Neurobiology of Addiction, Growing Threat of Synthetic and Polysubstance Drug Abuse including a Potentially Lethal Street Drug - Xylazine

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DISCLOSURE

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No financial relationships or conflicts of interest to disclose with ineligible companies.

The presentation contains pictures of wounds
Working with communities to address the opioid crisis.

• SAMHSA’s State Targeted Response Technical Assistance (STR-TA) and State Opioid Response Technical Assistance (SOR-TA) grants created the Opioid Response Network to assist states, individuals and other organizations by providing the resources and technical assistance they need locally to address the opioid crisis.

• Technical assistance is available to support the evidence-based prevention, treatment, and recovery of opioid use disorders.

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Working with communities to address the opioid crisis.

- The Opioid Response Network (ORN) provides local, experienced consultants in prevention, treatment and recovery to communities and organizations to help address this opioid crisis.
- The ORN accepts requests for education and training.
- Each state/territory has a designated team, led by a regional Technology Transfer Specialist (TTS), who is an expert in implementing evidence-based practices.
OBJECTIVES

• Neurobiology of Addiction

• Synthetic and Polysubstance Overdose Crisis

• Pharmacology, Mechanism of Action, Toxicity and management of Xylazine Overdose
The overdose crisis is worse with fentanyl

Unintentional Drug Overdose Deaths by Drug Type, Connecticut, 2021

- Any Opioid: 93%
- Fentanyl: 86%
- Cocaine: 43%
- Opioid+Benzos: 18%
- Heroin: 11%
- Xylazine+Fentanyl: 20%
- Methadone: 8%

“Tranq Dope”—The Heroin Combo That’s Been Putting Philly to Sleep

An animal tranquilizer is making street drugs even more dangerous

With overdoses at record highs, a veterinary tranquilizer spreading through the U.S. drug supply poses new threats
XYLAZINE (ZIE-LUH-ZEEN)

- Discovered in the 1960s.
- It is a sedating agent.
- It is FDA-approved as a tranquilizer for non-human use (veterinary medicine).
- It is NOT a federally controlled substance.
- Not known to have risks to bystanders or first responders.
Xylazine: The Basics

• Cheap to purchase online.
• May be used via injection, smoked, snorted, or swallowed.
• Onset within minutes.
• Lasts between 1-4 hours.
• When mixed with opioids it increases the duration of sedation, “gives it legs.”
Recent History of US Street Opioid Supply

1991-2013: Mexican black tar heroin west of Mississippi River; Colombian powder heroin east of the Mississippi; mixed supply in Midwestern cities like Chicago (Ciccarone & Bourgois 2003)

2013-2019: Mexican powder heroin displaces Colombian heroin from East Coast markets and fentanyl enters opioid supply chains primarily on the East Coast (Ciccarone 2021)

2017: Xylazine becomes increasingly prevalent in Rustbelt region, beginning in Philadelphia (Friedman, Montero, Bourgois et al. 2022), as fentanyl begins to spread west (Shover et al. 2020)

2020-present: Opioid supply on East Coast increasingly becomes a mix of fentanyl and xylazine ("tranq") as heroin disappears; Mexican methamphetamine enters East Coast/Rust Belt street markets formerly dominated by heroin and cocaine (Montero et al. 2022)
Missouri DHSS Statistics

- Sharp increase in xylazine involved deaths in Missouri from 39 deaths in 2021 to 109 deaths in 2022, a 180% increase.

- For all xylazine-involved deaths in 2019-2022, synthetic opioids were also found in 99.4% of these deaths.


