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What Now: Relevance of Xylazine in the Age of Opioid Use Disorder - Guidance for OUD Treatment Providers

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Attending Physician in Emergency Medicine
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Housekeeping

- Today's webinar is being recorded and all participants will be kept in listen only mode. There will be an opportunity to ask questions at the end of the webinar, so we encourage you to please submit your questions throughout the webinar in the Q&A box located at the bottom of your screen.
- The recording and slides will be made available on the PCSS-MOUD website within 2 weeks.
- Within 24 hours of today's session, you will receive an email from grantededucation@aaap.org with evaluation and certificate claiming information.



*The content of this activity may include discussion of off label or investigative drug uses.
The faculty is aware that is their responsibility to disclose this information.*

Funder Information

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- The overarching goal of PCSS-MOUD is to increase healthcare professionals' knowledge, skills, and confidence in providing evidence-based practices in the prevention, treatment, recovery, and harm reduction of OUD.

Today's Speaker



Daniel Rosa, MD, FASAM

Senior Medical Director, Acacia Network NYC
Attending Physician in Emergency Medicine,
Philadelphia VA Medical Center

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Disclosure to Learners

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All disclosures have been reviewed, and there are no relevant financial relationships with ineligible companies to disclose.

All speakers have been advised that any recommendations involving clinical medicine must be based on evidence that is accepted within the profession of medicine as adequate justification for their indications and contraindications in patient care. All scientific research referred to, reported, or used in the presentation must conform to the generally accepted standards of experimental design, data collection, and analysis.

Educational Objectives

At the conclusion of this activity participants should be able to:

- Discuss the prevalence of xylazine and its relevance to opioid use disorder.
- Describe medical issues associated with xylazine use and effective strategies to address these.
- Examine treatment options for xylazine use.



What Now: Xylazine in the Age of Opioid Use Disorder



Acacia Network



Photo credit: Honan, K. (2019).

My Professional Background



Poll: Level-setting on Xylazine Knowledge

How familiar are you with xylazine?



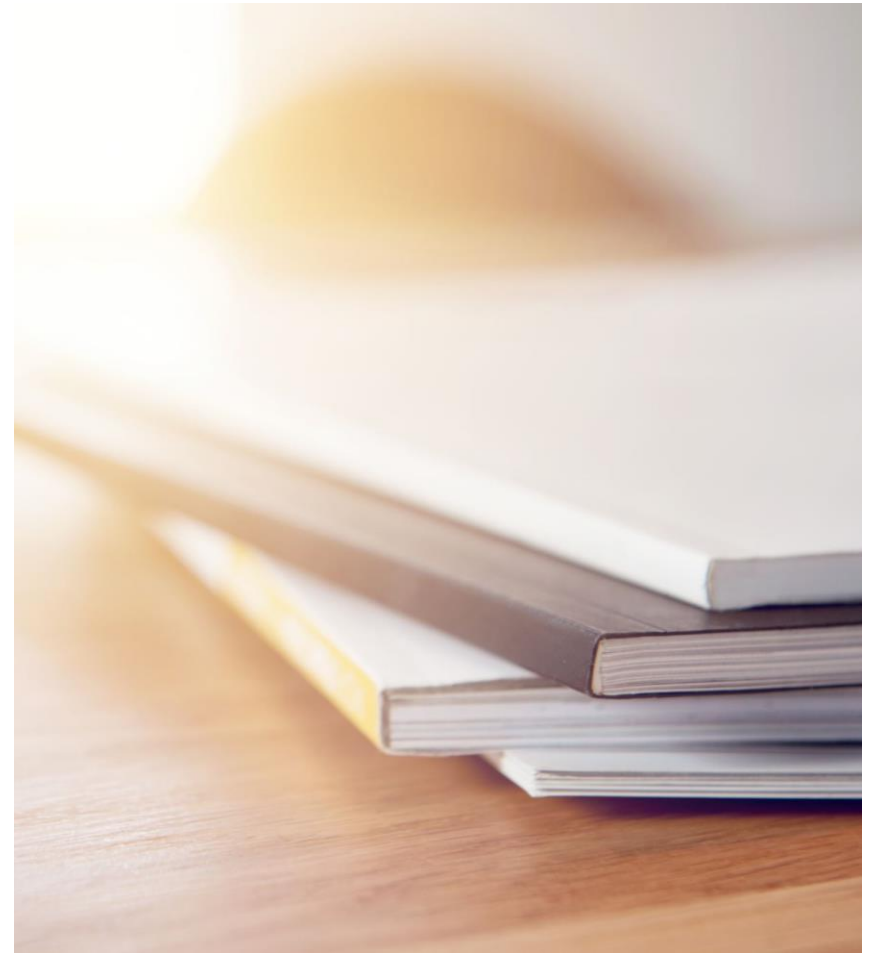
- a. I haven't heard the term before
- b. I've heard the term before, but don't really know anything about it
- c. I know some things about it
- d. I know a lot about it

My Introduction to Xylazine



Scholarly Articles on Xylazine

- Rodríguez N, Vargas Vidot J, Panelli J, Colón H, Ritchie B, Yamamura Y.
- *GC-MS confirmation of xylazine (Rompun), a veterinary sedative, in exchanged needles.*
- Drug Alcohol Depend. 2008 Aug 1;96(3):290-3. doi: 10.1016/j.drugalcdep.2008.03.005. Epub 2008 May 9. PMID: 18472231; PMCID: PMC2527692.



