

INTERESTING ADDICTION MEDICINE CASES

NYSAM

FEBRUARY 6, 2021

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Addiction Medicine

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No Disclosures



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“All things are poisons, for there is nothing without poisonous qualities. It is only the dose which makes a thing poison.”



Philippus Aureolus Theophrastus Bombastus von Hohenheim, who published under the name **Paracelsus** was a Renaissance physician, botanist, alchemist, astrologer, and occultist. (1493—1541)

Courtesy Timothy Wiegand, MD



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Case of Overdose with Drug X

- ◆ Patient is a 34 yo female with hx of AUD, Depression
- ◆ Suicide Attempts in the past: Alcohol/Acetaminophen, Alcohol/Sertraline
- ◆ Found by spouse on the floor, unresponsive, with syringe and vial of X drug, and fresh needle mark in the right antecubital fossa.
- ◆ In ED: hypotensive, bradycardic, sedated, RR=8, hyperglycemic, miotic pupils
- ◆ No response to Naloxone Nasal Spray 4mg X2
- ◆ UTOX: Neg-Opiates, Heroin, 6-MAM, Benzo, Fentanyl, PCP, Cocaine, Bupe, Methadone, Barbiturate,
- ◆ Blood Alcohol Level: 140mg/dl
- ◆ Routine Labs: WNL except for hyperglycemia-330
- ◆ Patient made complete recovery with supportive therapy: IV fluids, IV insulin X-1



Case of Overdose with Drug X

- ◆ Patient and Spouse are both Animal Lovers
- ◆ ? Occupation of Patient
- ◆ Veterinarian
- ◆ ? X Drug

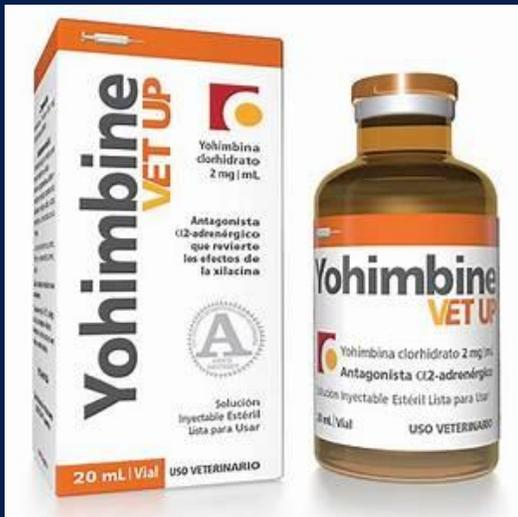
◆ **Xylazine**



Xylazine: History

- ◆ 1962: Developed by Bayer for Hypertension
- ◆ Never FDA Approved for Humans: Adverse Effects: ↓BP
- ◆ FDA Approved for Veterinary Use: Sedation, Analgesia, Muscle Relaxant: Dogs, Cats, Horses, Deer, Elk
- ◆ Brand Names: Rompun, Anased, Sedazine, Chanazine
- ◆ Not a Controlled Medication
- ◆ Cases of Human Poisoning(+/- Fatal) Dating to 1970s
- ◆ Adulterating Agent: Heroin, Fentanyl, Cocaine





Veterinary Medications Dispensed Prescribed

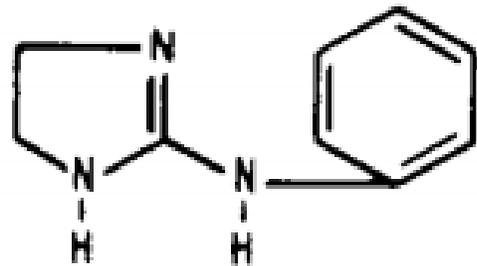


Xylazine: Pharmacology

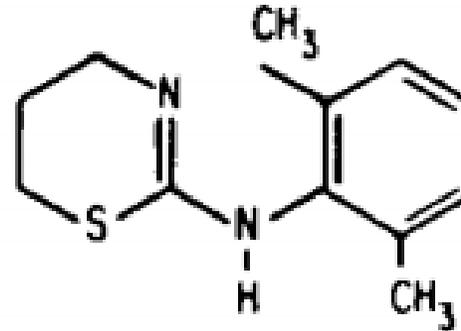
- ◆ Alpha-2 Adrenergic Agonist → ↓NE → ↓BP
- ◆ Analogue Clonidine and Phenothiazines
- ◆ Vagal Stimulation → Bradycardia
- ◆ Lipophilic: Rapid Onset: 15-30 mins.
- ◆ $1/2$ Life ~ 3hrs in Humans



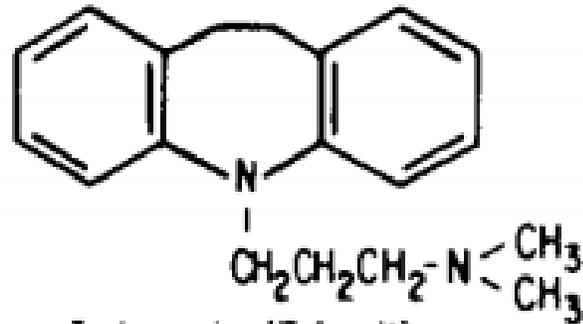
For the Biochemists



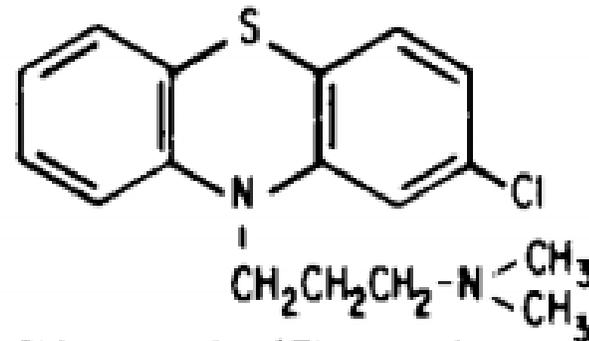
Clonidine (Catapres, St 155)