(U) Figure 2. Number of Xylazine-Positive Overdose Deaths by Region

<table>
<thead>
<tr>
<th>Region</th>
<th>2020</th>
<th>2021</th>
<th>Percent Increase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Northeast</td>
<td>631</td>
<td>1,281</td>
<td>103%</td>
</tr>
<tr>
<td>South</td>
<td>116</td>
<td>1,423</td>
<td>1,127%</td>
</tr>
<tr>
<td>Midwest</td>
<td>57</td>
<td>351</td>
<td>516%</td>
</tr>
<tr>
<td>West</td>
<td>4</td>
<td>34</td>
<td>750%</td>
</tr>
</tbody>
</table>

Source: DEA
Fentanyl Beyond “Potency”

- Experience of fentanyl consumption (vs. heroin)
  - Duration of effect / withdrawal symptoms
  - Quality of “high” \(\text{(Montero et al. 2022; Ciccarone, Ondocsin, and Mars 2017)}\)
  - Fentanyl deficiencies open space for new additives and substances (xylazine, meth)
Mechanism of Action

• Agonist at the alpha-2 adrenergic receptors
• Acts as a central sympathetic antagonist decreasing release of norepinephrine and dopamine
• Lipophilic, allowing BBB crossing
• Rapidly metabolized by CYP450, excreted via kidneys as 2,6-xylidine
• Causes dangerously low blood pressure, respiratory rate and heart rate \( \Rightarrow \) increases risk for life threatening overdose
• Vasoconstriction properties can result in more serious skin/soft tissue infections leading to ulceration/necrosis

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4822969/#:~:text=Xylazine%20is%20a%20strong%20\%CE%B12,decreased%20perception%20of%20painful%20stimuli.

Routes of Administration/Dosing

- IV most common, IM, SQ
- Ranging from 40 mg to 4300 mg
  - Average fatal dose 1,200 mg
Notable effects of Xylazine

• Profound sedation
• Blurred vision
• Super dry mouth
• Low blood pressure
• Bradycardia
• Weak reflexes
• Respiratory depression
• Disorientation
• Drowsiness
• Slurred speech
• Overdose

• Severe skin wounds

Xylazine wounds do not pose an infectious risk to responding officers, still wear gloves!
The biological mechanisms behind xylazine-related skin wounds have not been fully elucidated in the clinical and public health literature (as of spring 2023). However, clinicians and the Puerto Rican public health literature have offered the following likely explanations:

- Lack of oxygenation to skin
- PWUD often inject into wounds due to difficulty finding veins
- PWID also inject into wounds to provide pain relief, as xylazine is an anesthetic
- “Bed sores” from xylazine-induced sleep
- Skin picking leads to excoriation
Xylazine-Related Skin Wounds

WARNING:
The following two slides contain graphic depictions of xylazine-related skin wounds
Xylazine-Related Skin Wounds

Photos by Kimberly Sue, MD/PhD, Yale University
• Deep sedation, hypotension (low blood pressure), bradycardia (low heart rate)
• Time to effect 1-2 minutes, lasts ~4 hours
• Recovery position, airway maneuvers to clear airway
• Pulse oximetry, airway monitoring, supplemental oxygen as needed
• No known antidote
• Naloxone administration recommended if uncertain cause of OD
Best Practices for Responding to a Xylazine Overdose

- Administer naloxone!
- Place in recovery position.
- Check signs of life (pulse and breathing)
- Supportive management until drug wears off and sedation resolves
  - Keep people’s airways open (jaw thrust)
  - Provide rescue breathing (consider a face shield or ambu bag)
  - Continuous pulse oximetry, supplemental oxygen if hypoxia
  - Reposition every 2 hours, roll to opposite side, gently massage

*No commercially available antidote for xylazine yet!*
Xylazine’s Transformations to Harm Reduction Landscape

- Xylazine has introduced new problems:
  - Not opioid (need for new overdose reversal agents to complement, *not replace*, naloxone)
  - Ulcers/extensive skin wounds
  - Risk of sexual assault and muggings
  - Not just overdose: withdrawal and detox
Xylazine Withdrawal and Dependence

• Xylazine withdrawal has not been well defined in the literature yet, but patients report anxiety, insomnia, dysphoria, jitteriness

• Some overlap with opioid withdrawal symptoms – treat

• Treat similar to benzo/alcohol withdrawal

• Symptom management with medications

Sources: Reed et al. 2022; Kimberly Sue, MD/PhD, Yale University
Testing for Xylazine

- Rapidly eliminated from the body
  - Half-life 23-50 minutes
  - Difficult to detect on testing [1]
- Xylazine remains undetected in the most frequently performed urine drug screenings (UDS)
- Urine samples can be confirmed using gas chromatography-mass spectrometry or liquid chromatography-tandem mass spectrometry [2]

