

Substance Use Disorder ECHO

RUTGERS



RUTGERS
New Jersey Medical School



Hub Team Introductions



Mohammad Addar
Master Black Belt,
Operational Excellence
Cooper University Healthcare



James Bailey, DO,
NeuroMusculoskeletal Institute
Rehabilitation Medicine
Rowan University



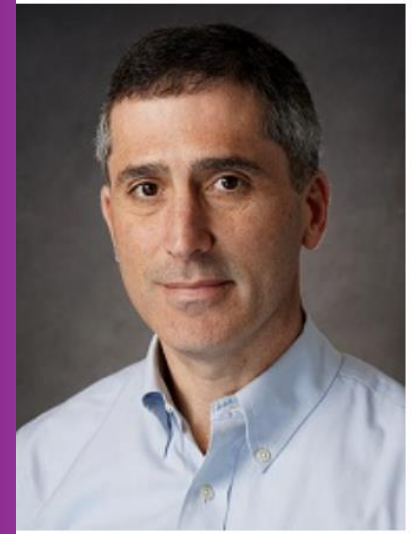
Clement Chen, PharmD
Clinical Pharmacist/Academic Detailer
Rutgers New Jersey Medical School



Lanvin Taylor II, DO,
NeuroMusculoskeletal Institute
Rehabilitation Medicine
Rowan University

Speaker Spotlight

- He/him
- Classically trained musician
 - Orchestral conducting
 - Viola
- Addiction Medicine Medical Director for
 - In-patient consult service
 - Research
- MPH candidate at the Bloomberg School of Public Health, Johns Hopkins University



**Matthew
Salzman, MD**

Assistant Professor,
Department of
Emergency Medicine
Cooper Medical School of
Rowan University

Our Goal

- Combat the substance use crisis through education on best practices in a safe space for peer-to-peer learning
- Engage healthcare providers in the primary care setting to increase skills to safely and compassionately manage, treat, and support their clients with a substance use disorder
- Recognize the importance of reducing stigma to advance equity and improve access to care for patients with substance use disorders



Nov. 4, 2022

Adulterants in Drugs of Abuse and the Trouble with Tranq

Presented by:

Matthew Salzman, MD

Assistant Professor, Department of Emergency Medicine

Division of Medical Toxicology and Addiction Medicine

Cooper Medical School of Rowan University

Financial Disclosures

- The following sessions leader(s) have no relevant Financial relationships with ineligible companies to disclose:
 - Matthew Salzman

Learning Objectives

- Briefly describe the history of adulterants in illicit substances
- Describe clinical findings associated with these adulterants
- Focus on xylazine, an adulterant that is not new but more commonly found in illicit substances and overdose victims in the United States

Terminology

- Adulterant
- Contaminant
- Diluent
- Substitute

A call for decriminalization and regulation

- Opioids (heroin)
 - MPTP
 - Levamisole
 - Fentanyl and fentanyl analogues
 - Anthrax
 - Scopolamine
- Clenbuterol
- *C. botulinum*
- Strychnine
- Arsenic
- Quinine
- Xylazine
- Caffeine
- Procaine
- Deschloroketamine

Harm reduction is paramount

- Cocaine
 - Levamisole
 - Xylazine
 - Lead
 - Fentanyl
- Marijuana
 - Lead
 - Aluminum
 - Fentanyl
- Synthetic cannabinoids
 - Brodifacoumb
- MDMA
 - PMA
 - PMMA
 - Caffeine
 - Ephedrine and pseudoephedrine
 - (meth)amphetamine

What are we seeing in New Jersey?