Xylazine (Rompun)



Imipramine (Tofranil)



Chlorpromazine (Thorazine)

Journal of Analytical Toxicology, Vol. 9, September/October 1985

Xylazine: Metabolism/Excretion

- ◆ Extensive Hepatic Metabolism
- ◆ Major Metabolite: 2,6 dimethylaniline (20 other metabolites)
- ◆ Rats: 70% Renal, 30% Hepatobiliary, 8% unchanged in urine



Xylazine: Misuse

- ◆ Mono Drug: Sedation, Anxiolytic
- ◆ Most Commonly Polysubstance: Heroin/Cocaine “Adulterant”
- ◆ USA: “Tranq Dope”
- ◆ Puerto Rico: “Anestecia de Caballo”
- ◆ Suicide: Sexual Assault: Homicide
- ◆ Accidental Exposure
- ◆ Veterinary Staff, Farm Workers, Horse Breeders, Hunters



Xylazine: Route of Administration

- ◆ IV, IM, SC, Inhalation, Ocular
- ◆ Animals: IV/IM
- ◆ Case Report: Eating Elk After Xylazine Used Prior to Slaughter



Severe intoxication from xylazine inhalation

ANDREW J. CAPRARO, MD, JAMES F. WILEY II, MD, JEFFREY R. TUCKER, MD

We present the first documented case of overdose from xylazine inhalation. The patient developed findings consistent with alpha₂ adrenergic agonist toxicity, eg coma, miosis, apnea, bradycardia, hypothermia, and dry mouth 2 hours after exposure. Standard dose naloxone did not reverse these effects. The patient fully recovered after appropriate supportive measures. A review of prior reports of xylazine exposure is provided.

drug, and feeling euphoric shortly thereafter. A xylazine level by gas liquid chromatography from blood drawn approximately 2 hours after inhalation was 0.54 µg/ml. His symptoms fully resolved 20 hours after initial exposure, and he was discharged with plans for follow-up substance abuse counseling.

This patient dried the xylazine on a compact disc case and inhaled the resulting powder. Therefore, estimation of dose is problematic. We independently determined that the maximum volume

CASE REPORT

TOXICOLOGY

*Hilke Andresen-Streichert¹, Ph.D.; Stefanie Iwersen-Bergmann¹, Ph.D.; Alexander Mueller¹, Ph.D.
Sven Anders¹, M.D.*

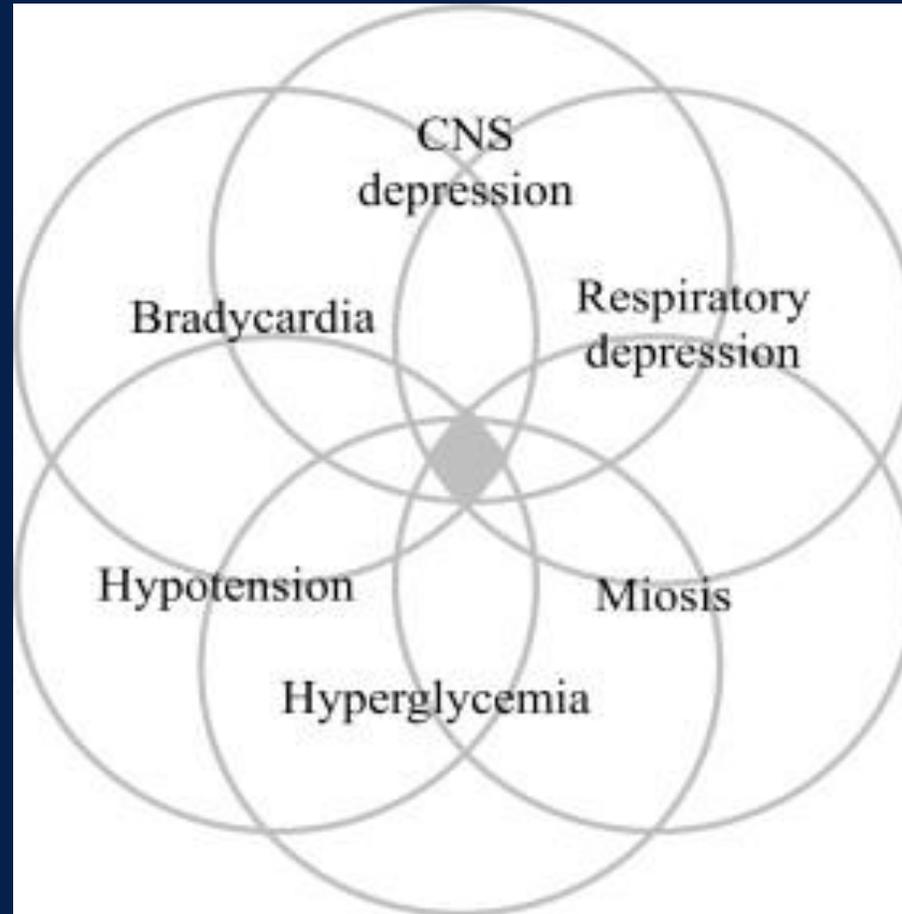
Attempted Drug-facilitated Sexual Assault— Xylazine Intoxication in a Child