Article Results from Collected Samples

- 37.8% of all samples collected were positive for xylazine (aka “Tranq”).
- Over 90% of samples that tested for Speedball (Cocaine/Heroin) tested positive for xylazine.
- Most of the samples positive for xylazine came from ranching communities.
- 38.5% of users had skin lesions vs 6.8% of non-users.



Trends in Xylazine Prevalence



- From 2019 to 2022, xylazine detection in drug samples **more than doubled** in 30 states. (Cano et. al., 2024)
- 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%). (Friedman et. al., 2022)

Philadelphia: Zooming in on xylazine presence in the drug supply

- 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.**



(Philadelphia Department of Public Health, 2022)

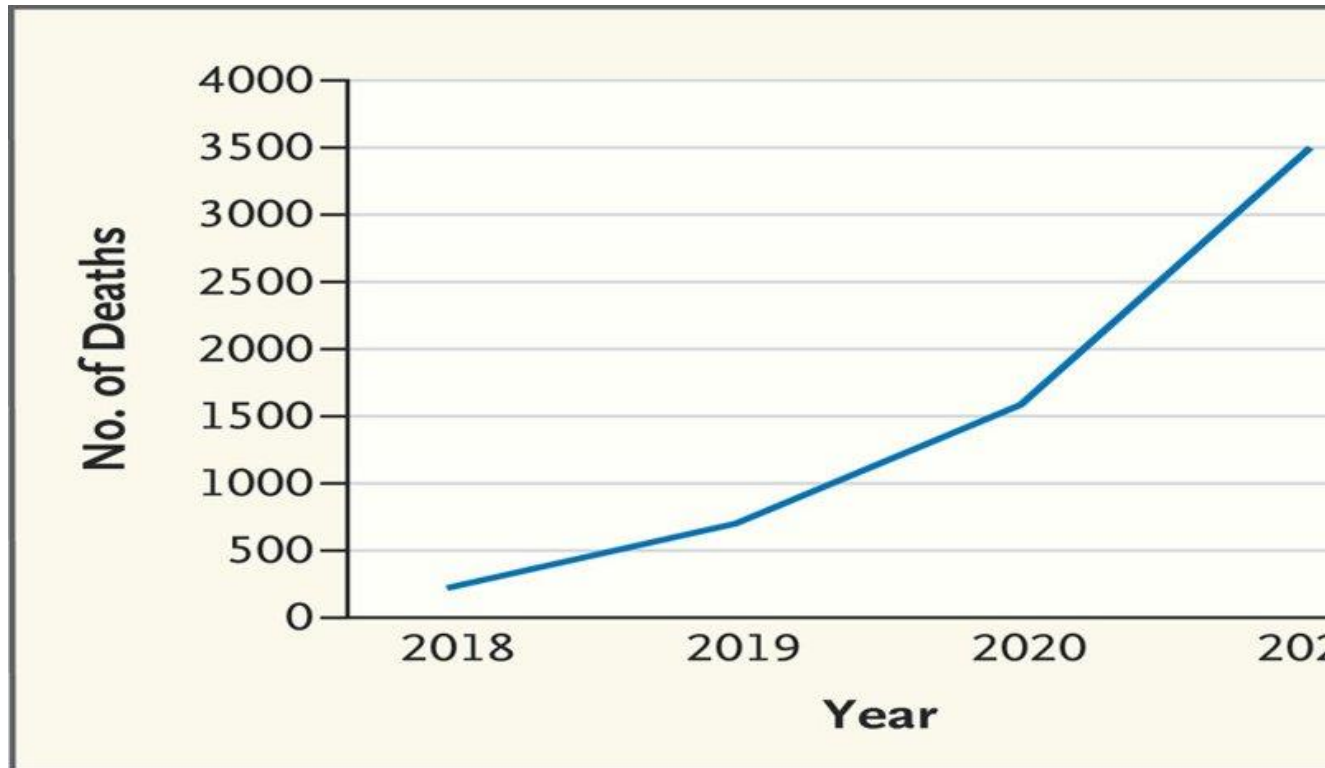
Photo credit: Heminghaus, D. (2022)

Xylazine Seen as an Emerging National Threat

Dr. Rahul Gupta,
Director of White
House National
Drug Control
Policy



Xylazine and Fatal Overdoses



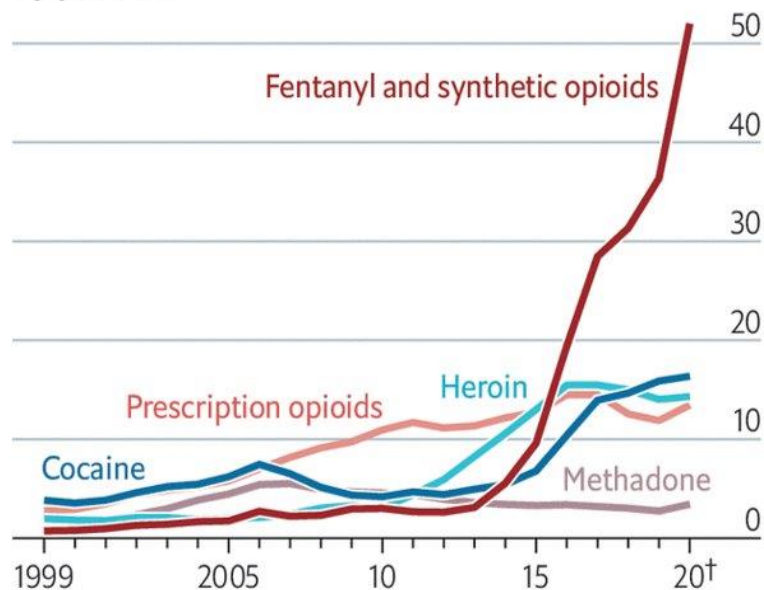
The estimated number of drug-poisoning deaths in the United States involving xylazine grew from 260 in 2018 to 3480 in 2021, an increase of 1238%

