



Getting Creative with Alpha Agonists:

Xylazine Withdrawal in the Outpatient Setting

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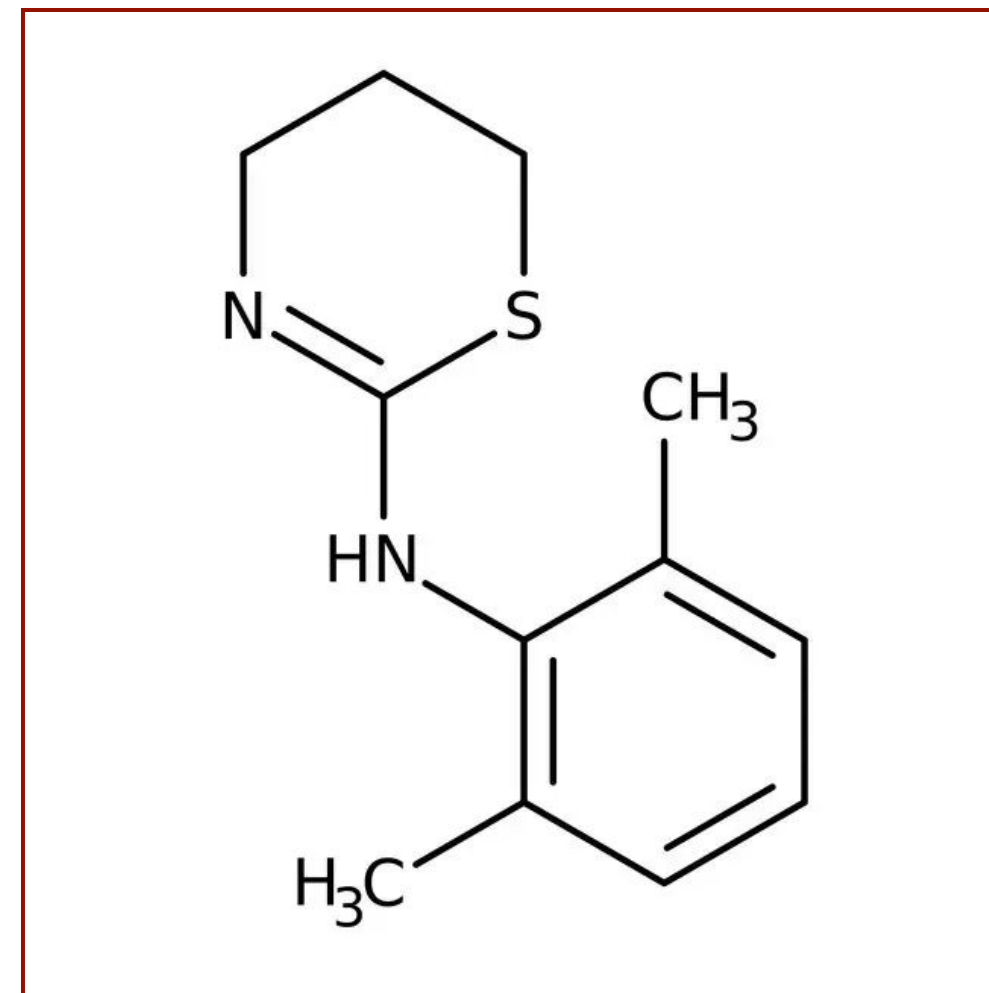
Xylazine Background

Alpha-2 agonist used in veterinary medicine as a **sedative for large animals**; commonly found as an **adulterant in illicit opioids** due to its ability to extend the duration of effects of opioids

Xylazine may **coactively increase heroin's toxic effects as well**

Actions on the central alpha-2 receptors causes **negative feedback** at neuronal synapses, ↓ the amount of **NE and dopamine** released, and thereby causing **CNS depression** along with **marked hypotension**

Wounds can occur in **both persons who inject and in persons who do not inject** substances; and either at injection sites or elsewhere → **local arterial alpha-1 adrenergic receptors**, leading to **vasoconstriction**



In 2021, **91%** of heroin and fentanyl samples in Philadelphia were **contaminated** with xylazine. In fact, it is not uncommon for 'dope' to **contain more xylazine than fentanyl**

