Toxicology:

Pearls, pitfalls & potpourri

Toxicology: Pearls, Pitfalls, & Potpourri

CLAIRE EPPERSON, DO

Assistant Instructor of Emergency Medicine,
Medical Toxicology Fellow
Dallas, Texas

UT Southwestern Medical Center

Parkland Memorial Hospital

lindsey.epperson@phhs.org

4th Annual Toxicology Education Day February 19, 2021

Relevant Disclosure and Resolution

Under Accreditation Council for Continuing Medical Education guidelines disclosure must be made regarding relevant financial relationships with commercial interests within the last 12 months.

Claire Epperson, DO

I have no relevant financial relationships or affiliations with commercial interests to disclose.

Learning Objectives

Upon completion of this session, participants will improve their competence & performance by being able to:

1. Identify analytical toxicology tests available to support the management of poisoned patients presenting to emergency departments.
2. Describe which medications require quantitative analysis to evaluate clinical effect.
3. Recognize advantages and disadvantages of commonly utilized clinical toxicology laboratory tests.
4. Explain the pitfalls of the basic urine drug screen.
5. Develop an organized, rapid clinical management plan for the acutely poisoned or overdosed patient.

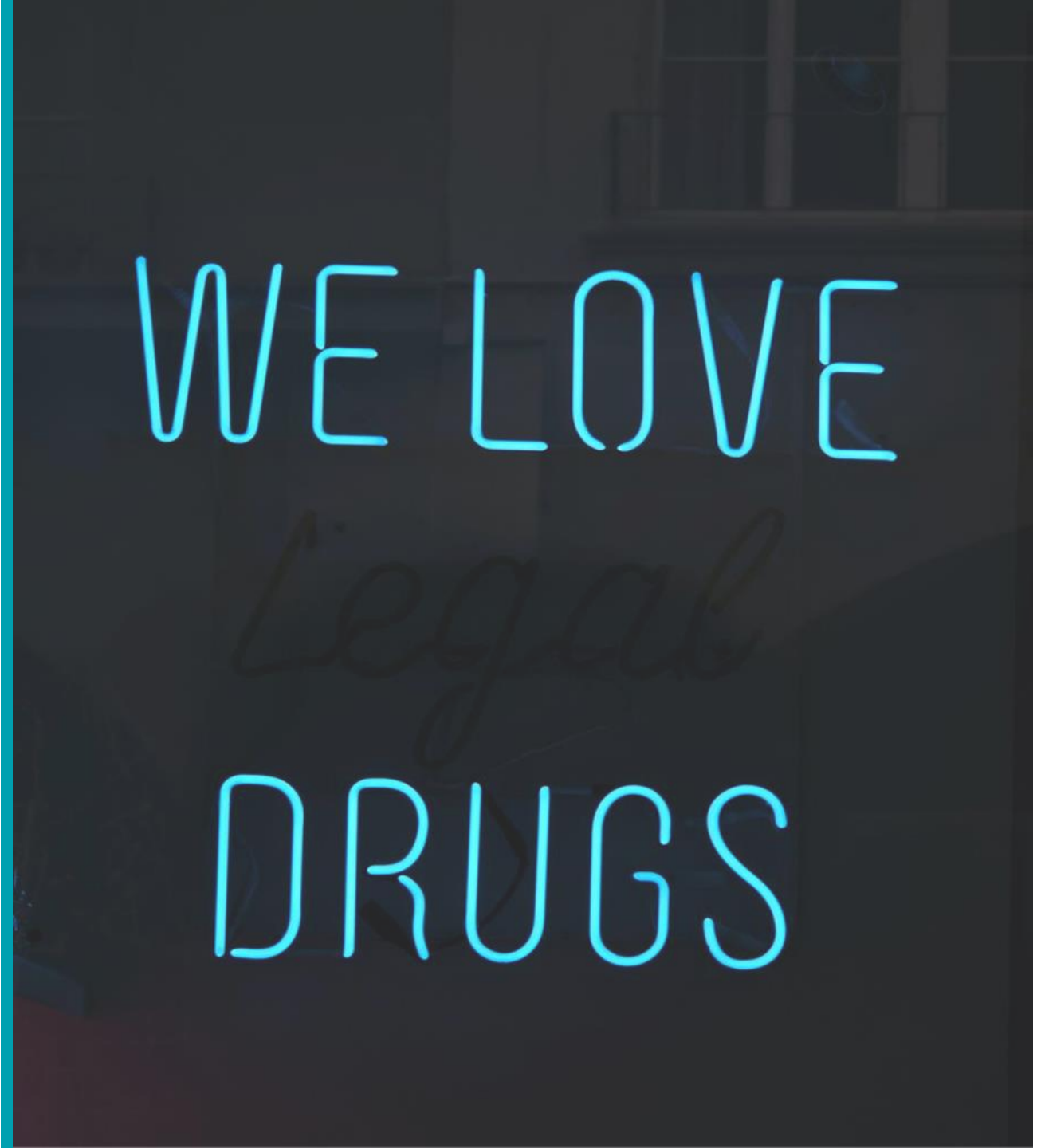
Professional Practice Gap

Gap 1: Practitioners in the emergency department, inpatient medicine, and the community can improve patient care by consulting poison experts when the need arises. Applying the principles discussed will provider practitioners with tools to confidently triage and manage the acute poisoned patient with the help of their local poison center.

Urine Drug Screens

Pearls & Pitfalls

Not a replacement for clinical diagnosis or decision making.



Urine Drug Screens

UDS is a relatively inexpensive and quick...

But how useful is it?

Before ordering, understand limitations

Management often doesn't change after UDS

So treat the ***toxidrome*** … Not the ***"drug"***

Toxidromes

- Opioid
- Sedative Hypnotic
- Sympathomimetic
- Serotonergic
- Anticholinergic
- Cholinergic
- Salicylate

Neurochemistry

Anticholinergic

Inhibit AcH receptors

Cholinergic

Stimulate AcH receptors

Opioid

Stimulate Endogenous Opioid receptors → Inhibitory

Sympathomimetic

Increase Norepinephrine → stimulatory
Increase Dopamine → stim / hallucinations
Increase Serotonin → stim / euphoric / hallucinations

Sedative Hypnotics

Stimulate GABA receptors → inhibitory
Inhibit electrical transmission → inhibitory

Opioid Toxidrome

- Signs: **CNS Depression**, Miosis, Respiratory Depression
  - Some agents have “other” effects:
  - Tramadol is serotonergic
  - Propoxyphene causes dysrhythmias
  - Cutting agents can alter presentations
- Drug Examples: Heroin, Fentanyl(s), U-47700MT45, Hydrocodone & Oxycodone

Pupils

Sedative Hypnotic Toxidrome

- Signs: **CNS Depression**, Respiratory Depression. Additional symptoms may vary a lot
- Drug Examples: Benzodiazepines, Barbiturates, Ethanol, Many Anti-Psychotics and Anti-Depressants, The “Z” Sleeping Agents, Muscle Relaxants, GHB

Sympathomimetic Toxidrome

- Signs: Think α & β agonism: CV- **↑HR**, ↑BP.
  Neuro- **Hyperactive**, Agitated, Delirium.
  Skin – Diaphoresis
  Pupils - Dilated
- Drug Examples: Amphetamines, Methamphetamine, Many Novel Psychoactive agents, Cocaine, Synthetic Cathinones (Bath Salts), Synthetic Cannabinoids

Reflexes

Serotonergic Toxidrome

- Signs: **Hyperreflexia**, Clonus, **Tremor**, **Tachycardia**, Diaphoresis, Diarrhea, Agitation
- Drug Examples: MDMA (Ecstasy) & many other similar drugs, Cough & Cold meds, BOMEs, SSRIs & SNRIs, Tramadol, Meperidine, Dextromethorphan, MAOIs

Arguments for UDS?

Psych clearance from the ED:

- ACEP: UDS doesn't impact psych med clearance from ED
- Clearance is based on UDS, but not on the confirmatory testing
- Psychiatrists often ignore the results
- Doesn't change management or impact treatment
- Costs money and wastes time

Pediatric pts in whom drug involvement suspected?

- More complicated… But again, many FP's and FN's.
- Rarely changes clinical management
- Generally, not worth resources or risk of a false result.

Urine Drug Screen...