Why is xylazine relevant to opioid use disorder? Considering opioid overdoses

The other epidemic

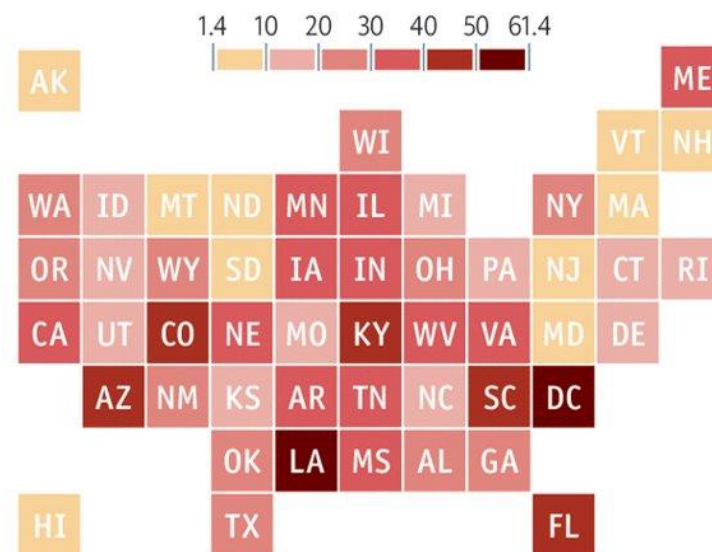
United States, drug overdose deaths*

By year, '000



Source: Centres for Disease Control and Prevention

By state, 2020†, % change on a year earlier



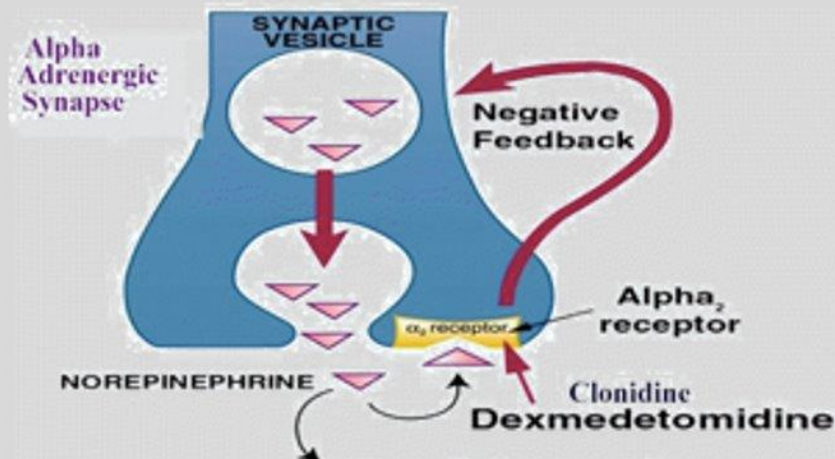
*Deaths involving multiple opioids counted in each category
†12-month ending August 2020, predicted

Why is xylazine relevant to opioid use disorder? Considering opioid contamination with xylazine

- The U.S. Drug Enforcement Administration (DEA) has seized xylazine and fentanyl mixtures in **48 of the 50 states**. (DEA, 2023)
- DEA Laboratory System reports show that of fentanyl seized in 2022, **23%** of fentanyl powder contained xylazine, while **7%** of fentanyl pills were also contaminated with xylazine (DEA, 2023)
- Because it is not an opioid, xylazine does not respond **to opioid reversal via naloxone**, potentially causing an increased number of deaths from opioid overdose (Alexander et. al., 2022)
- In 20 states and the District of Columbia, xylazine combined with illicitly manufactured fentanyl was present in **11% of drug overdose deaths in 2022**. (Kariisa et. al., 2023)

Xylazine Mechanism in the Human Body

Alpha-2 receptors are most plentiful in brain and presynaptic sympathetic neurons. Activation of α_2 receptors inhibits norepinephrine release. A specific α_2 receptor agonist is clonidine.



