• **Xylazine** is a NON-OPIOID chemical originally approved for veterinary use in 1972 as an animal sedative, but it has never been approved for use in humans because of serious harmful side effects. It is sometimes called “tranq” and might be sought by people who inject drugs to lengthen the duration of short-acting fentanyl injections. However, many people who suffer acute xylazine toxicity did not know they had ingested or injected it.

• Xylazine is already widespread in the illicit drug supply across the U.S. The DEA reports that though it is most common in the Northeast, all four regions of the country have seen an increase in prevalence of xylazine in overdose deaths, with the South having the largest increase: 193 percent between 2020–2021.

• In 2015, xylazine was involved in 0.36 percent of overdose deaths. In 2020, it was involved in 6.7 percent.

• Xylazine is essentially always encountered in combinations of multiple drugs. 98.4 percent of all xylazine-involved deaths also involved illicitly manufactured fentanyls. Other commonly associated drugs are cocaine (45.4 percent), benzodiazepines (28.4 percent), heroin (23.3 percent) and alcohol (19.7 percent).

• It is structurally similar to **clonidine** and similarly acts as a central nervous system (CNS) depressant. Thus, signs and symptoms of acute xylazine toxicity strongly resemble an overdose on opioids, benzodiazepines or other human CNS depressants. These symptoms include:
  
  • **Respiratory depression**, low blood pressure, slowed heart rate, hypothermia, pupil constriction and, sometimes, high blood sugar levels.
  
  • The pupil constriction and respiratory depression are particularly of concern, as these are very common and widely understood effects of an opioid overdose.
  
  • **Severe, necrotic skin ulcerations** are the most striking side effect of xylazine. Notably, while these skin ulcerations may appear at the site of injection, they may appear at a completely different site on the body altogether. Soft tissue infections are often associated with IV drug use of more conventional illicit substances such as opioids, but these are almost always located at the injection site.

• Despite the similarities to opioid overdose, naloxone **DOES NOT reverse a xylazine overdose**. If the patient used an opioid contaminated by xylazine, naloxone would act on the opioid in their system but not on the xylazine.
  
  • Yohimbine hydrochloride and tolazoline hydrochloride are used to reverse xylazine toxicity in animals, but it is UNKNOWN if these are safe for use in humans. Thus, the FDA warns against using these medications.

• Routine toxicology screenings—such as urine drug panels ordered in emergency departments—**DO NOT test for xylazine**. In fact, they currently do not screen for fentanyl either. Some laboratories can test for these chemicals, but, at present, there is no point-of-care test available for xylazine in hospitals. Xylazine test strips, which function similarly to fentanyl test strips, have been developed but as of now are not approved by the FDA to be marketed or used in clinical settings in the U.S.
• Repeated exposure to xylazine can cause chemical dependency and withdrawal symptoms, as is the case with other illicit substances. This can undermine treatment of any underlying opioid use disorder.

• There are currently no known medications for the treatment of xylazine that are equivalent to those used to treat opioid use disorder.

• There is a case study of buprenorphine in combination with gabapentin and clonidine being used to mediate xylazine withdrawal symptoms (Ehrman-Dupre et al.), but as of now, there are no FDA-approved medications specifically targeting xylazine dependence. Additionally, the soft tissue wounds still require extensive treatment, such as intravenous antibiotics.