How it works:

Urine Drug Screen

immune based test

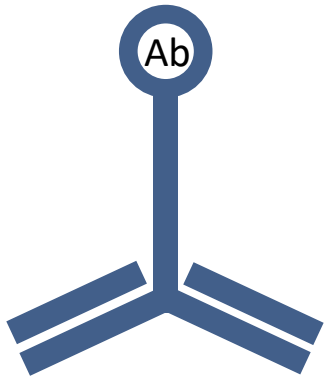
Confirmatory testing

LC-MS on positive UDS

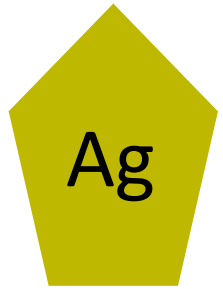
Talk to the patient

and interpret results

Uses **Antibodies...**



to detect specific Antigens



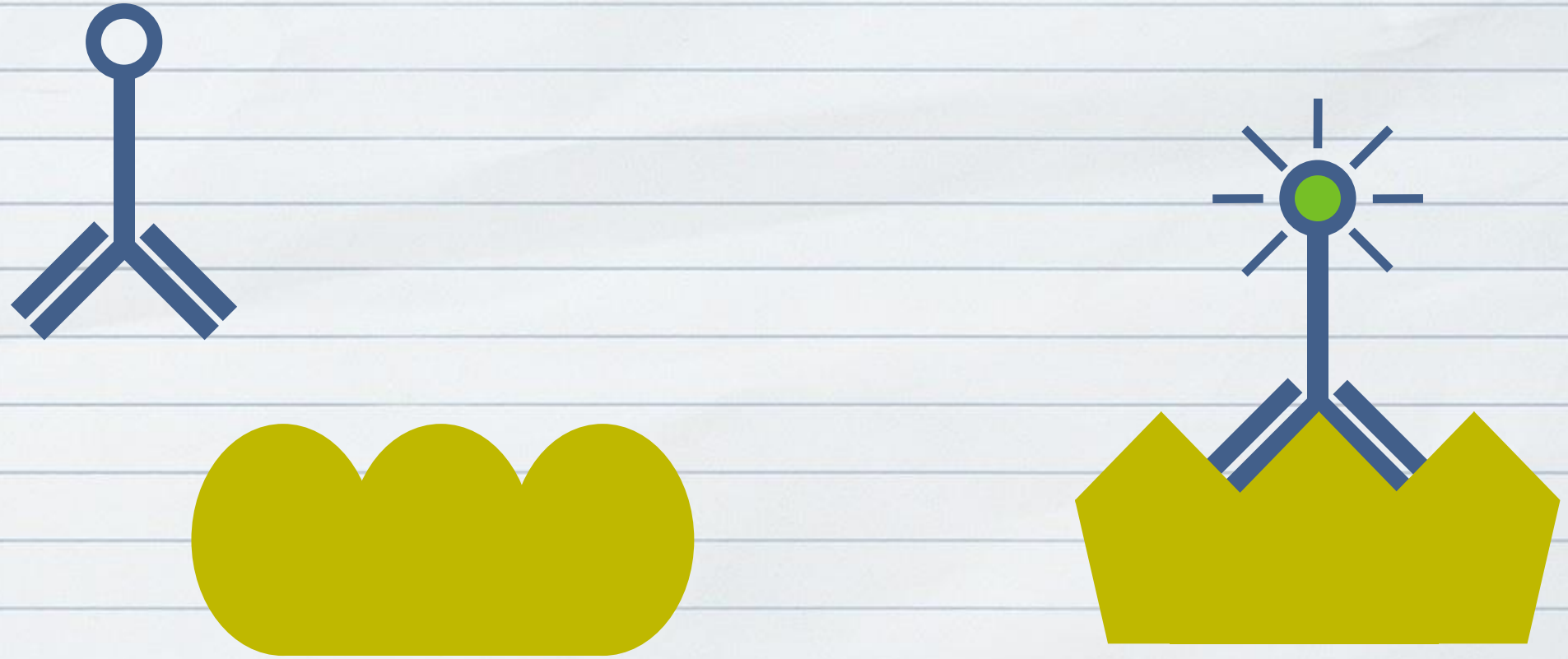
Urine Drug Screen...

How it works:

1. Antibody created to detect a particular Antigen
2. Attach a detector to the created antibody to signal when it binds the Antigen
3. Apply created Antibody to a *new* sample and look for the presence of detector

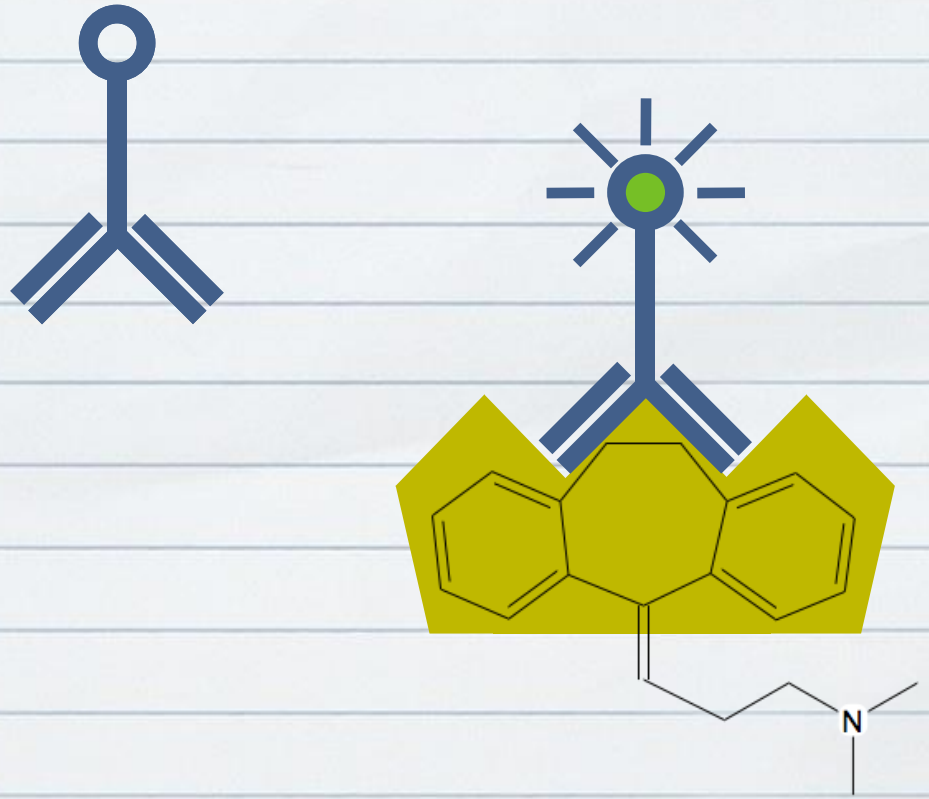
Urine Drug Screen...

How it works:

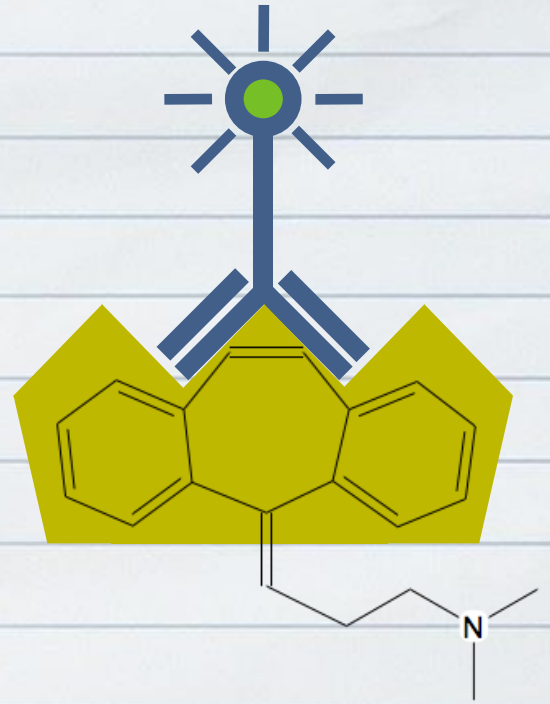


Urine Drug Screen...