Effects of Xylazine on Those Who Use it

XYLAZINE IMPACTS



CNS Effects

- Analgesia
- Sedation
- Amnesia
- Coma



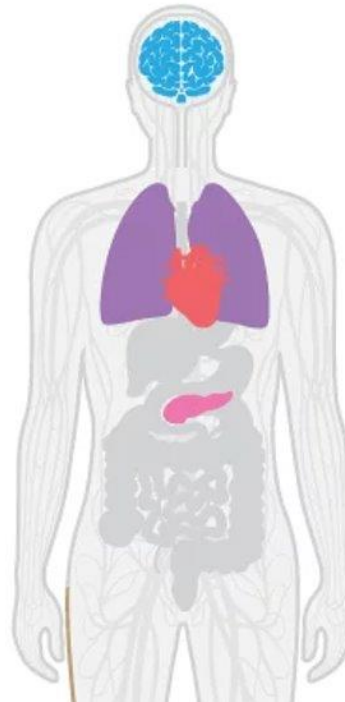
Respiratory System

- Respiratory depression



Skin Disorders

- Ulcers
- Tissue necrosis



Cardiovascular

- Hypotension
- Bradycardia
- Tachycardia
- Vasoconstriction



Metabolic/Endocrine

- Hyperglycemia

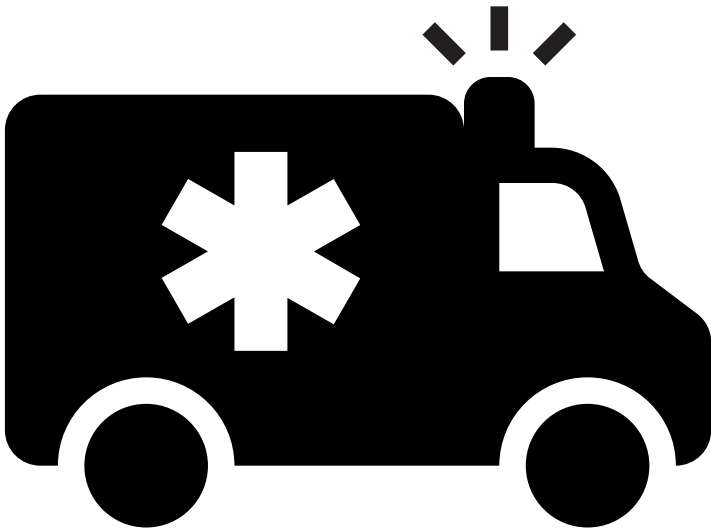
Stigma Surrounding Xylazine

Doctors Alarmed By Spread of Zombie Drug In New York: “Diabolical”



Xylazine, the “zombie drug” that’s causing alarm in the U.S., has been linked to several deaths on the American streets.

It Makes the Drug Deadlier!



- Xylazine makes the unregulated drug supply even potentially deadlier than it already is. (DEA, 2023)
- It is projected that the current drug overdose death toll will **increase** as the xylazine prevalence continues to rise. (DEA, 2022)

How do we treat xylazine use and its effects?



- **Harm reduction** is key approach (Zagorski et. al., 2023)
- **Counseling and Support**
- **MOUD (Medications for Opioid Use Disorder)**
- Consider **health-related social needs**:
 - Addressing Social Determinants of Health (housing, education, literacy, language, transportation concerns , etc.)
 - Mental Health
 - Primary Care

Poll: Case Study

- 40-year-old white male with known history of anxiety (on Xanax 1 mg tid) and opioid use disorder is found unresponsive and barely breathing in the bathroom of your facility (pulse oximetry 82%).
- He is administered Narcan nasally and his breathing normalizes with pulse oximetry of 99% and bounding pulse rate of 50.
- He is responsive to painful stimuli but still overly sedated.

What do you do next?



Poll: Case Study | Answer Options

- a. Start CPR
- b. Continue to give additional doses of nasal Narcan until he wakes up
- c. Give Flumazenil (Mazicon) to reverse likely Benzodiazepine overdose
- d. Immediately call 911 and apply O2 (if available) and monitor his breathing till help arrives
- e. Do nothing as this is probably a xylazine overdose and he will eventually wake up



Poll: Case Study | Answer Options

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- e. Do nothing as this is probably a Xylazine overdose and he will eventually wake up



Poll: Case Study | Reasoning behind the Correct Answer

- d. Immediately call 911 and apply O2 (if available) and monitor his breathing till help arrives**
- **Whenever you witness or respond to an overdose, call 911.**
 - Even if naloxone reverses the overdose:
 - There may be other health problems going on,
 - People who survive any type of overdose are at risk of experiencing other health complications because of the overdose
 - **Continue monitoring patient's breathing in case it worsens**

Poll: Case Study | Reasoning behind the Correct Answer cont.

d. Immediately call 911 and apply O2 (if available) and monitor his breathing till help arrives

- **Do NOT give more than 2 doses of naloxone**
 - If the second dose of naloxone does not revive them, something else is wrong:
 - It has been too long and the heart has already stopped, OR
 - There are no opioids in their system (other drugs may have caused the overdose), OR
 - The opioids are unusually strong and require more naloxone (can happen with Fentanyl, for example).

Treating Overdose in the Age of Xylazine

- Look for any signs of head or physical trauma.
- Check a Pulse Ox (if lower than 92%, provide supplemental O2).
- If possible, check a fingerstick glucose.

Overdose: Not just naloxone!

If someone took benzos or xylazine (*tranq/sleepdope*), naloxone may not be enough! What do you do?!?

If they aren't breathing:

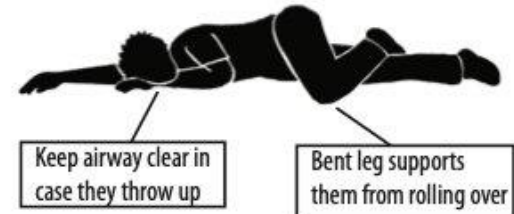
1. Try to **wake them up**
2. **CALL 911**, ask for EMS!!
3. **Use naloxone** to reverse fentanyl/opioid overdose. Give 1 or 2 doses. Naloxone takes 3-5 minutes to work!
4. While you are waiting for the naloxone, perform **rescue breathing**:
 - Take a deep breath, pinch their nose, cover their mouth with yours, blow into their lungs like blowing up a balloon
 - Two breaths to start then 1 every 5 seconds
5. **Keep checking for breathing**
 - Put your ear near their mouth and nose
 - Feel, look, listen for breathing, check for color returning
6. If they are still not breathing, **continue rescue breaths until EMS arrives**

If they are breathing, but not waking up:

There may be other drugs involved like benzos or xylazine (*tranq/sleepdope*). More naloxone won't help!

Roll them into **recovery position**:

- Roll them on their side, with one side's arm and leg straight, the other side's arm and leg bent. This position will keep them on their side so they won't choke if they vomit



Treating Xylazine Use



Monitor and **support** the acute intoxication

(remember that the period of sedation may be quite long after Narcan rescue – hours).



