STAT Reporting from the frontiers of health and medicine

Sedative ‘Dex’ Is Replacing ‘Tranq’ In Illegal Drug Supply And Causing Excruciating Withdrawal

Medetomidine, the new adulterant to illegal fentanyl, can damage heart and brain

By Lev Facher
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The era of “tranq” may be ending.

But tranq, as the powerful veterinary tranquilizer xylazine is known in the illicit drug supply, is being replaced at least in part by a dangerous new sedative: medetomidine. In the past year, the anesthetic has become an increasingly common element in the drug supply, with cities and states including Philadelphia, Pittsburgh, Chicago, and San Francisco reporting cases of medetomidine-involved overdoses.

In Philadelphia in particular, reports of medetomidine have skyrocketed. When the city first began testing for the substance in May 2024, it found medetomidine in 29% of fentanyl samples analyzed, according to data from the city’s public health department. Six months later, medetomidine’s prevalence had increased threefold to 87% — while xylazine’s dropped from 100% early in the year to 42% in November.

For years, illegal U.S. drug suppliers have “cut” the fentanyl they sell with sedatives like xylazine, likely because it is more cost-effective than selling fentanyl alone. Since its entry into the drug supply, many drug users have encountered it inadvertently in substances marketed as fentanyl, while others have actively sought it, despite its powerful sedative effects and tendency to cause severe skin wounds. And as law enforcement officials have cracked down on xylazine, a pharmacologically active form of medetomidine known as dexmedetomidine or “dex” has rapidly taken its place.

Already, medetomidine is causing severe health complications among many people who use drugs, even compared to xylazine. Reports from local doctors and public health officials indicate that overdose reversals, already made more difficult by xylazine, have taken on a new character with

medetomidine, with low heart rates and “profound” sedation. And withdrawal symptoms, already severe among those who only use fentanyl, have taken on a new and potentially deadly wrinkle.

“The supply has just shifted so heavily from xylazine to medetomidine, and there is an overwhelming amount of medetomidine in the supply,” said Sam Huo, an emergency and addiction medicine physician and assistant professor at the University of Pennsylvania’s Perelman School of Medicine. “With withdrawal from medetomidine, severe cases can be life-threatening. And the scary part is that we don’t have a way right now to predict who will be at risk for severe withdrawal and who’s not.”

While drug overdoses involving medetomidine often cause severe drops in heart rate and blood pressure, Huo said that medetomidine withdrawal symptoms effectively amount to the opposite: the sympathetic nervous system “skyrocketing” and causing elevated heart rate and blood pressure that can damage organs including the heart and brain.

The experience also differs significantly from xylazine withdrawal, which is often mild and characterized by feelings of anxiety or restlessness and not associated with vital sign abnormalities, Huo added.

Medetomidine is classified as an alpha-2 agonist, placing it in the same family of medications as xylazine as well as clonidine, a common medication used as an antihypertensive as well as to treat ADHD and some forms of pain, among other uses.

Like xylazine, formulations of medetomidine are sometimes used in veterinary settings. But they are used to treat humans, too, often under the brand name Precedex, a medication that is used for sedation in both adult and pediatric settings but not typically associated with misuse or addictive potential.

Medetomidine’s rapid proliferation throughout Pennsylvania’s drug supply happened soon after the state took action to crack down on xylazine. After temporarily classifying xylazine as a Schedule III controlled substance in 2023, Gov. Josh Shapiro (D) made the measure permanent in May 2024, the same month Philadelphia health officials began testing for medetomidine.

In an interview, Nabarun Dasgupta, a University of North Carolina pharmacoepidemiologist and activist focused on increasing access to naloxone, said the proliferation of dexmedetomidine was inevitable.

“We saw our first dexmedetomidine samples in 2022, and it was like: Duh, it’s obvious that this is what’s going to replace xylazine when xylazine gets cracked down on,” he said. “When you look at all the sister molecules in this family, dexmedetomidine is the obvious one to go to next because it has a lot of manufacturing, is used in every hospital, and is a pretty well-known drug that is known to be very safe and does not have known skin complications. So it was just a matter of time before the market would have switched to dex anyways.”

Legislation targeting xylazine, Dasgupta said, created market pressure for a replacement with similar properties. But future efforts to similarly crack down on medetomidine, he argued, could jeopardize access to a medication that is critical to many health providers’ day-to-day responsibilities.

The substance’s presence in the illicit drug supply adds a new layer of uncertainty to the current U.S. overdose epidemic. Broadly speaking, trends are positive: The running death toll per 12-month period is down from its high of roughly 111,000 in late 2023 to approximately 81,000 as of November, the last month for which data is available.

Like xylazine, however, medetomidine does not respond to naloxone, the common medication used to reverse opioid overdoses. And despite the decreasing death rate, however, medetomidine threatens to further complicate treatment, overdose response, and post-overdose care.

“It’s really changed opiate withdrawal from something that typically can be handled at home, sometimes in behavioral health facilities like detoxes that are not hospital level of care, to this opioid-plus-medetomidine withdrawal, which can be life-threatening,” Huo said.

Still, the withdrawal can be treated, typically with some combination of short-acting opioids for pain, another alpha-2 agonist like clonidine, anti-nausea drugs, and other medications used for sedation or to treat high blood pressure.

Despite the debilitating pain of medetomidine withdrawal, and the complications it has caused for health providers, it may have a silver lining. Xylazine has grown infamous for causing deep skin wounds, infections, and the death of body tissue, known as necrosis. Medetomidine, by contrast, has not been known to cause similar wounds.

Recently, the worlds of public health, medicine, and harm reduction have taken steps to respond to a new normal in the drug supply, in which medetomidine is widespread. Last week, dozens of researchers mostly based in or near Philadelphia gathered for an online forum with local public health officials, at which Huo presented her assessment of how to treat medetomidine withdrawal. A handful of states have issued warnings in the past year, too, and BTNX, a Canadian company known for selling fentanyl and xylazine test strips, has already made medetomidine test strips available for purchase.

Dasgupta, the University of North Carolina researcher, said dexmedetomidine poses a new level of danger for many drug users. Beyond potentially heightened risk for hard-to-reverse overdoses and medically perilous withdrawal, he said, its powerful sedative properties leave many individuals increasingly vulnerable.

“Xylazine and dex are inherently different,” Dasgupta said. “They look almost identical, but they have very different properties.”

But “they share one very similar property, which is knocking people out,” he added. “Dex is way more sedating than even xylazine was. So you’re going to have people waking up in compromised positions and maybe situations where their [stuff] has been stolen or they’ve been assaulted. That’s already a fear with xylazine. It’s something where we warn people to be careful of their surroundings. It’s even more so with dex.”