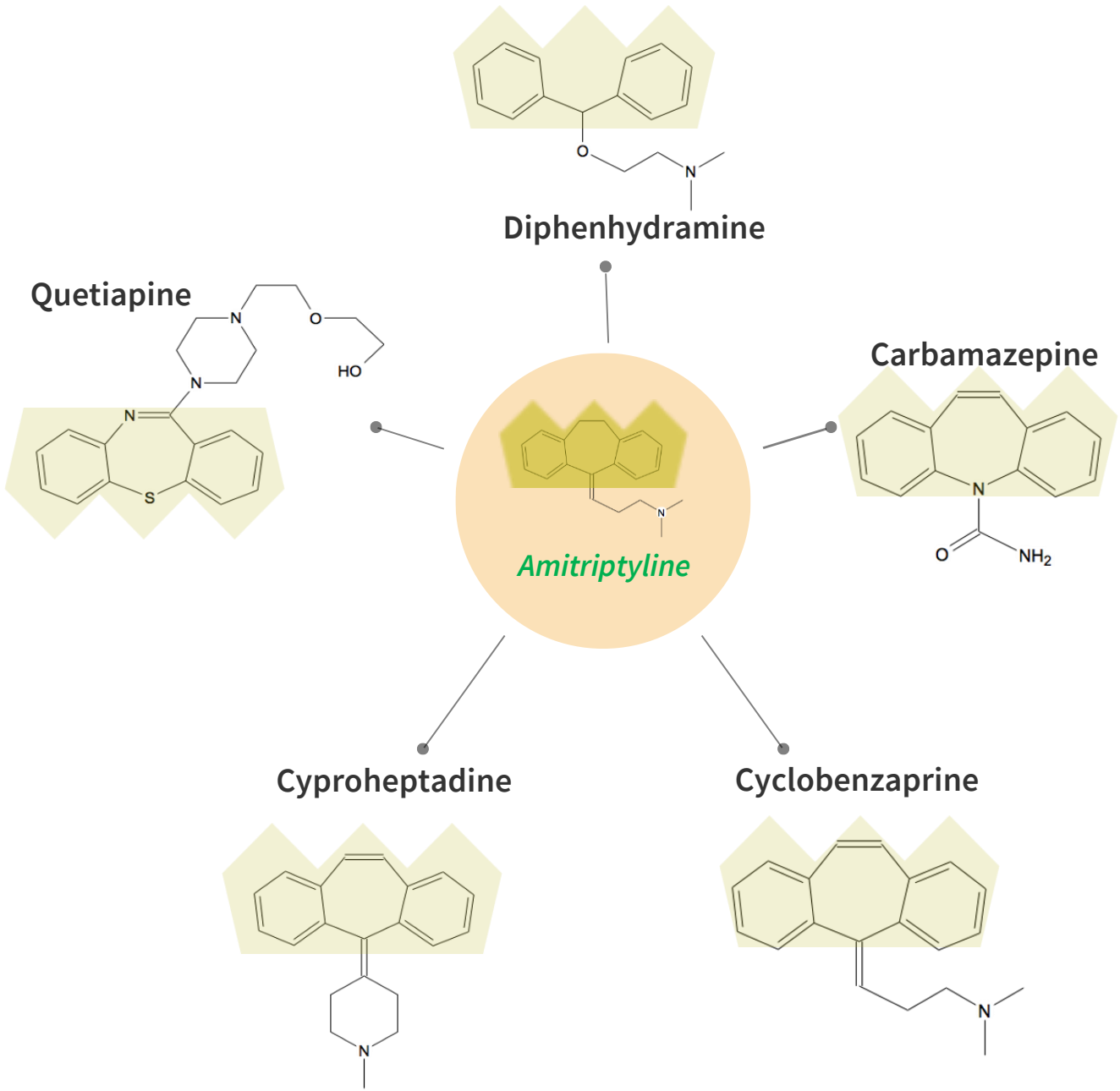
False Positives:



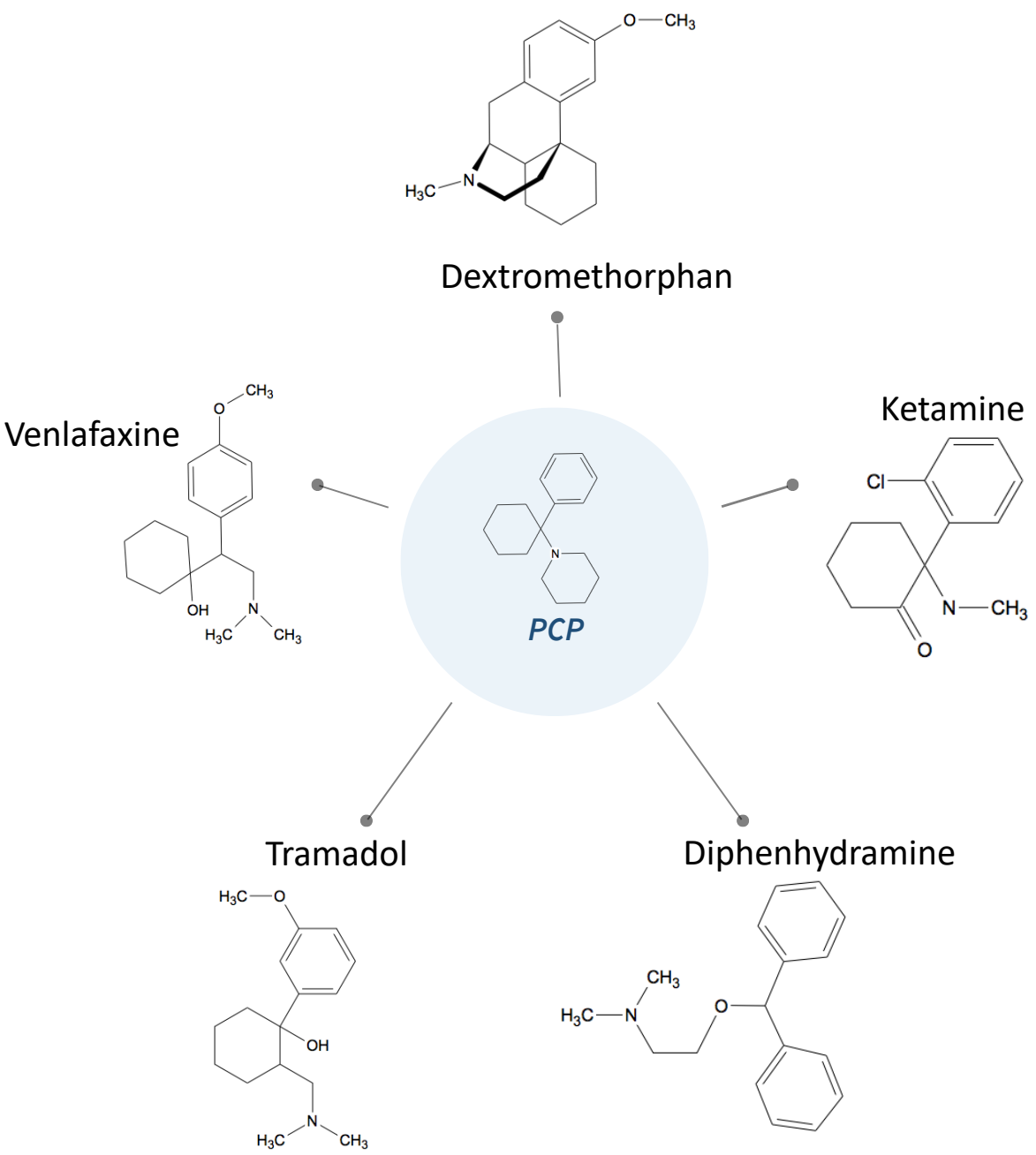
Amitriptyline (TCA)