- Fentanyl, etc
- Xylazine
- Procaine
- Deschloroketamine
- Pregabalin
- Methamphetamine
- Tramadol
- 4-ANPP
- EZ Pass
- Summer Jam
- The Joker
- White Magic
- Stimulus Check

Levamisole



- Noted cocaine adulterant in 2003
 - Found in approximately 69% of cocaine seized by DEA
- *Levo* enantiomer of tetramizole
 - Imidazothiazole derivative
- Anti-helminthic
- Immunomodulator

Clenbuterol

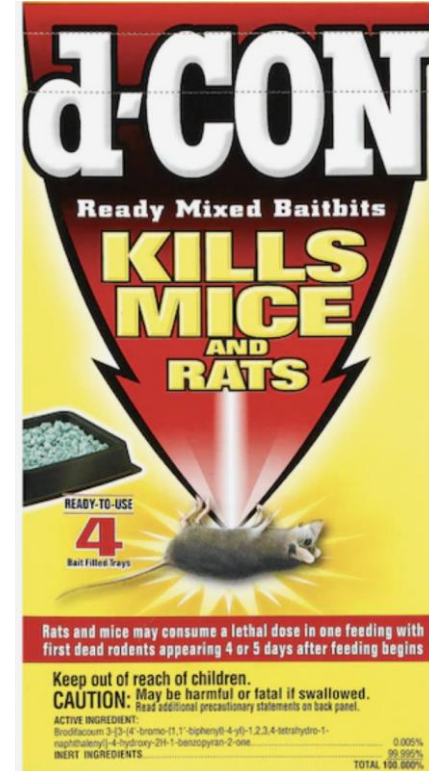
- Noted heroin adulterant in 2005
 - 26 cases reported in NJ, NY, Philadelphia region
 - 12 deaths reported in Philadelphia in 2008
- Elimination $t_{1/2}$ 25–39 hours
- Oral bioavailability 80%–90%
- β_2 adrenergic agonist at striated muscle
 - Increased muscle protein deposition
- β_3 adrenergic agonism at adipocytes
 - Promotes lipolysis
 - Abused by bodybuilders

Clenbuterol

- Hypotension
- Tachycardia
- Hypokalemia
 - Stimulation of Na-K ATPase resulting in intracellular shift
 - Increased risk for cardiac dysrhythmia
- Hyperglycemia
- Hyperlactemia

Brodifacoumb

- “Super-warfarin”
- Vitamin-k epoxide cycle antagonist
- INR>12



Brodifacoumb

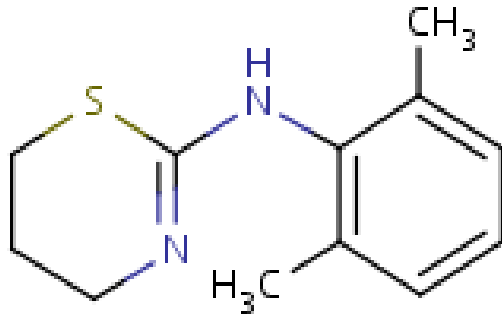


- Chicago, 2018 (n=155)
 - 4 deaths
- Florida, 2021 (n=52)
 - 4 deaths
- Other states including
 - Pennsylvania
 - Wisconsin
 - Maryland

The Trouble With Tranq (not Tribbles)



Xylazine



- 7 deaths in Philadelphia, 2006
- 262 deaths in Philadelphia, 2019
- 36 deaths in Puerto Rico, 2008–2010
- Antihypertensive agent
 - Large animal sedative–analgesic
- *Anestica de caballo, “tranq”*
- Partial central alpha-2 agonist
 - Blocks NE release
 - Inhibits Ach release
 - Has affinity for multiple receptors

Xylazine



- Hypertension followed by hypotension
 - Orthostatic hypotension
- Respiratory depression
 - Potentially lethal dose: 40-2400 mg
- Skin lesions/ulcers
 - Decreased skin oxygenation
 - Increased infection+decreased healing

Xylazine Complications



Picture courtesy of Michael Coletta, MD

Krokodil



- Desomorphine
- Codeine derivative
- Never confirmed in the US



Xylazine withdrawal???