Withdrawal presents similar to Opioid withdrawal C/f: **hypertensive emergency**

Need: Be able to manage xylazine withdrawal concurrently with opioid withdrawal

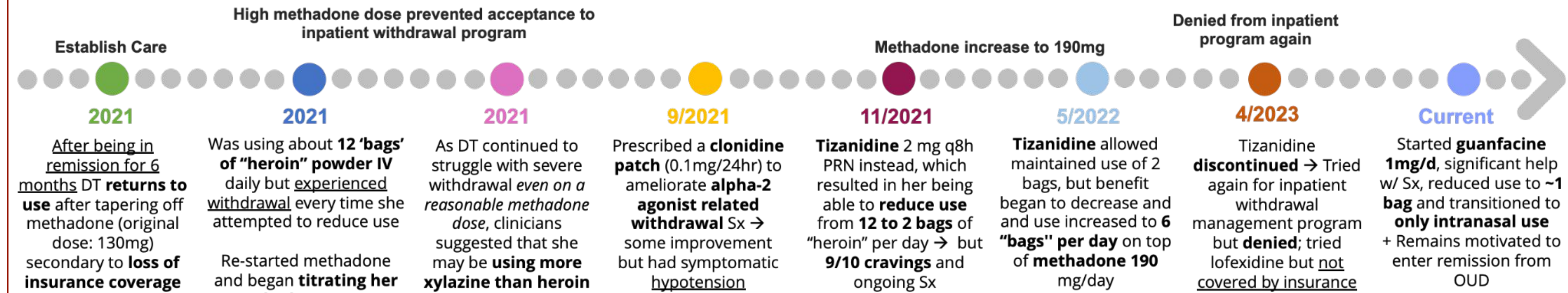


Case Description

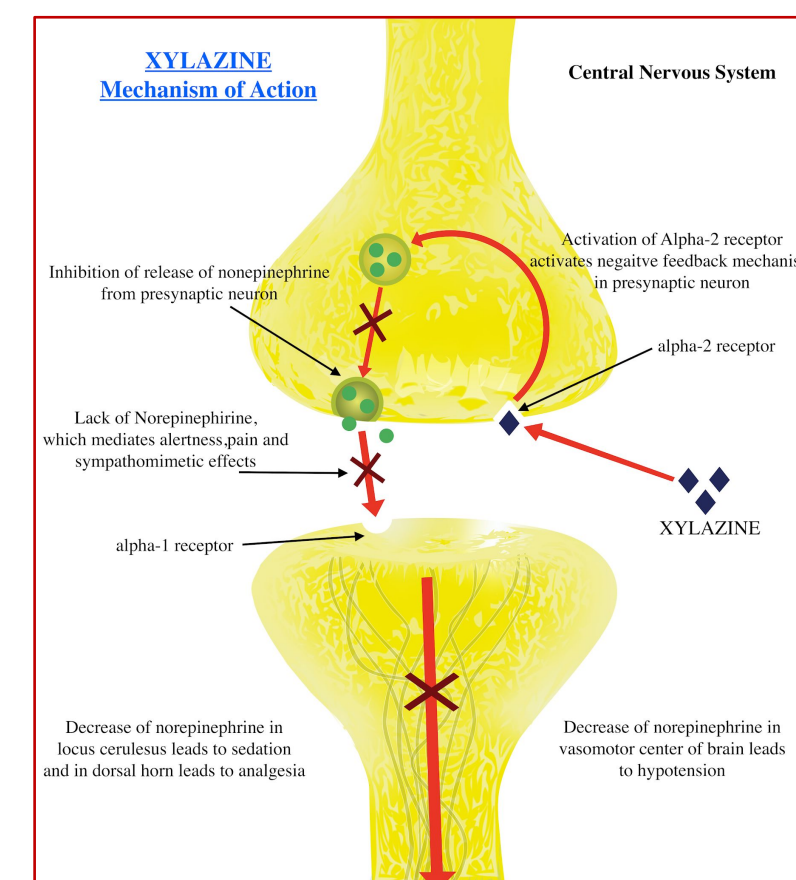
DT is a cis gender woman in her 40s with opioid and sedative hypnotic use disorders who established care at the Cooper Center for Healing in 2021 after experiencing a return to use while tapering off methadone (original dose 130mg) secondary to a loss of insurance coverage. DT struggled to reduce her fentanyl use even after re-titrating her methadone to 170mg. DT was interested in inpatient withdrawal management but struggled to find placement while on methadone, and with multiple complex psychosocial barriers.

As DT continued to struggle with severe withdrawal even on a presumably therapeutic methadone dose, clinicians suggested that she may be using more xylazine than fentanyl, and struggling with xylazine withdrawal. In the outpatient setting, DT's care team trialed multiple pharmacotherapeutic interventions to alpha agonist withdrawal, eventually discovering significant benefit with guanfacine. A full timeline of trialed interventions is above. On guanfacine, pt was able to significantly reduce fentanyl/xylazine use and remains motivated to reduce and eventually discontinue us all together.

Management Timeline



Xylazine Pharmacology



<https://www.statpearls.com/point-of-care/155900>

Other Alpha Agonists

	Route of Admin.	Summary of Action	Receptor Action: α-1: peripheral vasoconstriction, HTN α-2A- central, reduces sympathetic tone, has sedative hypnotic effects α-2B- peripheral, causes vasoconstriction α-2C- central
Clonidine	PO	Primarily α-2A selective → good sedative/hypnotic effect, but with significant hypotensive action	
Tizanidine	PO	Less selective for α-2A and α-2C → less hypotensive effect than clonidine.	
Guanfacine	PO	More selective for α-2A - more sedative/hypnotic effect Less selective for α-2B → less hypotension	
Lofexidine	PO	Similar to Guanfacine, much more \$\$\$	
Dexmedetomidine	IV	Even more α-2A than clonidine. Critical care. Risk for hypotension.	

Conclusions, DEI

- Case illustrates importance of identifying and managing withdrawal symptoms from adulterants in the opioid supply, and the benefits of being creative with pharmacotherapeutics in the treatment of xylazine withdrawal
- While alpha 2 agonists such as clonidine are commonly used, branching out into less common agents like tizanidine, guanfacine and lofexidine allows for a greater pharmacotherapeutic repertoire
- DT's case shows many systemic barriers patients face in seeking appropriate treatment for their substance use disorders
- Common for pts on methadone to have difficulty with placement in residential or inpatient treatment
- Growth of co-morbid benzodiazepine use disorders and now xylazine dependence in patients on methadone → increasingly necessary to have access to inpatient treatment for patients on methadone
- **We hope stories like DT's will help us continue to push for policy and systemic reform**

References

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