J Forensic Sci, January 2017, V
doi: 10.1111/1556
Available online at: onlinelibra



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General Toxidrome for Xylazine



Forensic Science International
Volume 240, July 2014, Pages 1-8

Xylazine: Overdose

- ◆ Supportive
- ◆ Hemodialysis: Not Helpful
- ◆ Naloxone: For Opioids and ? For Xylazine
- ◆ Alpha-Adrenergic Antagonists: Phentolamine, Yohimbine, Tolazoline



The Emerging of Xylazine as a New Drug of Abuse and its Health Consequences among Drug Users in Puerto Rico



Xylazine: Detection

- ◆ Suspicion if Any Veterinary/Farm Connection
- ◆ Suspicion Based on Si/Sx of Intoxication
- ◆ Not by Immunoassay: GC/MS: Blood/Urine
Syringes: 38% + PR, 90% + cocaine/heroin



Analytical findings in used syringes from a syringe exchange program

Taís Regina Fiorentin^{a,*}, Barry K. Logan^{a,b}^aThe Center for Forensic Science Research and Education (CFSRE), 2300 Stratford Ave, Willow Grove, PA, 19090, USA^bNMS Labs, 200 Welsh Road, Horsham, PA, 19044, USA**Table 1**

Table of the major compounds found by prevalence order, divided by class.

Class	Substances	N	%
Opioids	Heroin/related substances ¹	198	72.0
	Fentanyl/related substance ²	37	13.5
	Furanylfentanyl	10	3.6
	Fluoroisobutyrylfentanyl	5	1.8
	Tramadol	5	1.8
	Methadone	2	0.7
Stimulants	Cocaine/related substance ³	96	34.9
	Methamphetamine/related substance ⁴	21	7.6
	N-Ethyl Pentylone	2	0.7
Adulterants	Quinine/Quinidine	51	18.5
	Levamisole	33	12.0
	Caffeine	32	11.6
	Lidocaine	32	11.6
	Phenacetin	19	6.9
	Diltiazem	6	2.2
	Hydroxyzine	6	2.2
	Xylazine	6	2.2
	Dextromethorphan	3	1.1
	Diphenhydramine	2	0.7
Benzodiazepines	Gabapentin	1	0.4
	Alprazolam	1	0.4
	Clonazepam	1	0.4
Other	Cotinine	3	1.1
	Quetiapine	2	0.7
	Olanzapine	1	0.4

357 syringes collected by NYC-DOH from 11 Syringe Exchange Programs between March 2017—June 2017

77% + for one or more substances

23% - for all substances (?rinsed/not used)

2.2% + Xylazine

Xylazine: Users Beliefs

Focus Group in Puerto Rico: n=89

- ◆ Able to Detect: Effects, Taste, Color(Brown), Odor
- ◆ Odor in Breath, Sweat, Urine-- Post Use
- ◆ Skin Lesions: 35% Puerto Rico (? Secondary to ↓Tissue Oxygenation Due to Hypotension/Bradycardia and Analgesia)
- ◆ N=89: 80% reported xylazine use/ 42% with “speedball”

Reyes, et al: Journal of Urban Health, Vol. 89, No. 3



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Xylazine: Recommendations

- ◆ Educate Veterinary/Farm/Horse Personnel on Harms Associated with Xylazine/Other Veterinary Medications
- ◆ Stronger Warning Labels on Veterinary Medications
- ◆ Tighter Requirements on Storage of Unused Medications
- ◆ Naltrexone: Xylazine + Opioids
- ◆ DEA Scheduling
- ◆ Improve PDMP usage



Addicts using pets to score drugs, veterinarians warn

BY JENNIFER EARL

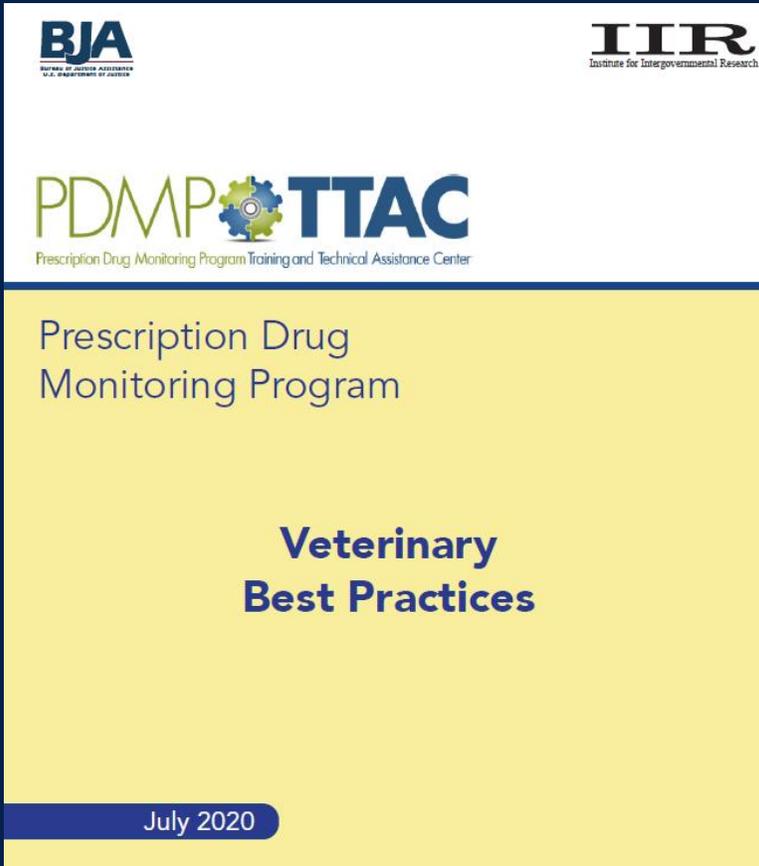
FEBRUARY 24, 2017 / 4:52 PM / CBS NEWS



In Kentucky, police say, a dog owner named Heather Pereira, 23, cut her dog with razor blades just so she could take the dog's pain medication in 2014. She was sentenced to four years in prison