- Analogous to clonidine withdrawal?
- Hypertensive emergency???
- Compassionate care



Xylazine withdrawal management



	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6
Hydromorphone	Patient-controlled anesthesia (PCA) pump; settings: no basal rate, bolus 1 mg q 10 minutes	PCA pump; settings: basal rate 1 mg/hour, bolus 1 mg q 12 minutes	PCA pump; settings: basal rate 1.5 mg/hour, bolus 1 mg q 12 minutes	PCA pump; settings: basal rate 1.5 mg/hour, bolus 1 mg q 12 minutes	PCA pump; settings: basal rate 1.5 mg/hour, bolus 1.2 mg q 12 minutes	PCA pump; settings: basal rate 1.5 mg/hour, bolus 1.2 mg q 12 minutes
Phenobarbital	Load (per institution's intensive care unit alcohol withdrawal protocol)	Taper (per institution's intensive care unit alcohol withdrawal protocol)	Taper (per institution's intensive care unit alcohol withdrawal protocol)	Taper (per institution's intensive care unit alcohol withdrawal protocol)	<i>Discontinued (taper completed)</i>	
Dexmedetomidine	Infusion	Infusion	Infusion	Infusion	<i>Discontinued</i>	
Tizanidine	4 mg q 6 hours PO	<i>Discontinued</i>				
Clonidine		0.3 mg q 8 hours PO	0.3 mg q 8 hours PO	0.3 mg q 8 hours PO	0.3 mg q 8 hours PO	0.3 mg q 8 hours PO
Buprenorphine				300 mcg once buccal	300 mcg BID buccal	450 mcg BID buccal
Gabapentin				300 mg q 8 hours PO	300 mg q 8 hours PO	300 mg q 8 hours PO
Ketamine				Infusion during dressing changes	Infusion during dressing changes	Infusion during dressing changes

Xylazine withdrawal management



	Day 7	Day 8	Day 9	Day 10	Day 11	Day 12
Hydromorphone	PCA pump; settings: basal rate 1.5 mg/ hour, bolus 1.2 mg q 12 minutes	PCA pump; settings: basal rate 1 mg/ hour, bolus 1.3 mg q 12 minutes	PCA pump; settings: no basal rate, bolus 1.3 mg q 12 minutes	PCA pump; settings: no basal rate, bolus 1.3 mg q 12 minutes	PCA pump; settings: no basal rate, bolus 1.3 mg q 12 minutes	PCA pump; settings: no basal rate, bolus 1.3 mg q 12 minutes
Clonidine	0.3 mg q 8 hours PO	0.3 mg q 8 hours PO	0.3 mg q 8 hours PO	0.3 mg q 8 hours PO	0.3 mg q 8 hours PO	0.3 mg q 8 hours PO
Buprenorphine	2 mg twice daily sublingual	2 mg three times daily sublingual	4 mg q 4 hours sublingual	2 mg four times daily sublingual	4 mg four times daily sublingual	4 mg four times daily sublingual
Gabapentin	300 mg q 8 hours PO	300 mg q 8 hours PO	300 mg q 8 hours PO	300 mg q 8 hours PO	300 mg q 8 hours PO	300 mg q 8 hours PO
Ketamine	Infusion during dressing changes	Infusion during dressing changes	Infusion during dressing changes	Infusion during dressing changes	Infusion during dressing changes	<i>Discontinued</i>