Discuss chemical dependency treatment options

(i.e. immediate Buprenorphine induction, high dose) or link to outpatient Buprenorphine induction or Methadone maintenance.



Examine the patient for skin lesions and if noted, exercise simple local wound care if possible. If severe, seek expert consultation.

A Note about Xylazine Withdrawal

- As an ER Doc, I rely heavily on evidence-based flowcharts and algorithms to guide my approach to medical urgencies.
 - Xylazine toxicity has redefined the landscape of the withdrawal syndrome
 - Can be a bit daunting
 - Evidence-based guidelines are still in their infancy.

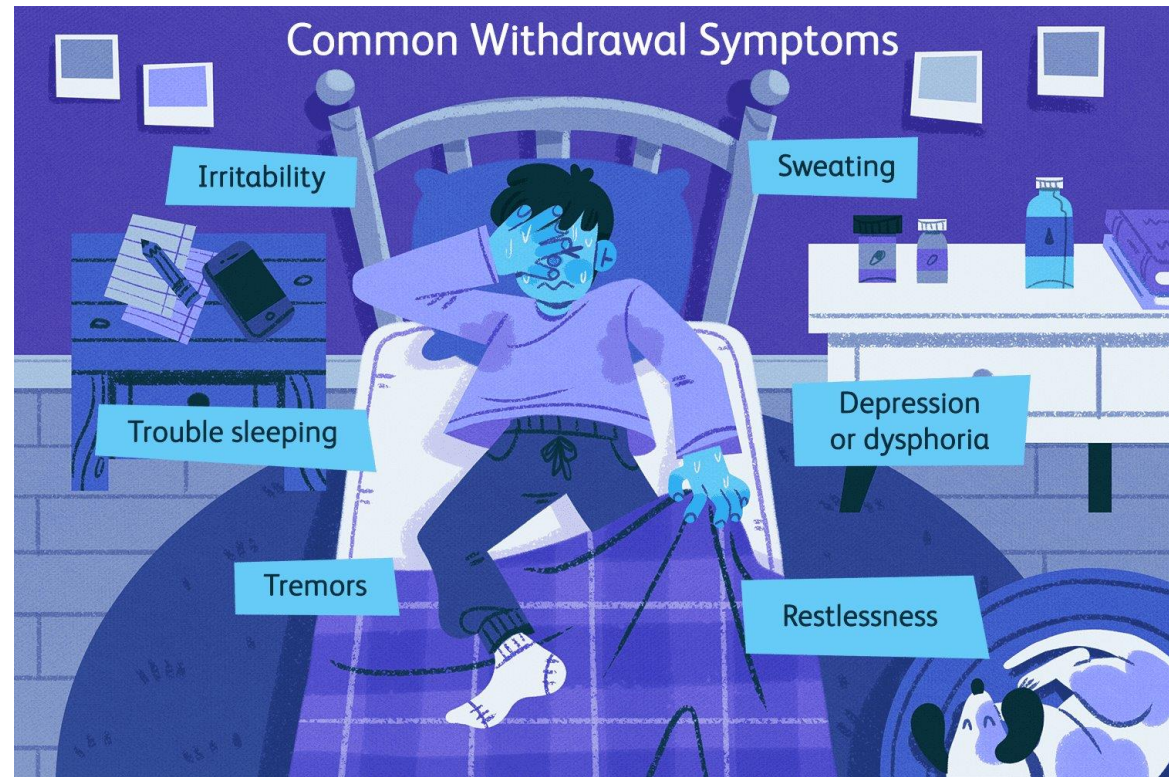
A Note about Xylazine Withdrawal

Though not evidence based my common-sense approach is to **target the receptors with medications known to share similar neurochemistry**

- **No known antidotes exist** (Papudesi et. al., 2023)

Symptoms of Xylazine Withdrawal

- Timing of withdrawal symptoms may be difficult to predict and even more difficult to treat due to the conflation of substances and their half lives of the parent drug and adulterant.
- Watch for signs and symptoms of severe withdrawal:
 - Elevated blood pressure
 - Tachycardia
 - Severe Anxiety
 - Delirium
 - Autonomic dysregulation



First-line Medications for Treating Xylazine Withdrawal

**For use in all patients unless contra-indicated.*

Clonidine:

0.1mg PO q6-8hrs.
scheduled (not PRN)
and titrated to effect,
up to a max dose of
0.3mg PO Q8h.

- Alpha2-adrenergic agonist; antihypertensive; efficacy in opioid withdrawal attributed to binding to central alpha-2 adrenergic receptor that shares potassium channels with opioids and blunts symptoms of withdrawal
- Monitor for signs of hypotension and oversedation especially in patients with ESRD, advanced age or compromised renal function.

OR

Tizanidine

2-4mg PO q6-8 hrs.
(not PRN)

- Another alpha 2 agonist
- Has less effect on heart rate and blood pressure and is ideal for withdrawal spasms associated with typical symptoms of withdrawal.

Adjunct Medications to Consider

Hydroxyzine
(Vistraril): 25-50
mg q 6-8 hrs PRN.

During early to moderate symptoms of anxiety associated with withdrawal.

Olanzapine
(Zyprexa): 5 mg PO
x 1 dose.

During worsening agitation or hyperactivity.

Quetiapine
(Seroquel): 50-200
mg q 12 hrs.

For moderate to severe agitation.

Gabapentinoids

For structural or neuropathic painful complaints.