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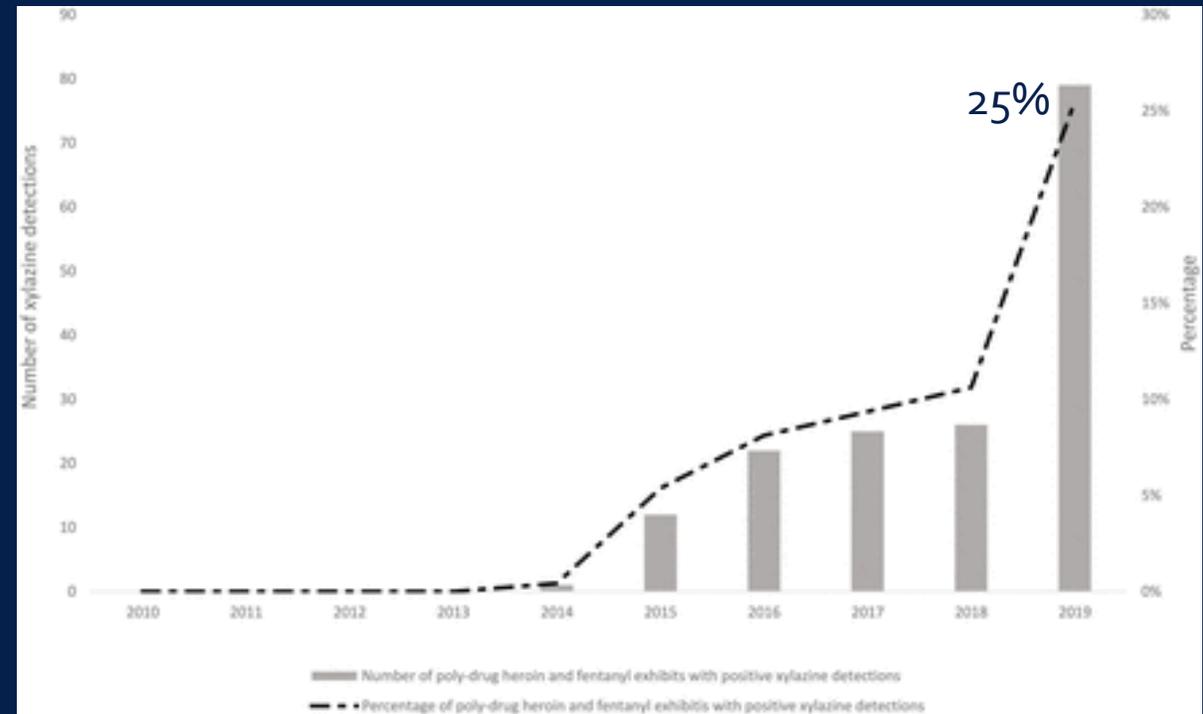
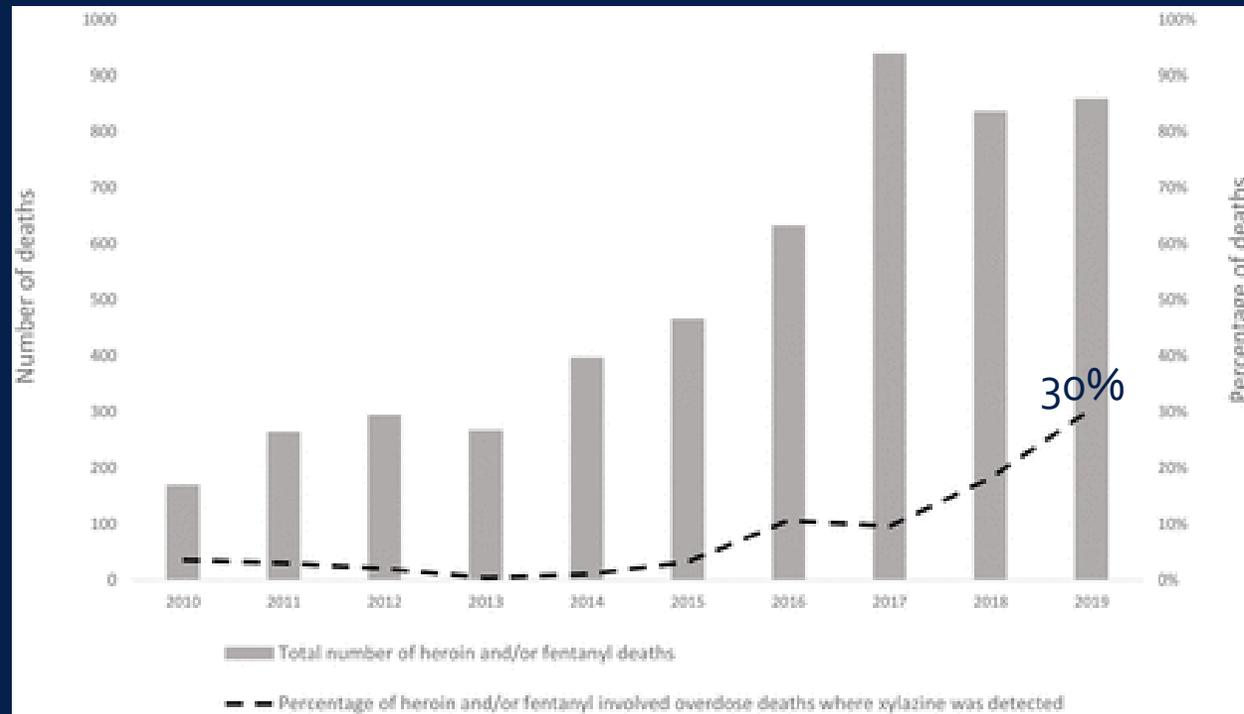
1. A prescription issued by a veterinarian must not only incorporate the information that other practitioners are required to provide, but also information such as the species of the animal and the name of the animal and/or its owner. This additional information must be reported to PDMPs by states that require a veterinarian to report medications dispensed.
2. Indiana—A practitioner who is a veterinarian treating an animal may obtain PDMP information about the owner of the animal or the individual to whom an opioid or benzodiazepine will be dispensed for the animal from the PDMP before prescribing an opioid or a benzodiazepine for an animal.
3. States where veterinarians are specifically excluded from PDMP: California, Michigan (if the substance is prescribed by a veterinarian and will be dispensed by a pharmacist), Nevada, New Hampshire, **New Jersey, New York, Texas, Wyoming**
4. **The majority of PDMPs do not require veterinarians who dispense controlled substances to report the information to the PDMP. Only 18 states required dispensing veterinarians to report.**