Xylazine withdrawal management



	Day 13	Day 14	Day 15	Day 16	Day 17	Day 18
Hydromorphone	PCA pump; settings: no basal rate, bolus 1.3 mg q 12 minutes	PCA pump; settings: no basal rate, bolus 1.3 mg q 12 minutes	PCA pump; settings: no basal rate, bolus 1 mg q 15 minutes	PCA <i>discontented</i> ; 2 mg q 3 hours IV PRN pain	2 mg q 3 hours IV PRN pain	2 mg q 4 hours PO PRN moderate pain, 2 mg q 4 hours PO PRN severe pain
Clonidine	0.3 mg q 8 hours PO	0.3 mg q 8 hours PO	0.3 mg q 8 hours PO	0.3 mg q 8 hours PO	0.3 mg/24 hours transdermal patch	0.3 mg/24 hours transdermal patch
Buprenorphine	4 mg QID sublingual	4 mg QID sublingual	4 mg 5 times daily sublingual	4 mg 5 times daily sublingual	4 mg 6 times daily sublingual	4 mg 6 times daily sublingual
Gabapentin	300 mg q 8 hours PO	300 mg q 8 hours PO	300 mg q 8 hours PO	300 mg q 8 hours PO	300 mg q 8 hours PO	300 mg q 8 hours PO

References

- Kelkar AH, Smith NA, Martial A, Moole H, Tarantino MD, Roberts JC. An Outbreak of Synthetic Cannabinoid-Associated Coagulopathy in Illinois. *N Engl J Med*. 2018 Sep 27;379(13):1216-1223. doi: 10.1056/NEJMoa1807652. PMID: 30280655.
- *Notes from the field: acetyl fentanyl overdose fatalities – rhode island, march–may 2013*. *MMWR Morb Mortal Wkly Rep*. **62**(34): p. 703–4.
- *Scopolamine poisoning among heroin users--New York City, Newark, Philadelphia, and Baltimore, 1995 and 1996*. *MMWR Morb Mortal Wkly Rep*, 1996. **45**(22): p. 457–60.
- *Atypical reactions associated with heroin use--five states, January–April 2005*. *MMWR Morb Mortal Wkly Rep*, 2005. **54**(32): p. 793–6.
- *Nonpharmaceutical fentanyl-related deaths--multiple states, April 2005–March 2007*. *MMWR Morb Mortal Wkly Rep*, 2008. **57**(29): p. 793–6.
- *Agranulocytosis associated with cocaine use – four States, March 2008–November 2009*. *MMWR Morb Mortal Wkly Rep*, 2009. **58**(49): p. 1381–5.
- Ehrman-Dupre R, Kaigh C, Salzman M, Haroz R, Peterson LK, Schmidt R. Management of Xylazine Withdrawal in a Hospitalized Patient: A Case Report. *J Addict Med*. 2022 Sep–Oct 01;16(5):595–598. doi: 10.1097/ADM.0000000000000955. Epub 2022 Jan 11. PMID: 35020700.

References

- Busse, F., et al., *Lead poisoning due to adulterated marijuana*. N Engl J Med, 2008. **358**(15): p. 1641-2.
- Busse, F.P., et al., *Lead poisoning due to adulterated marijuana in leipzig*. Dtsch Arztebl Int, 2008. **105**(44): p. 757-62.
- Decker, W.J., et al., *Two deaths resulting from apparent parenteral injection of strychnine*. Vet Hum Toxicol, 1982. **24**(3): p. 161-2.
- Hamilton, R.J., et al., *A descriptive study of an epidemic of poisoning caused by heroin adulterated with scopolamine*. J Toxicol Clin Toxicol, 2000. **38**(6): p. 597-608.
- Johnson J, Pizzicato L, Johnson C, Viner K. Increasing presence of xylazine in heroin and/or fentanyl deaths, Philadelphia, Pennsylvania, 2010-2019. Inj Prev. 2021 Aug;27(4):395-398. doi: 10.1136/injuryprev-2020-043968. Epub 2021 Feb 3. PMID: 33536231.
- Kazandra Ruiz-Colón, Carlos Chavez-Arias, José Eric Díaz-Alcalá, María A. Martínez, Xylazine intoxication in humans and its importance as an emerging adulterant in abused drugs: A comprehensive review of the literature, Forensic Science International, Volume 240, 2014, Pages 1-8, ISSN 0379-0738, <https://doi.org/10.1016/j.forsciint.2014.03.015>.



Thank you!

Any questions?

salzman-matthew@cooperhealth.edu