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A NEW DRUG EPIDEMIC SWEEPING ACROSS AMERICA

Xylazine's Horrifying Impact

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USE OF THE VETERINARY DRUG XYLAZINE is having a profound impact on the health of those who use illicit substances across the United States. Originally developed by the pharmaceutical company Bayer in 1962 as a large animal sedative containing a muscle relaxant with analgesic properties, xylazine was never intended for human consumption and therefore identified as a non-classified drug by the Food and Drug Administration (FDA), requiring only a veterinarian's prescription (Reyes et al., 2012; Karissa et al., 2021; NIDA, 2022; NASTAD, 2023). In humans, xylazine acts on the central nervous system and may cause drowsiness, slowed breathing, decreased heart rate, lowered blood pressure, and even amnesia (NASTAD, 2023). So when did this veterinary drug enter into the street drug supply chain, and how did it get there?

Xylazine was first documented among those using illicit drugs in Puerto Rico in 2000 (Silva-Torres et al., 2014). Xylazine's presence steadily increased among recreational street drugs, exacerbating the need for research concerning xylazine use as well as amplified media coverage to inform the public and alert those who use illicit substances of the presence and danger of Xylazine (Rodriguez et al., 2008; Torruella, 2011; & Reyes et al., 2012). Added to multiple other illicit drugs, xylazine can be ingested, inhaled, and injected (Capararo et al., 2001; & Stillwell, 2003). Xylazine is also used as an adulterant (McAward, 2021), primarily in combination with fentanyl, but also added to heroin and cocaine to increase their bulk size and to alter these drugs' effects, such as a prolonged high when added to fentanyl (Johnson et al., 2021, & Thompson, 2023). While some individuals who use illicit substances are aware of the presence of xylazine, the vast majority of drug users are unaware that this additional substance has been added to their drug supply (Reyes et al., 2012; Johnson et al., 2021; D'Arrigo, 2022; & Friedman et al., 2022) . The unaware addition has serious implications as xylazine is an anesthetic similar to those used during a surgical procedure and in the case of too much xylazine, such as an overdose or near overdose, the individual affected is unable to fully wake up. This sleep-induced effect also carries other potentially severe consequences in cases not resulting in overdose, especially for individuals who may be given the drug without their knowledge which can lead to victimization through sexual assault, theft, and other acts of violence (D'Arrigo, 2022; & Vestal 2023).

By 2019, the spread of xylazine in street drugs increased, with rapid expansion reaching epidemic levels during the pandemic in 2020 (Vestal, 2023). Initially documented in cities in the northeastern United States, particularly Philadelphia, Boston, and New York, xylazine is now prevalent in the recreational street drug supply in 36 states and Washington, D.C. (Bebinger, 2022, & Hoffman, 2023). Street names for xylazine include 'tranq', 'tranq dope', 'sleep cut', and 'speedball' when mixed with cocaine and heroin in the United States, and 'anestecia de caballo' (horse anesthesia) in Puerto Rico (Reyes et al.; McAward, 2021; & Hoffman, 2023). Regardless of its street name, xylazine is a dangerous drug, addictive in its own right, responsible for contributing to increased drug overdoses, and can potentially lead to significant bodily tissue damage, often with dire consequences such as amputation (Thompson, 2023; Vestal, 2023; & Hoffman, 2023). Xylazine also remains a significant challenge concerning treatment as there is no known antidote for xylazine exposure that is safe for humans (FDA, 2022).

Overdose and Xylazine

Xylazine, despite increased public awareness, has not been fully studied in the United States, even with documentation of the presence of xylazine via post-mortem toxicology reports or listed on an individual's death certificate as a contributing cause due to other drugs identified in the coroner's report (Karissa et al., 2019). For example, in the 2019 State Unintentional Drug Overdose Reporting System (SUDORS) conducted through the Centers for Disease Control and Prevention (CDC) analyzing overdose data from 28 states, 45,676 deaths were determined as unintentional or undetermined causes of death, with 826 (1.8%) being xylazine positive in 25 states, and 531(1.2%) as xylazine involved in

23 states (NIDA, 2022). This translates to a 64.3% increase in cases where xylazine was detected (NIDA, 2022). In all xylazine-involved deaths, the individual's toxicology report showed one or more other illicit substances as contributing to the cause of death with 98.7% xylazine positive, and 99.1% xylazine involved. In 2015, death from xylazine overdose rose from 0.36% to 6.7% in 2020, and from 2019 to 2020, the drug's prevalence in overdose deaths grew by 44.8% (D'Arrigo, 2022). These numbers were especially significant in the northeastern United States, with the presence of xylazine in overdose deaths at 25.8% in Philadelphia, 19.3% in Maryland, 10.2% in Connecticut, and in Vermont, steadily rising from 29 deaths in 2021 to 54 deaths by October 2022 (D'Arrigo, 2022; Friedman et al., 2022; & Vestal, 2023). In overdose deaths involving cocaine or heroin, there is an increasing presence of xylazine: in cocaine-related cases, 32.1% were xylazine positive with 29.6% xylazine involved, and in heroin-related cases, 26% were xylazine positive, and 28.4% xylazine involved. As a contributor to the cause of death, the presence of xylazine was evident in nearly half of all deaths in which it was detected, with the majority of overdose deaths involving fentanyl use (NIDA, 2022).