Low Dose
Benzodiazepines

Particularly when Bz or alcohol are suspected of exacerbating the withdrawal.

Poll: Level-setting on Xylazine Wounds

Have you seen xylazine-related wounds in your practice?

- a. I haven't seen these wounds in my practice
- b. I have seen wounds in my practice that I didn't recognize at the time, but that may have been xylazine-related
- c. I have seen these wounds a few times in my practice
- d. I have seen these wounds several times in my practice



Poll: Fill in the Blank

Xylazine-related lesions (wounds)...

- a. Are only seen in people using intravenous drugs
- b. Only occur at sites of injection
- c. Are present in all people using or exposed to xylazine
- d. Will always require surgical intervention
- e. All of the above
- f. None of the above



Poll: Fill in the Blank | Correct Answer!

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- f. **None of the above**



Poll: Fill in the Blank | Reasoning behind the Correct Answer

Xylazine-related lesions (wounds)...

- Can occur in **anyone** using xylazine via **any route of administration**
- Can occur **anywhere** on the body (not just at injection sites)
- Are **not present in all people** using or exposed to xylazine
- **Do not always require surgical intervention** – many wounds can be resolved with consistent, basic wound care



Xylazine-related Lesions: Leveraging Sonography

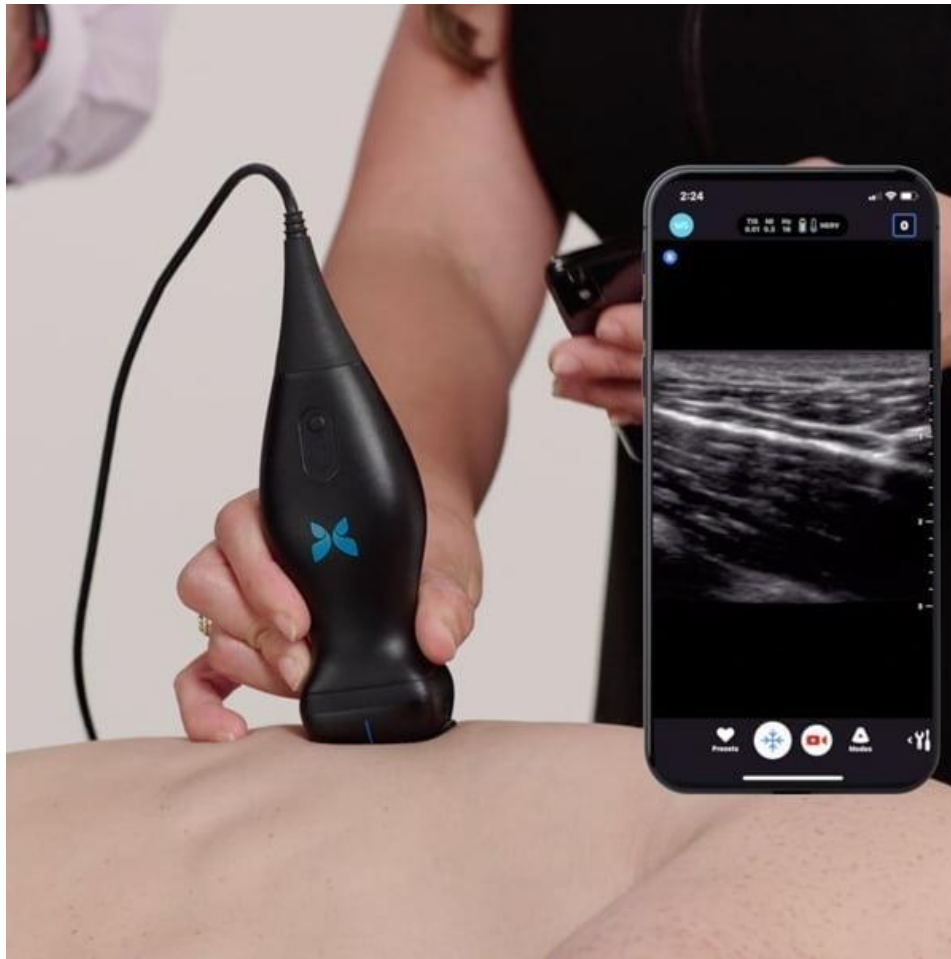
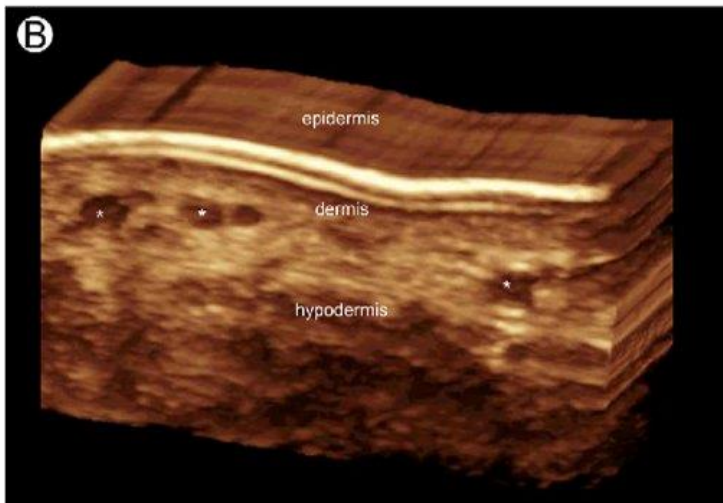
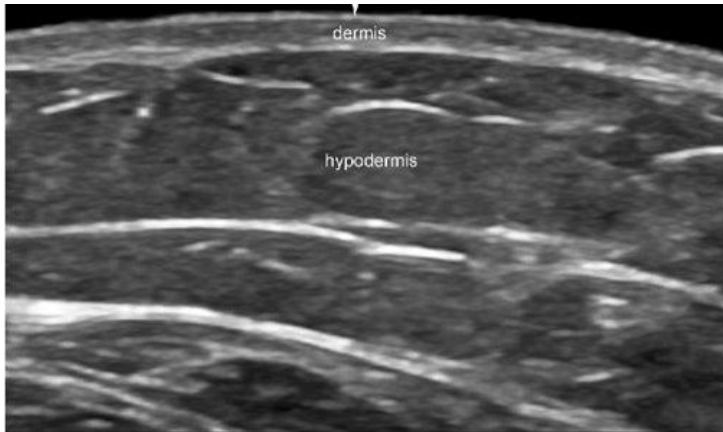