Increasing presence of xylazine in heroin and/or fentanyl deaths, Philadelphia, Pennsylvania, 2010–2019

Johnson J, et al. *Inj Prev* 2021;

Jewell Johnson , Lia Pizzicato, Caroline Johnson, Kendra Viner



Did She or Didn't She?

What Will the Clinician Predict?



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71 yo Female Requesting Amb. Opioid “Detox”

5/18/20

- ◆ Domiciled, Retired, Last Opioid “Detox” many years ago . Hx OUD
- ◆ Rx’d Oxycodone IR for chronic LBP—20mg QID- ~15 years
- ◆ Claims mild withdrawal when oxycodone “wears off”
- ◆ Uses heroin (skin popping) to alleviate withdrawal si/sx
- ◆ Claims no misuse of prescribed oxycodone
- ◆ Wants to continue with Rx IR oxycodone, but not use heroin
- ◆ COWS=2
- ◆ Metformin, Gabapentin(DPN), Trazodone, NSAIDS, Acetaminophen
- ◆ Patient was given 20mg methadone and enrolled in amb. “detox”



71 yo Female in Ambulatory “Detox”

- ◆ After patient left, case was presented to me.
- ◆ The patient was called and asked to bring her original pharmacy bottle of oxycodone, which was dispensed on 5/2/20, with all the tablets remaining when she returns tomorrow to continue “detox”
- ◆ Patient says “I’ll try”



Which Scenario Do You Predict?

1. Patient will not return for next appointment
2. Patient will return and forget to bring the oxycodone Rx
3. Patient will return and claim partner threw out oxycodone
4. Patient will return and have correct pill count
5. Patient will return with empty bottle or few oxycodone pills

◆ **Patient will return and have correct pill count**



Rx Written	Rx Dispensed	Drug	Quantity	Days Supply
05/26/2020	05/27/2020	oxycodone hcl 20 mg tablet	120	30
04/28/2020	05/02/2020	oxycodone hcl 20 mg tablet	120	30
03/31/2020	04/03/2020	oxycodone hcl 20 mg tablet	120	30
02/27/2020	03/04/2020	oxycodone hcl 20 mg tablet	120	30
10/20/2019	10/22/2019	oxycodone hcl 20 mg tablet	120	30
10/02/2019	10/02/2019	oxycodone hcl 20 mg tablet	90	22
09/25/2019	09/25/2019	oxycodone hcl 20 mg tablet	30	7
08/28/2019	09/03/2019	oxycodone hcl 15 mg tablet	120	30
07/30/2019	08/02/2019	oxycodone hcl 15 mg tablet	120	30
07/02/2019	07/02/2019	oxycodone hcl 15 mg tablet	120	30

Patient Name: Theresa Figueroa
Address: 177-14 106 AVE JAMAICA, NY 11433

Birth Date:
Sex: Female

Rx Written	Rx Dispensed	Drug	Quantity	Days Supply
01/28/2020	02/04/2020	oxycodone hcl 20 mg tablet	120	30
01/07/2020	01/11/2020	oxycodone hcl 20 mg tablet	120	30
12/10/2019	12/13/2019	oxycodone hcl 20 mg tablet	120	30
11/17/2019	11/18/2019	oxycodone hcl 20 mg tablet	120	30