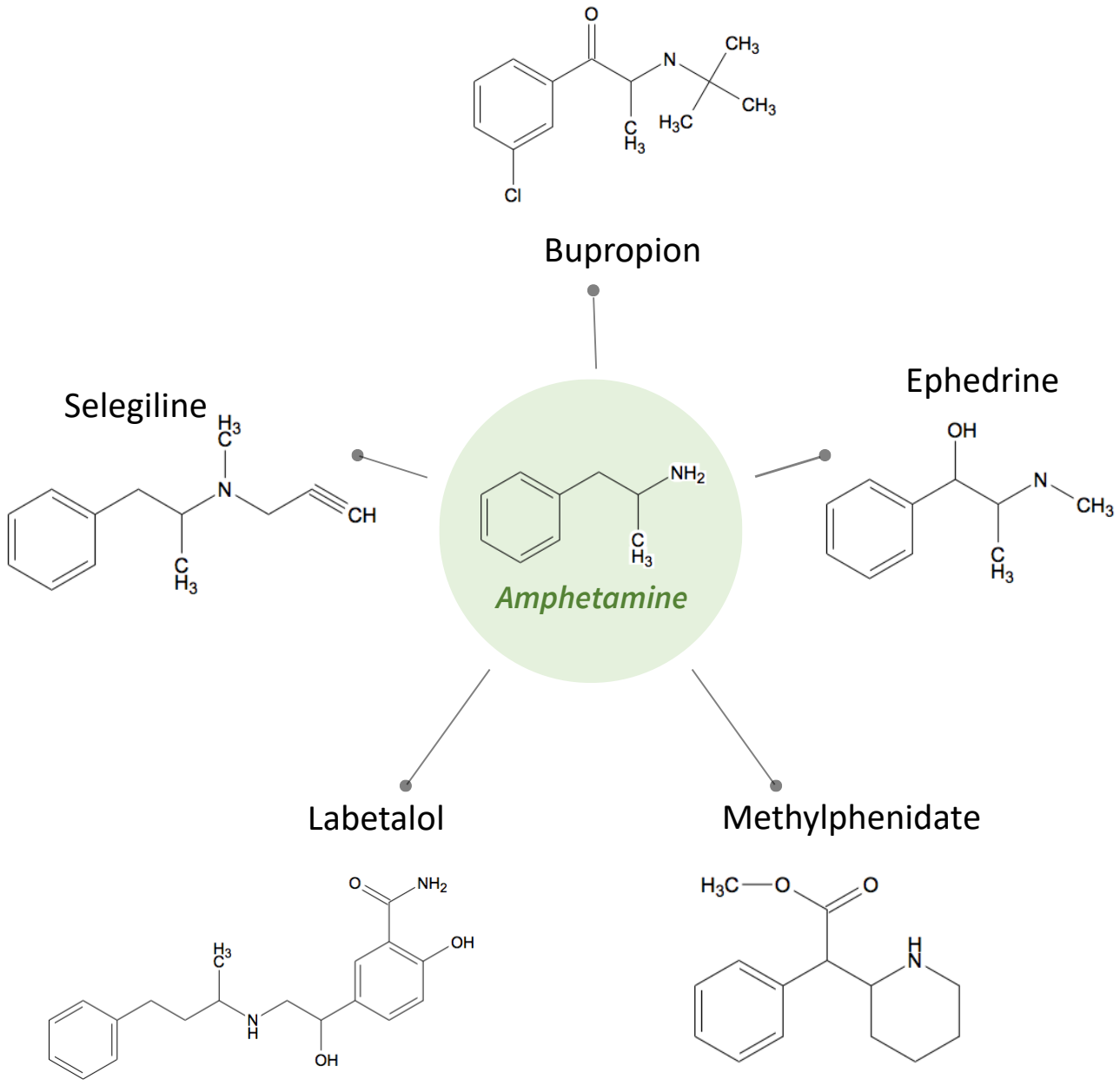
Cyclobenzaprine



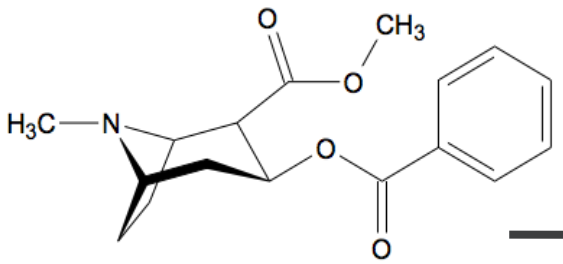
False Positives: TCA's



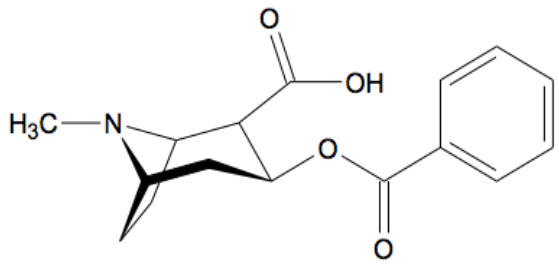
False Positives: PCP



False Positives:
Amphetamines



Cocaine ✓



Benzoylecgonine

False Positives:

Cocaine

False positives are uncommon with cocaine due to high accuracy and low cross reactivity

Urine Drug Screen…

Other limitations:

- False Negatives
- Won’t detect many newer agents

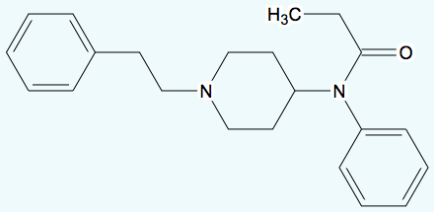
Drug	Time
Alcohol	7-12 h
Amphetamine/Methamphetamine	48 h
Barbiturate	
Short-acting	24 h
Long -acting	3 wk
Benzodiazepine	
Short-acting	3 d
Long -acting	30 d
Cocaine metabolites	2-4 d
Marijuana	
Single use	3 d
Long-term heavy use	> 30 d

Drug	Time
Opioids	
Codeine	48 h
Heroin	48 h
Hydromorphone	2-4 d
Methadone	3 d
Morphine	48-72 h
Oxycodone	2-4 d
Propoxyphene	6-48 h
Phencyclidine (PCP)	8 d

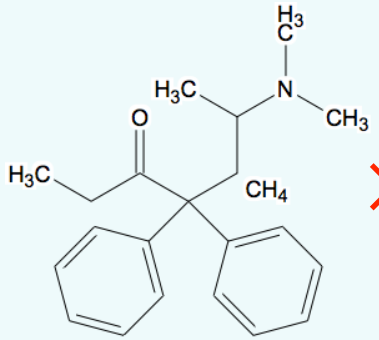
- Window of detection
  - If tested too early, might not trigger positive test
  - If too far out from exposure, no longer present in high enough of concentration to trigger positive test