Photo credit: Universal Diagnostic Solutions, (n.d.)

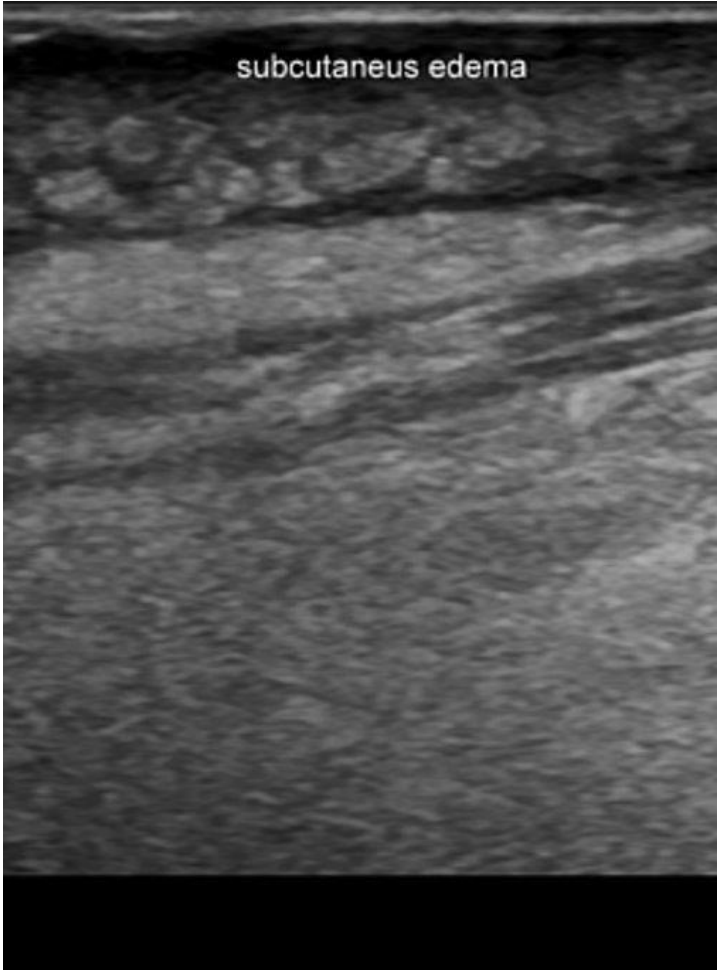
Xylazine-related Lesions – Quick Notes

Normal



- Most who have heard of xylazine are aware of the **risk for lesions**
- A good majority of people who use drugs intravenously have **expressed concerns** about these lesions.
- Majority of these lesions actually are **superficial** and amenable to simple wound care.
- **Many of these lesions are not at injection sites** but in many cases have been described to be at sites distal to injection sites and seen even in individuals who never injected drugs and used other routes of administration (i.e.: oral or nasal)

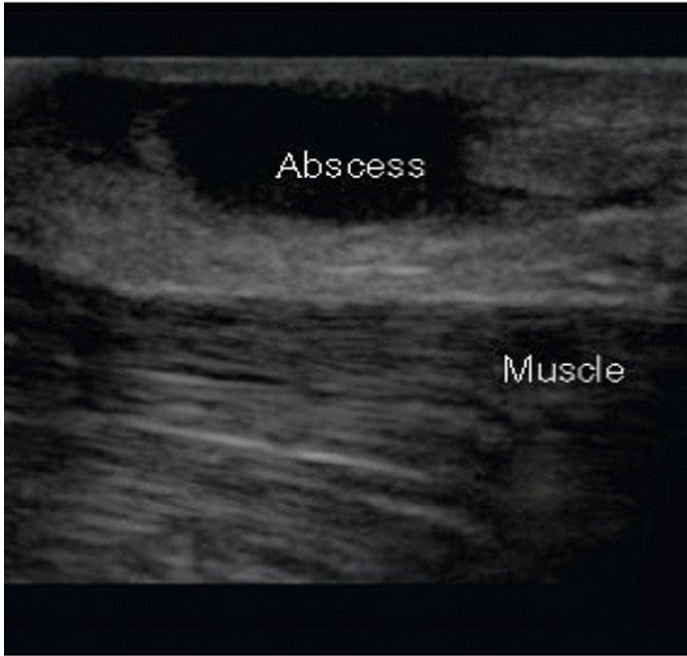
Treating Xylazine-related Lesions



subcutaneous edema

This is a longitudinal B-mode ultrasound image of skin. The top layer is the epidermis, followed by the dermis. Below the dermis, there is a thick, dark, hypoechoic layer, which is labeled as subcutaneous edema. The underlying muscle and subcutaneous fat layers are visible below the edema.