One Prescriber



5/18/2020

TESTS	RESULT	FLAG	UNITS	REFERENCE INTERVAL	LAB
734578 4+Alc-Scr+1-ReScr					
^A					01
Benzodiazepines ^A	Negative		ng/mL	Cutoff=300	01
Drug Screen Comment: ^A					01
This analysis is performed by immunoassay. Positive findings are unconfirmed analytical test results; if results do not support expected clinical finding, confirmation by an alternate methodology is recommended. Patient metabolic variables, specific drug chemistry, and specimen characteristics can affect test outcome. Technical consultation is available at otstoxline@labcorp.com , or call toll free 888-883-5017.					
Cannabinoid ^A	Negative		ng/mL	Cutoff=50	01
Cocaine (Metab.) ^A	Negative		ng/mL	Cutoff=300	01
Opiates ^A	Positive		ng/mL	Cutoff=300	01
Opiate test includes Codeine, Morphine, Hydromorphone, Hydrocodone.					
Methadone Screen, Urine ^A	Positive		ng/mL	Cutoff=300	01
Ethanol U, Qual ^A	Negative		%	Cutoff=0.020	01



5/18/20 → 5/27/20

TESTS	RESULT	FLAG	UNITS	REFERENCE INTERVAL
Oxycodone/Oxymorphone Confirm				
^A				
Oxycodone/Oxymorph ^B	Positive			Cutoff=100
Test includes Oxycodone and Oxymorphone				
Oxycodone ^B	Positive			
Oxycodone Confirm ^B	>10000		ng/mL	Cutoff=100
Oxycodone detected; this finding is consistent with use of medications that include Oxycontin, Percodan, Percocet, Tylox, or generic formulations. Drugs listed are representative of common sources of the compound detected and are not intended to include all possible sources.				
Oxymorphone ^B	Positive			
Oxymorphone Confirm ^B	2290		ng/mL	Cutoff=100
Oxymorphone detected; this finding is consistent with use of medications that include Numorphan, Opana, or drugs containing Oxycodone, or generic formulations. Drugs listed are representative of common sources of the compound detected and are not intended to include all possible sources.				



Patient returned with exact correct pill count

- ◆ Uses heroin as a means of not using more than 4 oxycodone/day
- ◆ When she does not have heroin she takes more than 4 per day
- ◆ When running out early uses heroin or illicit methadone
- ◆ Methadone is bought from someone in an OTP



Discussed Options with Patient 5/19/20

- ◆ Prior hx of OUD and methadone maintenance treatment
- ◆ Understands that a “detox” makes no sense while on 80mg oxycodone daily
- ◆ Ask prescriber to increase dose: tolerance vs OIH: Over CDC MME 160MME
- ◆ Ask prescriber to switch to ER/LA formulation oxycodone, or other ER/LA opioid analgesic (methadone—Pain and/or OUD --Complicated Nexus)
- ◆ Enroll in OTP for MMTP—could use IR oxycodone for breakthrough pain if needed
- ◆ Buprenorphine: patient reluctant
- ◆ OIH: taper to lower dose
- ◆ Non-pharmacologic treatments; Physical therapy, massage, etc,



Tunnel Vision, Jumping to Conclusions Mea Culpa



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54 yo Male on MMTP

- ◆ Admitted to MSBI on 12/7/20 for treatment of osteomyelitis L foot
- ◆ On MMTP 140mg X 5 years
- ◆ HTN, CAD, T₂DM
- ◆ Amlodipine, atorvastatin, HCTZ, gabapentin, insulin,
- ◆ Vancomycin, Piperacillin
- ◆ + Tobacco, ~10 EtOH drinks per week, denies illicit opioids since MMTP
- ◆ HgB=11, WBC=10, Platelets=301, BUN=23, Creatinine=1.84, EGFR=39
- ◆ No UTOX obtained on admission



54 yo Male on MMTP

- ◆ Rapid Response on 12/15/20 at 18:30— **8 days after admission**
- ◆ Patient was found unresponsive in bed by RN
- ◆ Glu=49, BP=105/55, HR=50, O₂ Sat=95% RA
- ◆ Patient given Naloxone 0.04 mg X 6 IV, D50W
- ◆ Patient responded but remained somnolent
- ◆ Transferred to MICU for 12 hours-naloxone drip-back to medicine
- ◆ BUN=50, Creatinine=3.73
- ◆ Consensus: Over sedation from methadone + hypoglycemia



54 yo male on MMTP

	12/15/2020 1650	12/17/2020 1224	12/20/2020 1458	12/23/2020 2144	12/24/2020 2207	12/28/2020 1136
TOX - URINE						
Acetylmorphine, Ur	<i>Negative</i> *					
AMPHETAMINES, URINE	<i>Negative</i> *					
BARBITURATES, URINE	<i>Negative</i> *					
BENZODIAZEPINE SCR...	<i>Negative</i> *					
Buprenorphine, Ur	<i>Negative</i> *					
CANNABINOID SCR, UR	<i>Negative</i> *					
EDDP (Methadon MET...	<i>Positive</i> * !					!
Fentanyl, Ur.	<i>Positive</i> * !					
Oxycodone, Ur	<i>Negative</i> *					
Tramadol, Ur	<i>Negative</i> *					
U-COCAINE	<i>Negative</i> *					
U-METHADONE	<i>Positive</i> * !					!
U-OPIATE	<i>Positive</i> * !					
U-PCP SCREEN	<i>Negative</i> *					



54 yo male on MMTP

- ◆ Did patient use heroin prior to somnolence & Rapid Response?
- ◆ If yes, did he bring into hospital or did visitor bring?
- ◆ Patients are not searched on admission.