Generally, most drugs become undetectable in the urine after about 72h

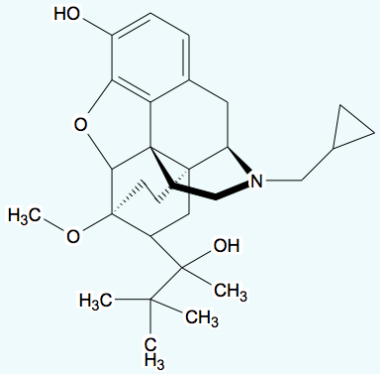
UDS Opioids



✗ Fentanyl

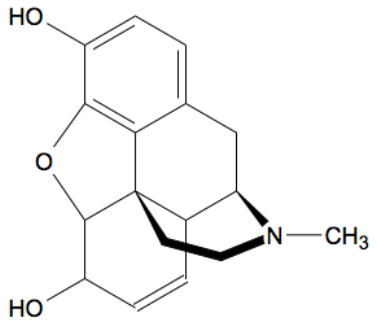


✗ Methadone



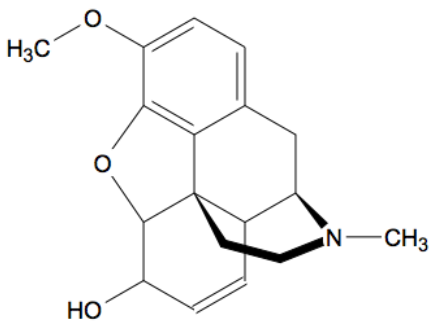
✗ Buprenorphine

False Negatives



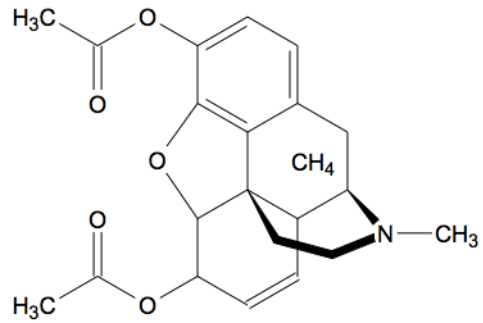
Morphine

Detected

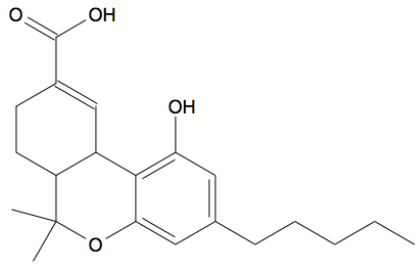


✓ Codeine

✓ Heroin

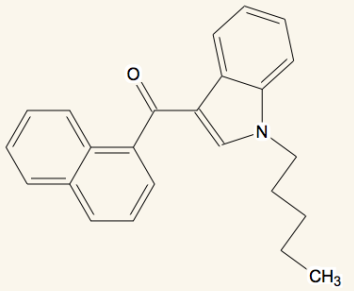


UDS False Negatives Cannabinoids

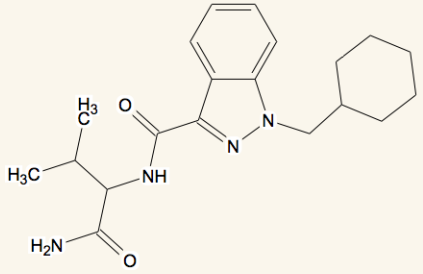


9-carboxy-THC

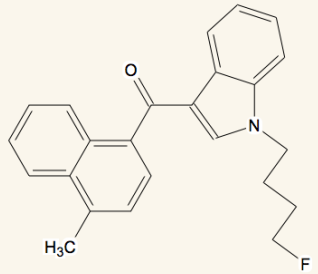
Synthetic cannabinoids will not show up



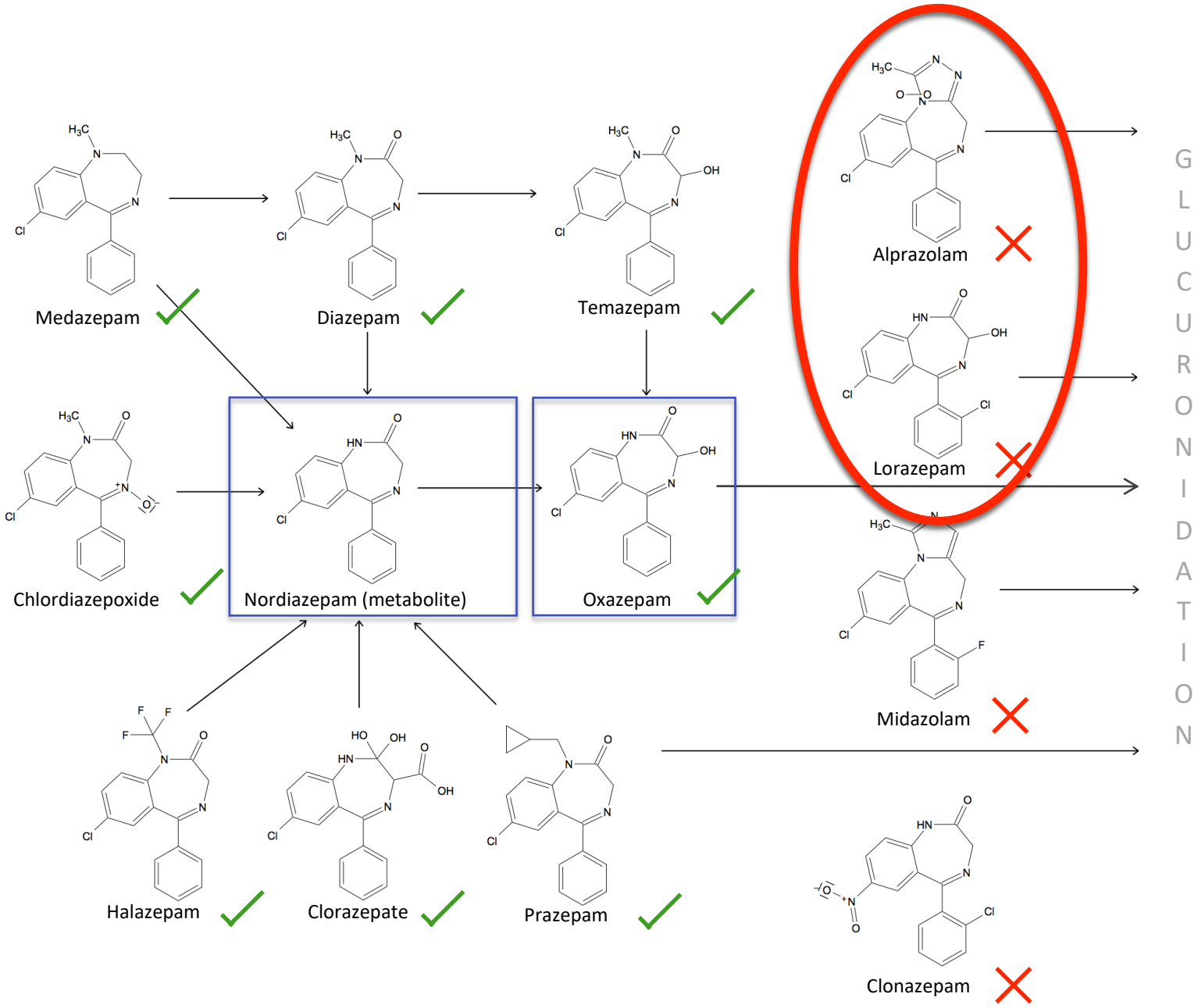
JWH-018 ✕



AB-CHMINACA ✕



MAM-2210 ✕



Alprazolam & lorazepam: commonly abused, but will not show up

UDS False Negatives Benzodiazepines

Drug	Immunoassay Target	False Positives	False Negatives
Amphetamines	D-amphetamine, D-methamphetamine	Amantadine, atomoxetine, bupropion, chloroquine, chlorpromazine, desipramine, doxepin, ephedrine, labetalol, metformin, phentermine, phenylephrine, promethazine, pseudoephedrine, ranitidine, selegiline, trazodone	MDA, MDMA, Most substituted cathinone derivatives, Most substituted phenethylamine derivatives
Barbiturates	Secobarbital	Ibuprofen, naproxen	Sodium Thiopental
Benzodiazepines	Nordiazepam, Oxazepam	Efavirenz, Ertraline, Oxaprozin,	Clonazepam, lorazepam, alprazolam, midazolam, flunitrazepam, Chlordiazepoxide
Cocaine	Cocaine, Benzoylecgonine	Coca tea, some forms of yerba mate	Fluconazole (However, this is with confirmatory testing)
LSD	LSD, 2-oxo-hydroxy-lsd	Amitriptyline, bupropion, buspirone, diltiazem, doxepin, ergonovine, fentanyl, fluoxetine, haloperidol, imipramine, labetalol, methylphenidate, metoclopramide, norfentanyl, prochlorperazine, risperidone, sertraline, trazodone, verapamil	N/A
Opioids	Morphine, Codeine	Dextromethorphan, imipramine, levofloxacin, naltrexone, ofloxacin, poppy seed containing foods, rifampin	Non-naturals (Hydrocodone, hydromorphone, oxycodone, fentanyl, tramadol, U-47700, methadone, buprenorphine)
	Oxycodone, Oxymorphone	N/A (Typically very specific to oxycodone & metabolites)	N/A
	Methadone, EDDP	Morphine, codeine, methadone, tramadol	N/A
	Buprenorphine, Norbuprenorphine	Diphenhydramine, doxylamine, quetiapine, tapentadol, verapamil	N/A
PCP		Dextromethorphan, diphenhydramine, ibuprofen, ketamine, lamotrigine, mdpv, O-desmethylvenlafaxine, thioridazine, tramadol, venlafaxine, zolpidem	N/A
THC	9-carboxy-thc	Some NSAIDs, efavirenz, promethazine, pantoprazole	Synthetic/Designer Cannabinoids
TCA's	Amitriptyline, Imipramine	Carbamazepine, cetirizine, cyclobenzaprine, cyproheptadine, diphenhydramine, hydroxyzine, quetiapine,	N/A

Table adapted from Urine Drug Screens in the Emergency Department: The Best Test May Be No Test at All, by Stellpflug, Samuel J. et al. Journal of Emergency Nursing, Volume 46, Issue 6, 923 - 931

Summary

Urine Drug Screens

- Inexpensive, quick results, low technical skill to operate, readily available
- Limitations: many FPs and FNs
- Not great at providing information regarding the length of time since last ingestion
- No information about overall duration of use
- No comment about state of intoxication when collected

Drug testing in general:

- Know what type of test you are ordering and interpreting
- Immuno-based tests: quick, inexpensive, but have many FP and FN results (low SN and SP)
- LC-MS has high SN and SP for urine drug detection, but takes longer and is more expensive
- Speak with the patient about the result to see if there is a medically acceptable explanation

Tox Consult! Dystonia vs NMS

Case

- 38 y.o. male, PMH psychosis +opioid use disorder
- CC: chest pain, back pain, lock jaw x1 day
- VS: Afebrile, HR 104, BP 141/86, SpO2 98%
- Diaphoretic, appeared uncomfortable
- Diffuse spinal tenderness
- Increased tonicity, spasms, neck stiffeness

DDX:

Dystonic reaction

- •Did not resolve with diphenhydramine
- •Never filled his risperidone prescription

Strychnine poisoning:

- •Rare contaminant in heroin
- •Convulsions with clear sensorium,
- •Sudden onset, quicker resolution

NMS:

- •Prescribed Risperidone but did not take it
- •No AMS, bradyreflexia, “lead-pipe” rigidity

Trismus due to orofacial infection

- •Wouldn’t explain diffuse body spasms

Tetanus:

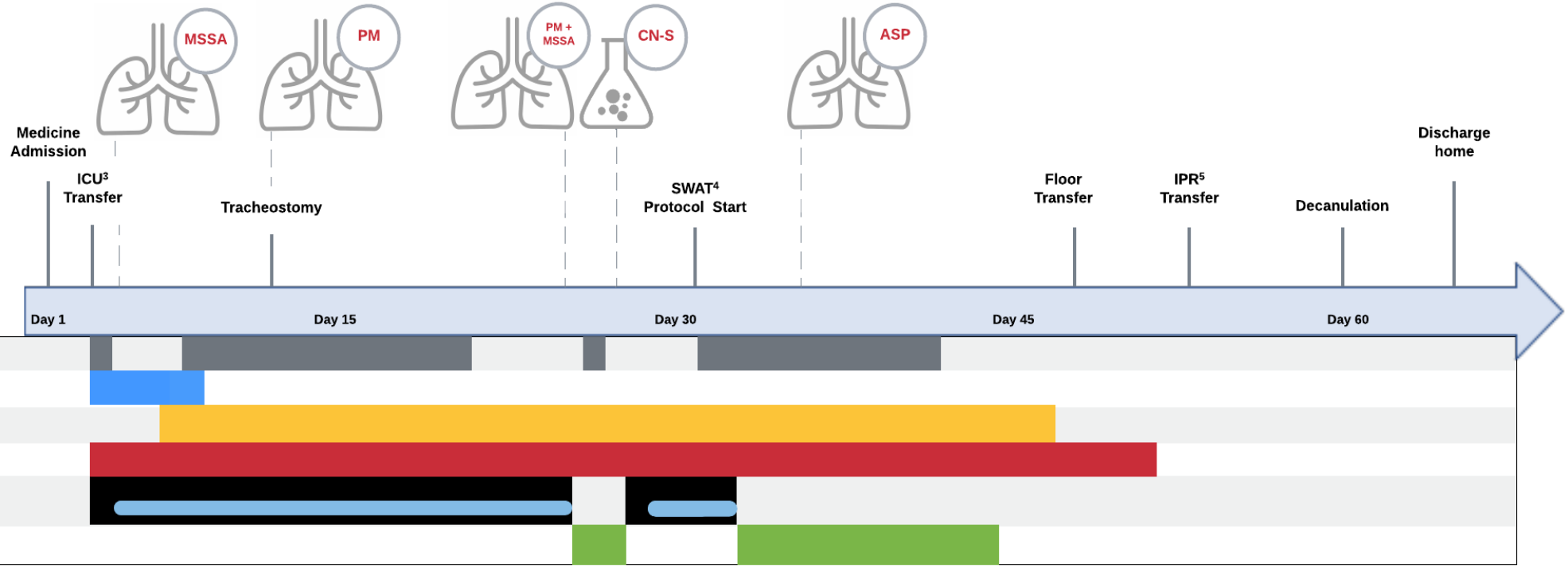
BLACK TAR HEROIN

Tetanus:

