recommendations for treating xylazine withdrawal are evolving, but currently include treating with alpha-2 adrenergic agonists (e.g., clonidine, dexmedetomidine, tizanidine, guanfacine) and/or benzodiazepines. Given the prevalence of the combination of fentanyl and xylazine in the drug supply, xylazine withdrawal may need to be managed simultaneously with opioid withdrawal.^{20,21}

Harm reduction messaging and approaches^{14,22}

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 and encourage harm reduction practices**, including:
 - **Have naloxone on hand**, and make sure you and family/friends know how to use it.
 - **Never take drugs alone and ensure you are safe.** Have at least one person who can check on you, call 911, or use naloxone. **Use xylazine test strips**, which you can get from harm reduction programs, syringe service programs, or purchase. A negative xylazine test strip result does not guarantee the substance is xylazine free.
- **Advise patients on xylazine sedation and unintended effects:**
 - Make sure you and your things are in a safe place. Before using, lay down or sit to avoid falls or injury from not moving for several hours. Ensure you are not laying on top of your arms or legs, as this could limit/reduce 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 blisters and can worsen quickly to deeper, larger wounds. If left untreated, wounds may become infected, require amputation, or become life-threatening.^{6,23}
- **Counsel patients on how to care for and monitor xylazine-related wounds:**
 - Encourage patients not to inject into wounds or areas around a wound.
 - Seek medical care for atypical skin or tissue wounds. Do not scratch or pop the wounds.
 - Keep the wounds as clean as possible and keep them covered. Change the wound dressing daily or whenever it gets wet.²⁴
 - **Self-care tips for xylazine-associated wounds:** Use mild soap and clean water to clean the wound, apply a layer of petroleum jelly or wound ointment on a clean bandage, and cover the wound. Use self-adhesive wrap to cover the wound and keep the bandage in place. Clean the wound and change the bandage daily if possible, but at least every 2-3 days. Avoid putting alcohol and hydrogen peroxide on the wounds (they can dry out the wounds too much).²⁴⁻²⁶



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Harm reduction messaging and approaches^{14,22} (continued)

- **Seek medical care if any of the following occur:** signs of infection (fever, chills, nausea, skin is red, feels hot or smells), severe pain at wound site, pieces of skin falling off, bone is showing, new numbness or tingling on skin, inability to move the body part where the wound is located.²⁵
- **Consider pain management if appropriate,** specifically prior to dressing changes. Topical or local analgesics can be used but may have limited effect.²⁷
- **Reduce injection-related risks:** Clean injection site with alcohol swab and let air dry before injecting, use sterile needles and do not share or reuse them, or take drugs in other ways besides injection.²⁸ If patients are not able to wait for a new/sterile needle, they can clean the needle using these instructions: <https://tinyurl.com/cdcccleansyr>.
- Encourage substance use treatment and refer to Harm Reduction/Syringe Services Programs. (See: <https://www.va.gov/recovery>.)
- Facilitate engagement in additional medical and mental health care as appropriate.

Resources

- CDC Xylazine handout: <https://tinyurl.com/CDC-overdose-prevention>
- SAMHSA *Opioid Overdose Prevention and Response Toolkit*: <https://tinyurl.com/overdose-kit>
- Substance Use Treatment For Veterans | Veterans Affairs (va.gov)
- SAMHSA mental health and substance use disorder treatment locator: <https://findtreatment.gov/locator>

Preventing overdose



HIV information for providers



Your path to recovery (va.gov)



Safer injection practices



REFERENCES:

1. Gupta R, et al. Xylazine—Medical and Public Health Imperatives. *N Engl J Med*. 2023 Jun 15;388(24):2209-2212.
2. Drug Enforcement Administration, U.S. Department of Justice. The Growing Threat of Xylazine and its Mixture with Illicit Drugs (2022). Accessed August 7, 2023: <https://www.dea.gov/documents/2022/2022-12/2022-12-21/growing-threat-xylazine-and-its-mixture-illicit-drugs>.
3. 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.
4. Kariisa M, et al. Illicitly Manufactured Fentanyl-Involved Overdose Deaths with Detected Xylazine—United States, January 2019–June 2022. *MMWR Morb Mortal Wkly Rep*. 2023 Jun 30;72(26):721-727.
5. 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.
6. FDA alerts health care professionals of risks to patients exposed to xylazine in illicit drugs November 8, 2022. Accessed August 7, 2023: <https://www.fda.gov/drugs/drug-safety-and-availability/fda-alerts-health-care-professionals-risks-patients-exposed-xylazine-illicit-drugs>.
7. 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>.
8. 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.
9. 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.
10. 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.
11. 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.
12. Elejalde JJ, et al. Drug abuse with inhaled xylazine. *Eur J Emerg Med*. 2003 Sep;10(3):252-3.
13. Capraro AJ, et al. Severe intoxication from xylazine inhalation. *Pediatr Emerg Care*. 2001 Dec;17(6):447-8.
14. Alexander RS, et al. Xylazine and Overdoses: Trends, Concerns, and Recommendations. *Am J Public Health*. 2022 Aug;112(8):1212-1216.
15. Torruella, RA. Xylazine (veterinary sedative) use in Puerto Rico. *Subst Abuse Treat Prev Policy* 6, 7 (2011).
16. 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.
17. Bishnoi A, et al. Skin ulcerations caused by xylazine: A lesser-known entity. *J Am Acad Dermatol*. 2023 Aug;89(2):e99-e102.
18. 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>.
19. 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>.
20. 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.
21. Mulders P, et al. Xylazine Dependence and Detoxification: A Case Report. *Psychosomatics*. 2016 Sep-Oct;57(5):529-33.
22. Centers for Disease Control and Prevention. What you should know about xylazine. Accessed September 3, 2024: <https://www.cdc.gov/overdose-prevention/about/what-you-should-know-about-xylazine.html>.
23. McFadden R, et al. Xylazine-associated Wounds: Clinical Experience From a Low-barrier Wound Care Clinic in Philadelphia. *J Addict Med*. 2024 Jan-Feb 01;18(1):9-12.
24. NASTAD. Wound Care & Medical Triage for People Who Use Drugs and the Programs that Serve Them: A Guide. Accessed September 3, 2024: <https://nastad.org/sites/default/files/2023-04/PDF-Wound-Care-And-Triage.pdf>.
25. California Department of Public Health. Xylazine. November 2023. Accessed September 3, 2024: <https://www.cdph.ca.gov/Programs/CCDPHP/sapb/CDPH Document Library/xylazine-wound-care-factsheet.pdf>.
26. Sue KL, Hawk K. Clinical considerations for the management of xylazine overdoses and xylazine-related wounds. *Addiction*. 2024 Apr;119(4):606-608.
27. Anekar AA, et al. WHO Analgesic Ladder. Accessed Aug 1, 2023: <https://www.ncbi.nlm.nih.gov/books/NBK554435>.
28. Centers for Disease Control and Prevention. Xylazine—Clinical Management and Harm Reduction Strategies for Patients. Accessed September 3, 2024: https://www.cdc.gov/ore/pdf/CDC_Xylazine-Clinician-Fact-Sheet_508.pdf.