Unlike a number of other illicit drugs, xylazine does not show up in a routine toxicology screen. Xylazine requires a full toxicology report to isolate the drug from other substances found in the body. Repeated use of xylazine can increase dependency as well as result in difficult withdrawal symptoms (FDA, 2022; NASTAD, 2023; & Vestal, 2023). Unlike opioids, there is currently no known treatment for xylazine exposure, and naloxone does not reverse the drug's effects. This is particularly problematic because xylazine is difficult to trace and, in the event of a drug overdose, treatment may be both delayed and unsuccessful. These concerns prompted the FDA to send a four-page letter to healthcare providers in November 2022 warning about the risks associated with exposure to xylazine (FDA, 2022). The FDA letter outlined specific physical signs and management of individuals exposed to xylazine. The letter sent to providers focused on two key issues: the significant danger of delayed diagnosis in the event of an overdose due to the increased risk of cardiac and respiratory failure, and the development of severe skin lesions in individuals exposed to the drug via injection. Primarily among these warnings was an alert to providers that lesions occurring from xylazine exposure may appear away from the injection site, and manifest on various other parts of the body, especially the arms, and legs. This warning carries significant merit because the infection induced by these lesions in some cases has resulted in amputation (FDA, 2022; Hoffman, 2023; & Thompson, 2023).

DISCUSSION

Combating the prevalence of xylazine within the recreational drug supply chain is complex. There is still no clear evidence as to how this drug intended for veterinarian use has deviated into public use. As a means to get ahead of xylazine's rapid spread, the Massachusetts Drug Supply Data Stream (MADDS) began examining samples of street drugs, reporting the concerning increase of xylazine's presence in 28% of drugs tested, with some areas of Massachusetts experiencing increases of 50% xylazine prevalence in 75% of tested drugs (Bebinger, 2022). As a result of the growing danger of the spread of xylazine among those who use illicit drugs, Tapestry Health, a non-profit community-based organization has literally taken their messaging to the streets. Tapestry Health used their street outreach team to alert substance users about xylazine through a dedicated public education campaign. The campaign includes information as to how xylazine differs from opioids, and how it is included in other illicit drugs (Bebinger, 2022). Other states are beginning to follow with similar outreach programs. In addition to the tracking and testing of illicit drug samples, New York, Philadelphia, Rhode Island, and North Carolina have developed novel rapid drug testing programs for illicit street drugs, coupled with targeted, localized messaging aimed at people who use illicit substances and healthcare providers to alert them of the dangers of xylazine. Maryland has created a pilot program to staff harm reduction centers with medical professionals trained to treat xylazine exposure (Vestal, 2023). Though states are taking the lead to reduce the flow of xylazine into the recreational illicit drug supply chain, to date, there is currently no national strategy for combating the widespread prevalence of xylazine within the United States. However, in February 2023, the FDA took an important first step by restricting the unlawful import of xylazine and ingredients used to make it, requiring a review of evidence from importers to insure that this drug is properly labeled, not adulterated, and intended for legal use by veterinarians (Reuters, 2023; FDA, 2023).

CONCLUSION

Numerous challenges remain for addressing the impact of xylazine and slowing the spread of this significantly dangerous drug. Treatment of xylazine exposure also remains challenging as there is currently no pharmaceutical available as an antidote to reverse the effects of xylazine. Steps necessary in reducing the harmful effects of xylazine exposure include quick diagnosis based on respiratory and cardiac symptoms in suspected cases of overdose, and treatment of bodily tissue damage from xylazine-induced lesions. Going forward, there is a significant need to standardize post-mortem toxicology testing for identifying exposure to xylazine and to strategically educate healthcare providers, those who use illicit substances, and the general public as to the associative level at which xylazine contributes to overdoses, overdose deaths, and potential long-term health effects. This will require advocacy through a network of influencers, including law enforcement, social service agencies, and city and local governments to persuade elected officials at the national level to set protocols and policies to manage and mitigate the growing threat of xylazine. Educating the public about the very real dangers of xylazine will also be paramount, requiring specific, targeted language accessible to multiple populations.

KEY POINTS

- Xylazine is an FDA non-classified, veterinary anesthesia drug never intended for human use.
- Many individuals are unaware that recreational street drugs contain xylazine.
- Xylazine does not show up in routine toxicology screens.
- There is no current treatment to reverse the effects of xylazine exposure.
- Xylazine-induced skin lesions can result in the amputation of limbs.
- A network of influencers will be necessary to persuade elected officials to set policies and protocols to manage and mitigate this potent drug.

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