Clinical Hospitalization Course

LEGEND	
MSSA	MSSA[1] VAP[2]
PM	Proteus mirabilis VAP[2]
PM + MSSA	Proteus mirabilis & MSSA[1] VAP[2]
CN-S	Coagulase negative Staphylococcal bacteremia
ASP	Aspiration Pneumonia

[1]*Methicillin Sensitive Staphylococcus Aureus*
[2]*Ventilator Associated Pneumonia*
[3]*Intensive Care Unit*
[4]*Slow Wean After Tracheostomy*
[5]*Inpatient Rehabilitation*



Tox Consult! Seisure --> Asystole

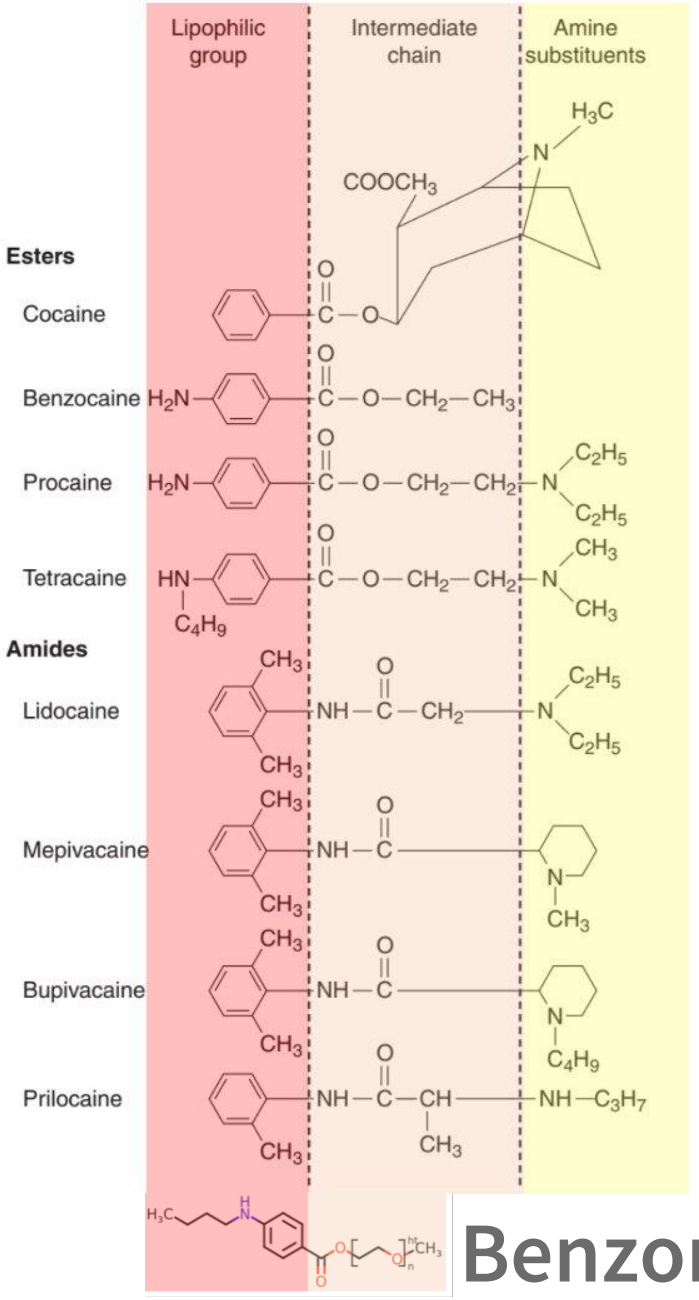
Case

- 10 month old male. Poison center call that patient was unresponsive with CPR in progress.

  Had a history of a recent eir infection and was started on amoxicillin.

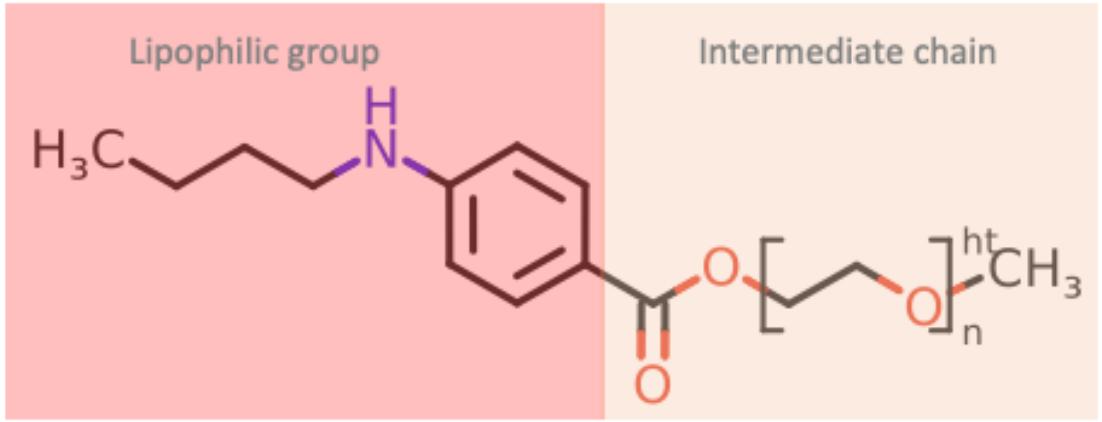
  Last seen normal playing at 9:20 AM. At 9:45 AM patient began drooling and foaming at the mouth, had a seizure, then went limp, and went into cardiac arrest. Mother called EMS and started CPR

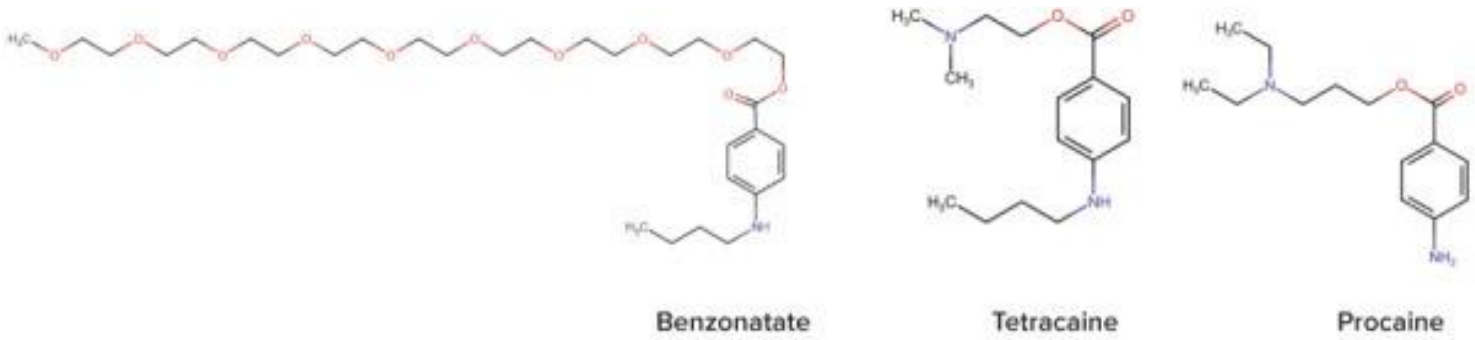
Little pills:



Benzonatate

Benzonatate (Tessalon®)