- ◆ Seemed like a reasonable scenario, if UTOX is consistent with recent use



54 yo male on MMTP

Rx Written	Rx Dispensed	Drug	Quantity	Days Supply
08/07/2020	08/07/2020	oxycodone-acetaminophen 5-325 mg tab	14	7
07/23/2020	07/23/2020	oxycodone hcl 5 mg tablet	42	14
06/07/2020	06/08/2020	oxycodone hcl 5 mg tablet	56	14
05/09/2020	05/09/2020	oxycodone hcl 5 mg tablet	84	14
04/09/2020	04/09/2020	oxycodone hcl 5 mg tablet	42	7
02/26/2020	02/26/2020	oxycodone-acetaminophen 7.5-325 mg tablet	45	7
02/03/2020	02/03/2020	oxycodone-acetaminophen 7.5-325 mg tablet	56	14

Denies any use of pharmaceutical fentanyl, morphine, codeine

Admits to occasional IN Heroin Use--1-2 X week



54 yo Male on MMTP

GC/MS 12/16/20

(NOTE)

Test Ordered: 737846 Opiates Confirmation, Urine

Opiates Positive [A] ng/mL XB

Opiate test includes Codeine, Morphine, Hydromorphone, Hydrocodone.

Codeine Negative XB

Reference Range: Cutoff=100

Morphine Positive [A] XB

Morphine Confirm 213 ng/mL XB

Reference Range: Cutoff=100

Morphine detected; this finding is consistent with use of medications that include Duramorph, MS-Contin, Roxanol, Kadian, or drugs containing Codeine, or generic formulations. This drug may also be detected from use of Heroin. Drugs listed are representative of common sources of the compound detected and are not intended to include all possible sources.

Hydromorphone Negative XB

Reference Range: Cutoff=100

Hydrocodone Negative XB

Reference Range: Cutoff=100

GC/MS 12/16/21

M3287303

Collect D/T: 12/15/2020 1650

Order a

Order physician:

MISC LABCORP TEST

MISC TEST CODE

737934

MISC TEST NAME

HEROIN METABOLITE 6 AM CONFIRMATION

MISC TEST SOURCE

URINE

MISC TEST RESULT

COMMENT

(NOTE)

Test Ordered: 737934 6-Acetylmorphine Confirm, Ur

6-Acetylmorphine Negative XB

Reference Range: Cutoff=10



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54 yo male on MMTP

	12/15/2020 1650	12/17/2020 1224	12/20/2020 1458	12/23/2020 2144	12/24/2020 2207	12/28/2020 1136
TOX - URINE						
Acetylmorphine, Ur	<i>Negative *</i>	<i>Negative *</i>				
AMPHETAMINES, URINE	<i>Negative *</i>	<i>Negative *</i>				
BARBITURATES, URINE	<i>Negative *</i>	<i>Negative *</i>				
BENZODIAZEPINE SCR...	<i>Negative *</i>	<i>Negative *</i>				
Buprenorphine, Ur	<i>Negative *</i>	<i>Negative *</i>				
CANNABINOID SCR, UR	<i>Negative *</i>	<i>Negative *</i>				
EDDP (Methadon MET...	<i>Positive *</i> !	<i>Positive *</i> !				!
Fentanyl, Ur.	<i>Positive *</i> !	<i>Positive *</i> !				
Oxycodone, Ur	<i>Negative *</i>	<i>Negative *</i>				
Tramadol, Ur	<i>Negative *</i>	<i>Negative *</i>				
U-COCAINE	<i>Negative *</i>	<i>Negative *</i>				
U-METHADONE	<i>Positive *</i> !	<i>Positive *</i> !				!
U-OPIATE	<i>Positive *</i> !	<i>Positive *</i> !				
U-PCP SCREEN	<i>Negative *</i>	<i>Negative *</i>				

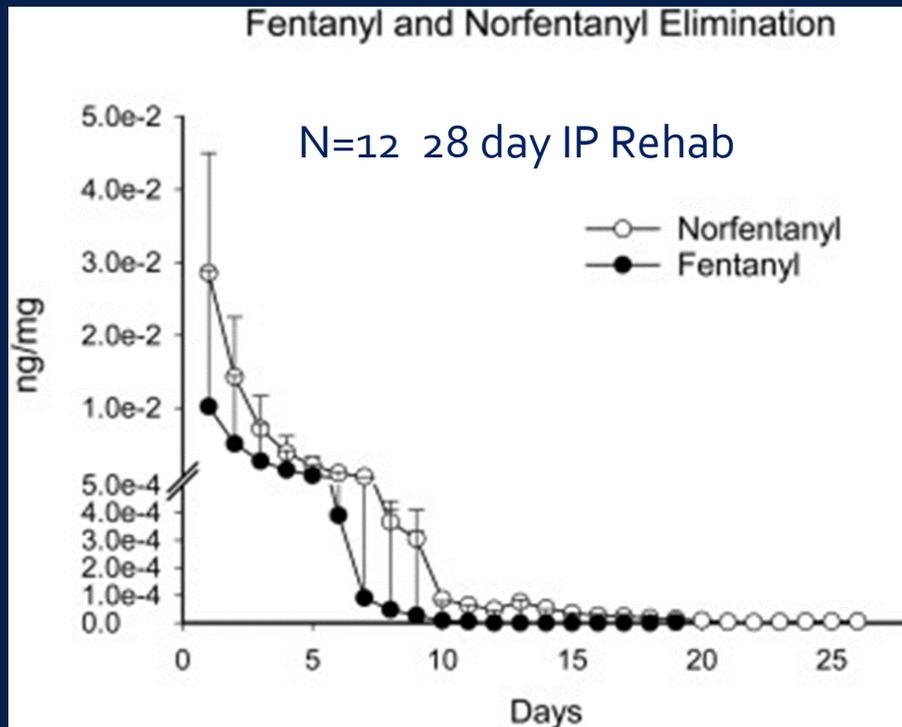


54 yo male MMTP

- ◆ Now admits to daily IN Heroin use
- ◆ Did not know heroin was contaminated with Fentanyl
- ◆ Patient did not have fentanyl patch on his body
- ◆ Methadone dose was decreased to 80mg daily



