



## Case Report

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# The Xylazine Crisis: The Growth of the Zombie Drug

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When initially approved by the U. S. Food and Drug Administration, Xylazine was intended to be used for sedation, muscle relaxation, pain relief and management of large animals and only under strict medical supervision. Its fast onset and extended duration make it very useful in the treatment of cattle, horses and dogs. It has been used in combination with other drugs which augment the effectiveness of xylazine in dental procedures on animals. There were no human medical or dental applications approved by the USFDA, which belies the fact that Bayer initially synthesized the drug in 1962 for its potential use as an analgesic, hypnotic, and an

esthetic for humans. Human clinical trials were terminated due to severe hypotension and central nervous system depressant effects. Xylazine is an  $\alpha$ -agonist like clonidine and belongs to a class of compounds known as phenothiazines, which primarily treat mental and emotional disorders. Human pharmacology studies are scarce, but xylazine decreases the release of norepinephrine and dopamine in the central nervous system resulting in analgesia, sedation, bradycardia and muscle relaxation [1]. Individuals who use xylazine may develop physiological dependence and withdrawal symptoms without the proper treatment (Figure 1).

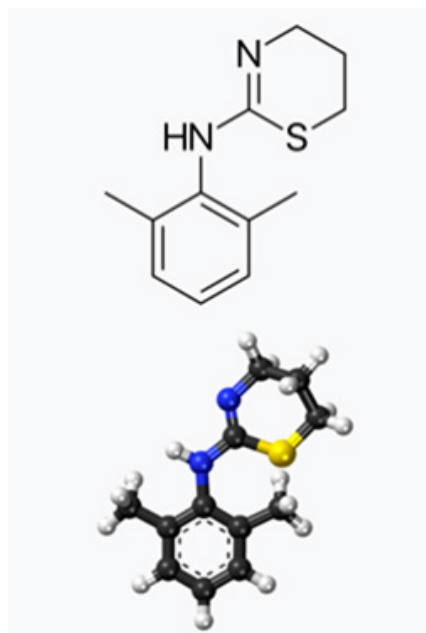


Figure 1:

For all its beneficial uses with animals, xylazine has unfortunately made its way into the human drug trade as a solo drug where it can be used in multiple forms, including oral use, smoking, snorting and injection [1]. It can also be used in combination with prescription medications (gabapentin, benzodiazepines), alcohol, and opioids like the synthetic opioid Fentanyl, where it prolongs the euphoria from the fentanyl usage [2]. As a result, the combination of these 2 drugs has been a growing concern in recent years, particularly in the southern United States and Mexico. Known on the street as “tranq dope”, “sleeping beauty” or “Zombie Drug”, this combination is less expensive to heroin. The drug is typically sold in powder or pill form, and it is often cut with other substances such as caffeine, benzodiazepines, or other opioids. Xylazine is similar in looks and texture to opioids so its combination with opioids allows users/dealers the ability to offer more product for less money.

The misuse of xylazine was initially reported in Puerto Rico in 2001; however, it did not become more widespread in the United States until 2006 and has been steadily growing since that time [1]. In February 2023, the Drug Enforcement Agency (DEA) issued an alert about the use of xylazine and the drug’s appearance in confiscated samples found in 48 of the 50 states [1]. In 2021, Philadelphia law enforcement reported that 90% of opioid samples obtained from the street contained xylazine. The majority of the deaths were black. According to the Centers for Disease Control and Prevention, 107, 735 Americans died between August 2021 and August 2022;

66% of those deaths were the of result opioid laced with fentanyl usage. Many of the deaths stem from the fact that typical reversal agents for opioids, like naloxone, do not reverse the harmful effects of xylazine [3]. Lack of rapid point-of-care testing for xylazine is a problem to be solved. There are mixed feelings toward the use of test strips to detect xylazine in drug samples even if earlier detection on the street would prevent deaths. One side argues that the use of the strips will potentiate the use of illegal drugs by eliminating tainted drugs and allowing safer use of the narcotics. Others argue that efforts should be directed toward complete reduction or elimination of drug usage.

Why is this information important to dentists? The answer is simple; a patient who has taken xylazine may walk into a dental office one day for treatment, and dentists should be prepared. The effects of xylazine/fentanyl use are readily apparent assuming the user does not die. There will be skin ulcers and tissue necrosis around the injection sites on the arms; the ulcerations have been misdiagnosed previously, leading to amputation. The necrosis may extend beyond the skin surface and cause tissue death. The dentist should refer to a physician or infectious disease specialist for a comprehensive evaluation and management. The user will also face withdrawal symptoms that are being treated with a regimen of clonidine and similar drugs. The withdrawal treatment will be more difficult if the xylazine were initially mixed with an opioid (Figure 2).



Figure 2:

As the use of xylazine continues to grow, there is ongoing discussion regarding future regulation of the drug by making it a controlled substance. Veterinarians are concerned about the impact that xylazine regulation will have on their ability to practice. It is apparent that more education, more testing opportunities, more research, and more regulation will be necessary in the future.

## References

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