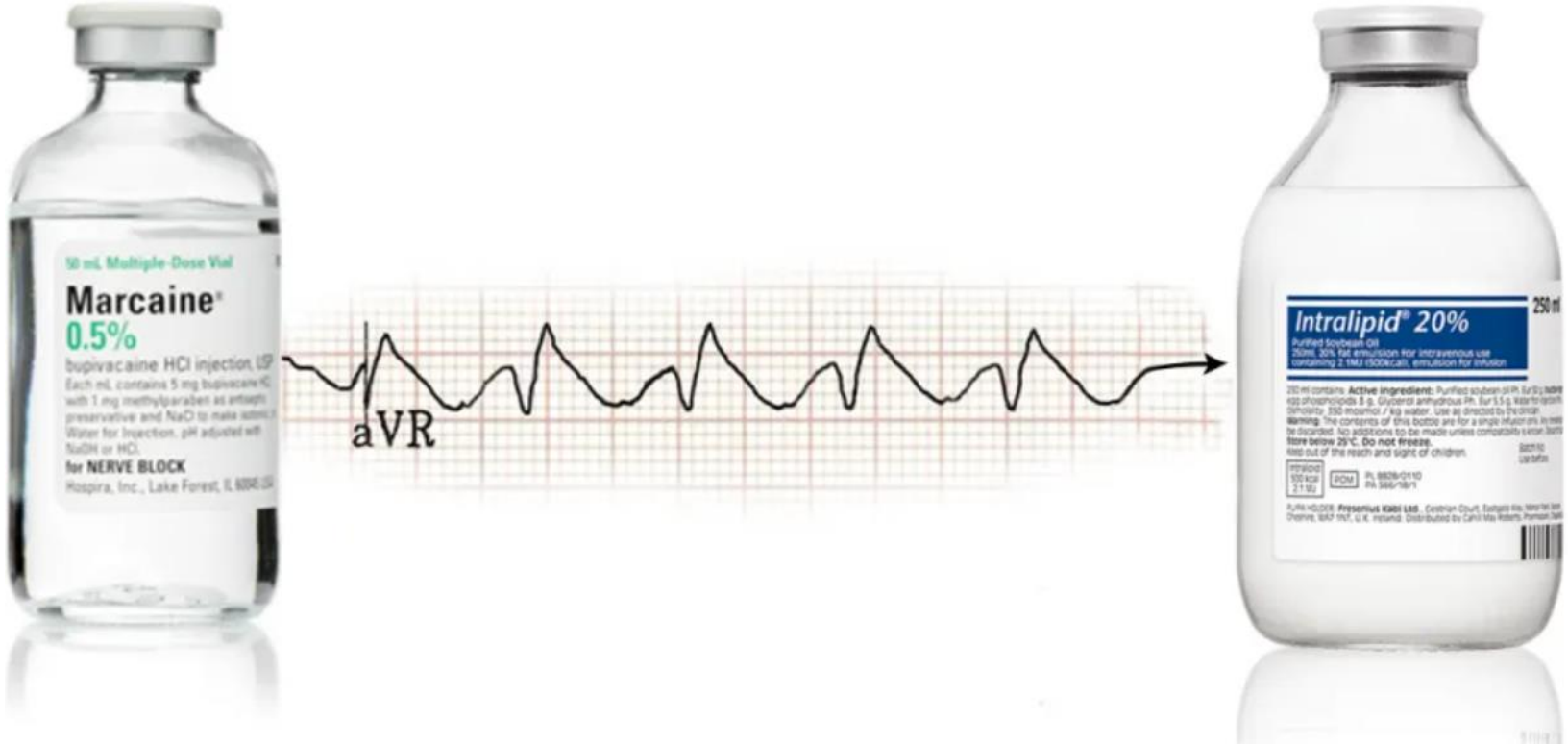




Benzonatate

Tetracaine

Procaine


50 mL Multiple-Dose Vial
Marcaine®
0.5%
bupivacaine HCl injection, USP
for NERVE BLOCK
Hospira, Inc., Lake Forest, IL
aVR
Intralipid® 20%
250 ml

Tox Consult! Bupropion Overdose

Wellbutrin SR/XL

Zyban

Contrave

Budeprion XL

FDA approved:

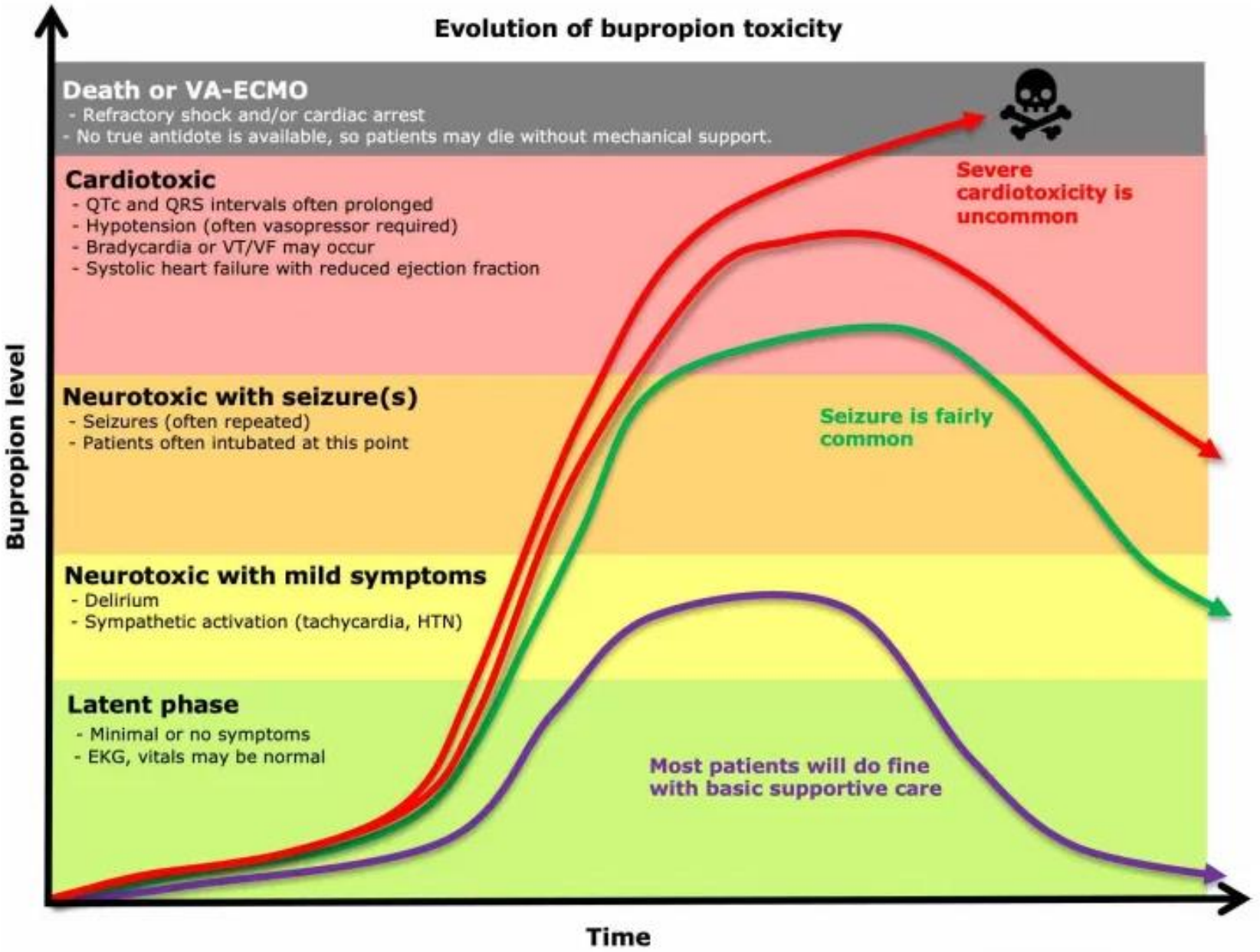
- MDD
- Seasonal Affective disorder
- Smoking Cessation (Zyban)
- Weight loss

Under investigation

- Stimulant use disorder
- Sexual dysfunction
- Bipolar disorder

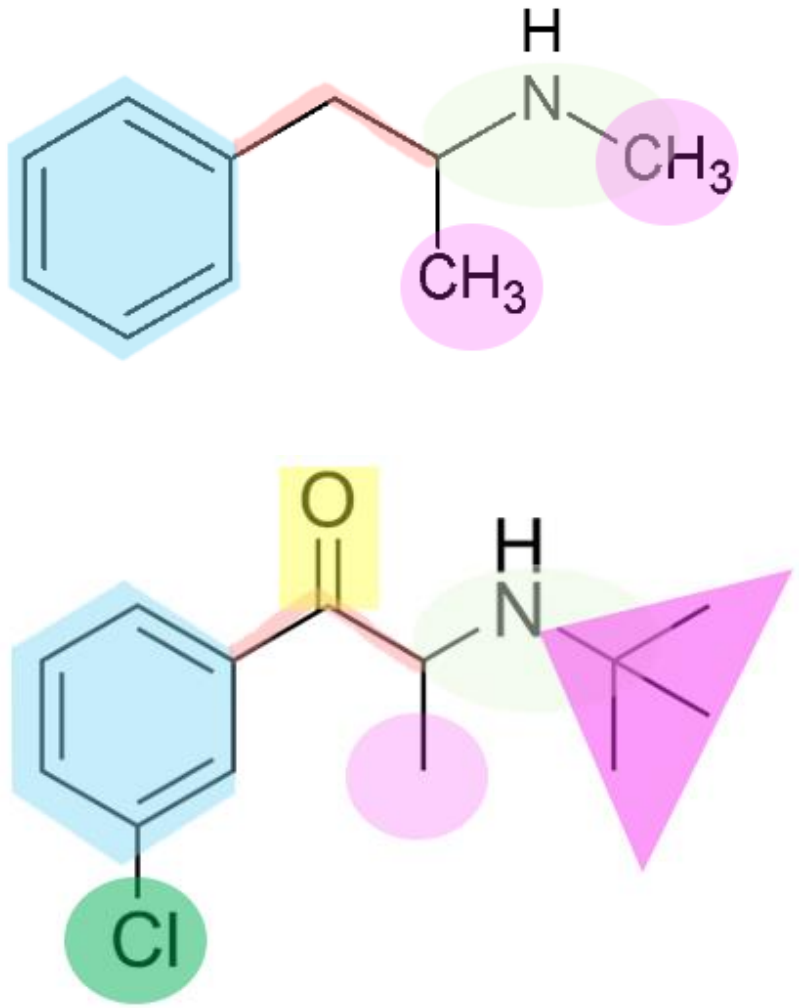
Bubropion

"ill-butrin"