Protracted renal clearance of fentanyl in persons with opioid use disorder

Andrew S. Huhn^{a,b,*}, J. Gregory Hobelmann^{a,b}, George A. Oyler^c, Eric C. Strain^a^a Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, MD, 21224, USA^b Ashley Addiction Treatment, Havre de Grace, MD, 21078, USA^c Department of Chemical and Biomolecular Engineering, Johns Hopkins University, Baltimore, MD, 21218, USA

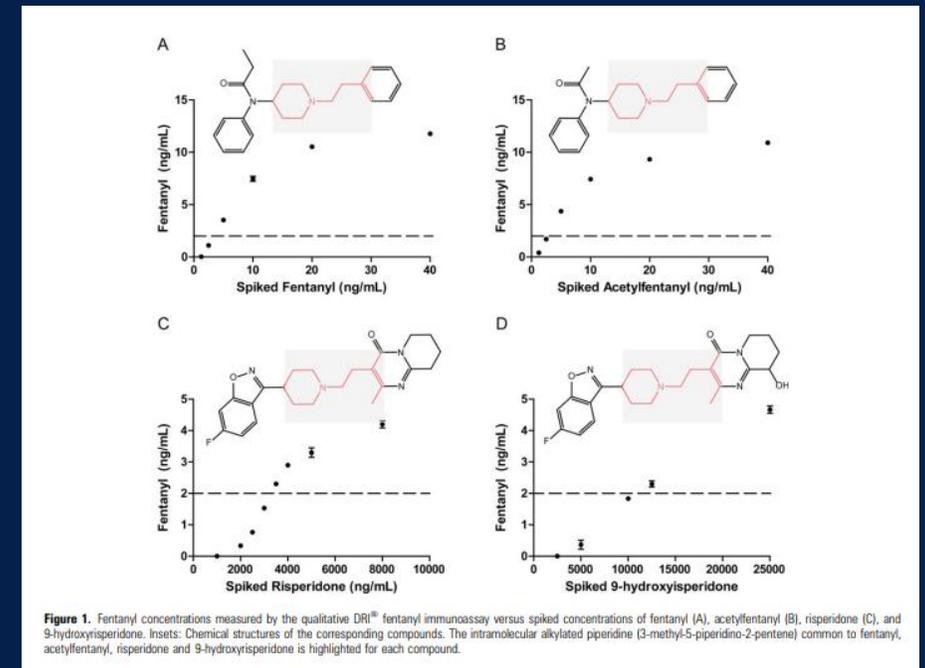
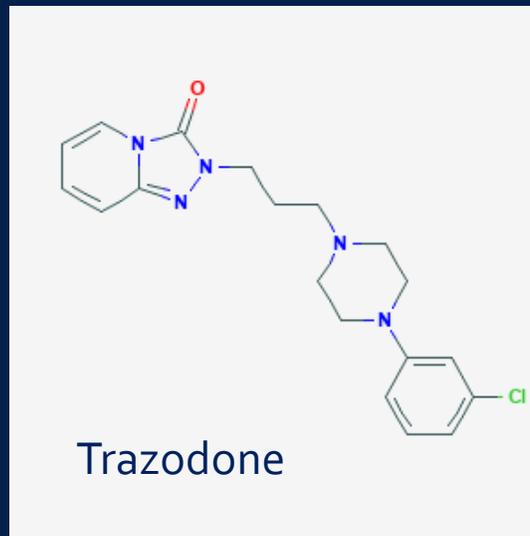
The mean (SD) time for fentanyl and norfentanyl clearance was 7.3 (4.9) and 13.3 (6.9) days, respectively.

One participant continued to test positive for fentanyl for 19 days and norfentanyl for 26 days following their last use, and left treatment without testing negative for norfentanyl.

Conclusion: Fentanyl clearance in persons with OUD is considerably longer than the typical 2–4 day clearance of other short-acting opioids. The findings of this study might explain recent reports of difficulty in buprenorphine inductions for persons who use fentanyl, and point to a need to better understand the pharmacokinetics of fentanyl in the context of opioid withdrawal in persons who regularly use fentanyl.

False Positive Fentanyl Immunoassay

- ◆ Trazodone
- ◆ Risperidone, Paliperidone, Iloperidone
- ◆ Some of the Fentanyl Analogues
- ◆ Not nor-fentanyl



Journal of Analytical Toxicology 2014;38:672–675

54 yo Male on MMTP Conclusions

- ◆ Has been regularly using illicit heroin contaminated with fentanyl prior to hospital admission
- ◆ Delayed clearance of Morphine and M-6-G/M-3-G – Impaired renal Function → accumulation of M-6-G. Do metabolites screen +morphine?
- ◆ Delayed clearance of Fentanyl— Lipophilicity/Tissue stores
- ◆ Rapid Response likely due to hypoglycemia
- ◆ Naloxone response expected in patient on methadone maintenance
- ◆ Lessons Learned by All