- **Superficial ulcerations** can be approached with simple wound care
- **Superficial abscesses** with can be approached simple I & D (incision and drainage)



Abscess

Muscle

This is a longitudinal B-mode ultrasound image showing a well-defined, anechoic (black) area labeled as an abscess. Below the abscess, the muscle layer is visible, characterized by its striated appearance. The label 'Muscle' is placed to the right of the muscle layer.

Treating Xylazine-related Lesions – Case Study



Final Knowledge Check!



Poll: Case Study

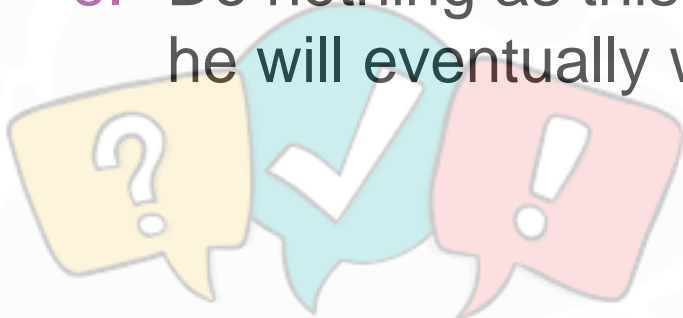
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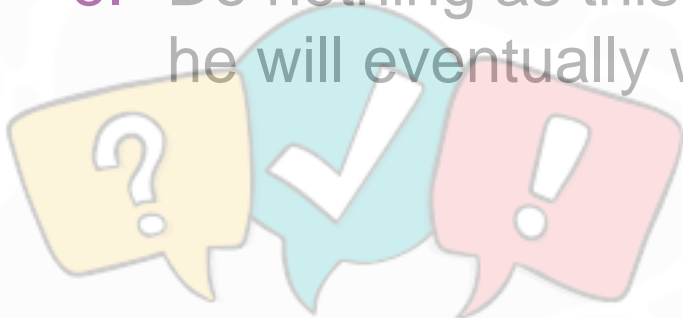
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Warning

The next 2 slides show somewhat graphic images of xylazine wounds

If you do not want to see these images, we suggest you look away

We will let you know once the images are no longer on-screen.

Xylazine Wounds: Before Treatment



Photo credit: Tracey McCann, (n.d.)

Xylazine Wounds: After Treatment



Photo credit: Tracey McCann, (n.d.)

Poll: Fill in the Blank

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In summary...

- 👉 Xylazine adulteration in the unregulated drug supply in the U.S. appears to be expanding exponentially
- 👉 The best response to treatment of an unresponsive patient who uses drugs is still naloxone (normalize breathing and STOP)
- 👉 Treatment options for xylazine use disorder include MOUD and adjuncts to help with prolonged effects of withdrawal from xylazine
- 👉 Xylazine-related lesions can be effectively treated with known techniques

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Questions?



Thank You!!!

Daniel Rosa: drosa@promesa.org

PCSS-MOUD Mentoring Program

- PCSS Mentor Program is designed to offer general information to clinicians about evidence-based clinical practices in prescribing medications for opioid use disorder.
- PCSS Mentors are a national network of providers with expertise in **addictions, pain, evidence-based treatment including medications for opioid use disorder (MOUD)**.
- 3-tiered approach allows every mentor/mentee relationship to be unique and catered to the specific needs of the mentee.
- No cost.

For more information visit:

<https://pcssNOW.org/mentoring/>

PCSS-MOUD Discussion Forum

Have a clinical question?

Ask a Colleague

A simple and direct way to receive an answer related to medications for opioid use disorder. Designed to provide a prompt response to simple practice-related questions.

<http://pcss.invisionzone.com/register>

Addiction Policy Forum	American College of Medical Toxicology
Addiction Technology Transfer Center*	American Dental Association
African American Behavioral Health Center of Excellence	American Medical Association*
American Academy of Addiction Psychiatry*	American Orthopedic Association
American Academy of Child and Adolescent Psychiatry	American Osteopathic Academy of Addiction Medicine*
American Academy of Family Physicians	American Pharmacists Association*
American Academy of Neurology	American Psychiatric Association*
American Academy of Pain Medicine	American Psychiatric Nurses Association*
American Academy of Pediatrics*	American Society for Pain Management Nursing
American Association for the Treatment of Opioid Dependence	American Society of Addiction Medicine*
American Association of Nurse Practitioners	Association for Multidisciplinary Education and Research in Substance Use and Addiction*
American Chronic Pain Association	Coalition of Physician Education
American College of Emergency Physicians*	College of Psychiatric and Neurologic Pharmacists
Black Faces Black Voices	

Columbia University, Department of Psychiatry*	Partnership for Drug-Free Kids
Council on Social Work Education*	Physician Assistant Education Association
Faces and Voices of Recovery	Project Lazarus
Medscape	Public Health Foundation (TRAIN Learning Network)
NAADAC Association for Addiction Professionals*	Sickle Cell Adult Provider Network
National Alliance for HIV Education and Workforce Development	Society for Academic Emergency Medicine*
National Association of Community Health Centers	Society of General Internal Medicine
National Association of Drug Court Professionals	Society of Teachers of Family Medicine
National Association of Social Workers*	The National Judicial College
National Council for Mental Wellbeing*	Veterans Health Administration
National Council of State Boards of Nursing	Voices Project
National Institute of Drug Abuse Clinical Trials Network	World Psychiatric Association
Northwest Portland Area Indian Health Board	Young People In Recovery



Providers
Clinical Support
System

Educate. Train. Mentor



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