- The Rapid Response Xylazine Test Strip by BTNX
  - Rapid test for the detection of xylazine that can be used for drug checking in an unregulated drug supply. [3]
  - Strips demonstrated high sensitivity (100%), specificity (85%) [4]

Sources:
1. https://www.fda.gov/media/162981/download#:~:text=Even%20with%20appropriate%20testing%2C%20overdoses%2C%20life%20of%2023%2D50%20minutes.
Addressing Misinformation

- Xylazine is not naloxone resistant, it is simply not an opioid.
- Like fentanyl, there is no known risk to first responders from xylazine exposure.
- Xylazine wounds are not contagious to officers/first responders.
- Sedation from xylazine will make people who use less able to respond and less able to follow directions.

Torruella (2011)
Malayala (2022)
Universal Precautions

• Both fentanyl and xylazine can be handled safely using standard precautions.
  • Gloves
  • Sharps safety
  • Masks/Eyewear (more because of COVID)
  • BVM (bag valve mask for resuscitation)
XYLAZINE PATIENT HANDOUTS
SCAN QR CODE TO DOWNLOAD FREE PDF
XYLAZINE PATIENT HANDOUTS
SCAN QR CODE TO DOWNLOAD FREE PDF

**WOUND CARE SUPPLIES**
- Sterile saline
- AD ointment
- Medical tape
- Coban
- Toilet paper
- Gauze
- Kerlix
- Soap

**SELF-CARE STEPS**
1. Clean hands with soap & water or hand sanitizer before touching wounds.
2. Gently wash wound with soap & water or with saline at least every 2-3 days.
3. Put ointment on gauge & place on entire wound. Cover with more dry gauge.
4. Wrap wound with kerlix and secure with medical tape. Make sure wrap is not too tight.
5. Cover dressing with ACE wrap or coban or with long sleeves/pants if no other option.
6. Change dressing every 1-3 days. Watch for red flag.

**XYLAZINE**
/ˈziː ləˌzen/  
AKA “Tranq” or “Tranq Dope”

A cutting agent making its way into the drug supply. Contamination with xylazine increases risk of sedation, overdose, and wounds that are hard to heal.

**XYLAZINE WOUNDS**
Xylazine wounds can appear anywhere on the body regardless of where you are injecting, particularly in YELLOW areas.
Check these areas regularly for any wounds that may develop.
Wounds can occur even if you’re just sitting or smoking.

**RED FLAGS to SEEK MEDICAL CARE**
- Fever or chills
- Skin turns dark or black
- Skin is red, hard, & hot to touch
- Thick, oval yellow or green drainage
- Severe or worsening pain at wound site
- Pain & decreased ability to move joint
- Pieces of tissue falling off
- Exposed bone or tendon
- New numbness

**HELPFUL TIPS**
- Keep your skin moisturized with A-D ointment
- Avoid using alcohol/hydrogen peroxide on wounds
- Keep wounds covered with a clean bandage
- Wear long sleeves, pants, socks, and gloves to prevent yourself from scratching your skin
- Eat protein. Stay hydrated to help with healing
- Avoid injecting into or around your wounds
- Use new supplies every time and avoid sharing
- Not every wound is infected. Avoid taking non-prescribed antibiotics

Even though xylazine isn’t an opioid, you should still give naloxone in an overdose as opioids are often present.
Calling or texting 988 or chatting 988Lifeline.org will connect you to compassionate care and support for mental health-related distress. #988Lifeline
Resources: Xylazine

General Information & Warnings:


• Kariisa M. Notes from the Field: Xylazine Detection and Involvement in Drug Overdose Deaths — United States, 2019. MMWR Morb Mortal Wkly Rep. 2021;70. doi:10.15585/mmwr.mm7037a4

Resources: Xylazine

Xylazine Data:


Skin and Soft Tissue:


References

References


References


Contact the Opioid Response Network

• To ask questions or submit a request for technical assistance:
  • Visit www.OpioidResponseNetwork.org