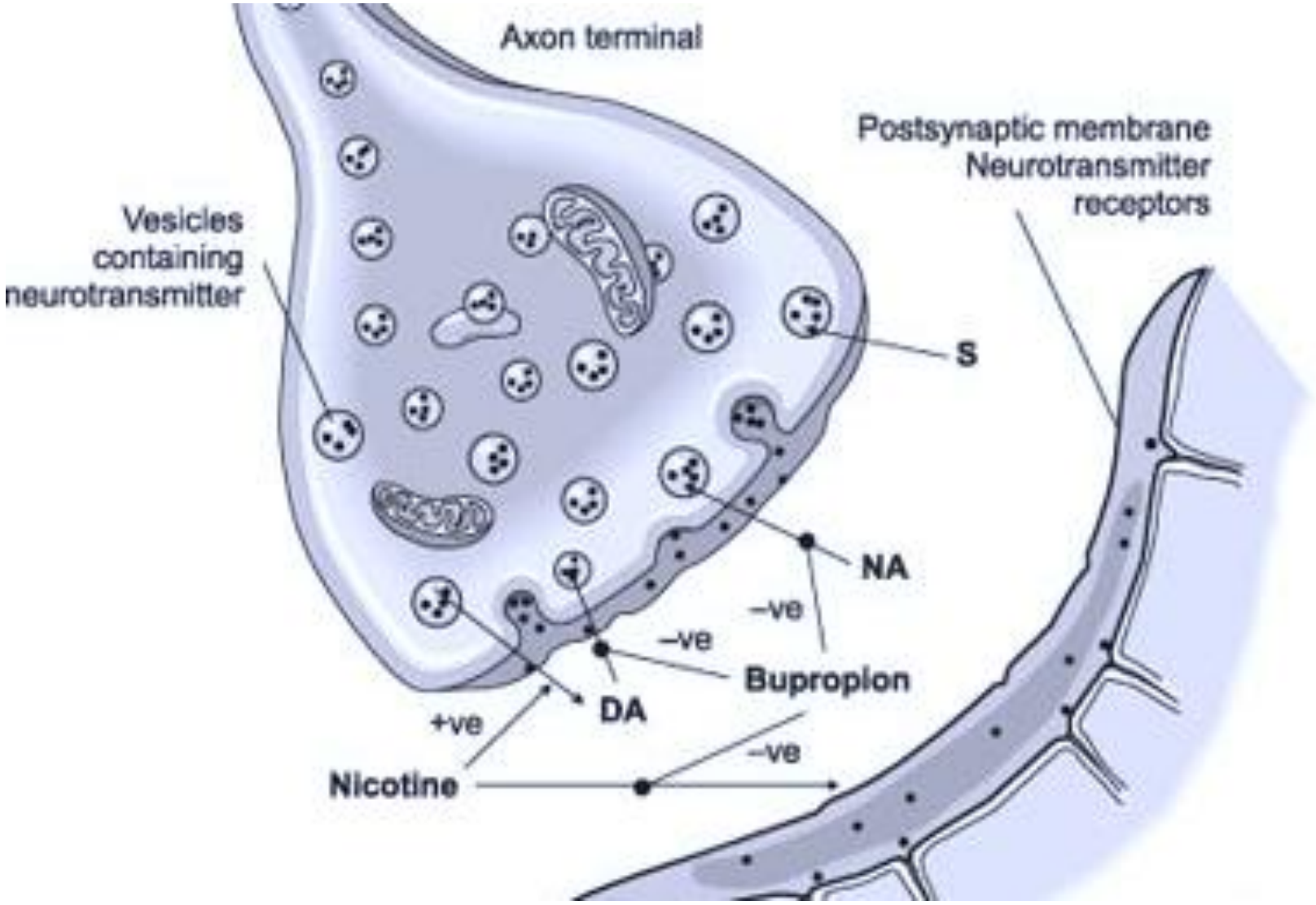
Stereotypical evolution of bupropion intoxication. This won't apply to every patient (for example, some patients may progress *directly* to seizures without developing mild neurologic symptoms).

-The Internet Book of Critical Care, by @PulmCrit


H
N
CH3
CH3
O
H
N
Cl

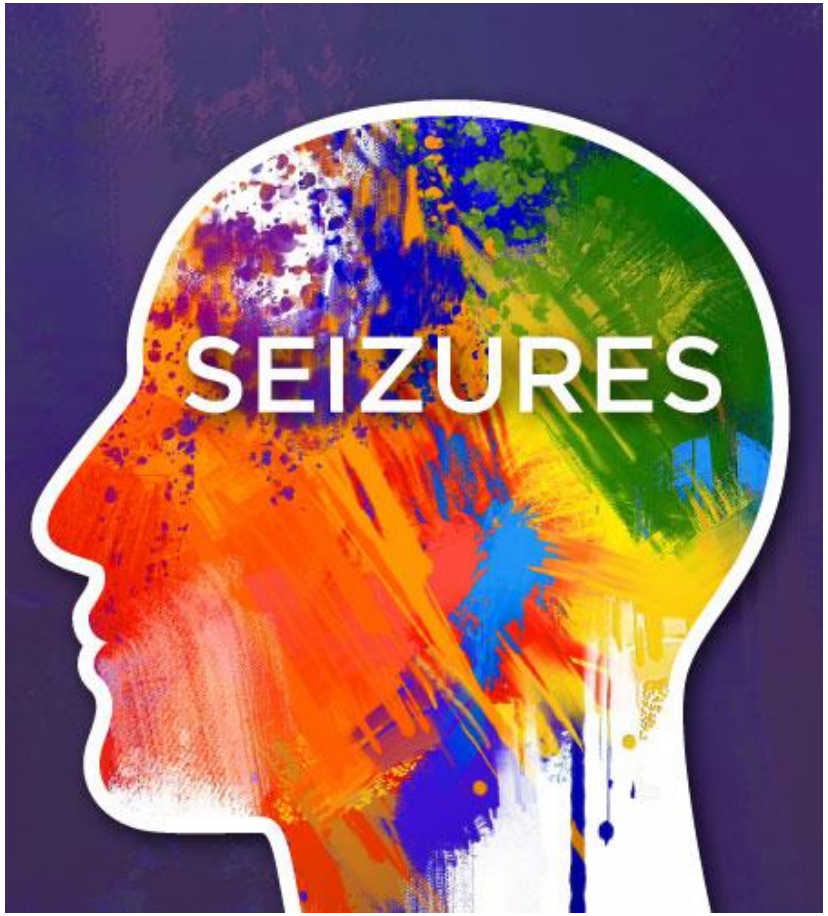
MECHANISM OF ACTION:

- DA and NE Re-uptake inhibition



Contraindications

1. Seizure disorder
2. Bulimia or anorexia
3. Discontinuation of Alcohol, BZD, Barbiturate, antiepileptic drug
4. MAOI use



Mechanism of Action:

- Nicotinic action: secondary

Nicotinic receptor antagonists as treatments for nicotine abuse

Peter A Crooks [1], Michael T Bardo [2], Linda P Dwoskin [3]

- Serotonin action: minimal

Antagonism by antidepressants of serotonin S1 and S2 receptors of normal human brain in vitro

T J Wander, A Nelson, H Okazaki, E Richelson

Pharmacokinetics

- Serum level peak: ~5 hours (XL)
- Metabolism: CYP 2B6
- Active metabolites: hydroxybupropion, erythrohydrobupropion, threohydobupropion
- Half life: ~24 hours

Predicting Toxicity by Dose?

- Not well defined
- Therapeutic range: 100-450 mg/day
- ~3 gram threshold? Seizures
- ~10 gram threshold? Cardiotoxicity

Delayed Absorption

- Minimal initial symptoms
- Tachycardia very common
- XL form: toxicity possible 24 hours out
- Observation period?

Bupropion associated seizures following acute overdose: who develops late seizures

Steve Offerman [1], Jasmin Gosen [2], Stephen H Thomas [3] [4], Angie Padilla-Jones [5], Anne-Michelle Ruha [5] [6], Michael Levine [7]

Neurotoxicity

- Delirium
- Sympathomimetic
- Myoclonic Jerks
- Seizures

Seizures

Progression of toxicity

Onset 30 min- 24 hours

Isolated vs Multiple

Status Epilepticus

Cause of Death in some cases

SO many publications on seizures and bupropion

Bupropion With Clozapine: Case Reports of Seizure After Coadministration

Allison Schmitz [1], Brandon Botner [1], Morris Hund [2]

New-Onset Seizure in Patient Medicated With Bupropion for Smoking Cessation: A Case Report

Donna Saffaei [1], Shannon Lovett [2], Megan A Rech [3]

Bupropion overdose and seizure

A B Storrow [1]

Seizure associated with bupropion and guanfacine

L B Namerow

Cardiotoxicity

- sympathomimetic effect
- **Tachycardia**
- **QTc and QRS prolongation**
- **Hypotension/ Brady/ VT or VF**
- **Refractory Shock**
- **Cardiac arrest**

QRS Prolongation

Case Reports > J Emerg Med. 2005 Oct;29(3):299-305. doi: 10.1016/j.jemermed.2005.01.027.

Intraventricular conduction delay after bupropion overdose

Steven C Curry [1], John S Kashani, Frank LoVecchio, William Holubek

---

Case Reports > Am J Ther. Mar-Apr 2009;16(2):193-6. doi: 10.1097/MJT.0b013e3180a5bd83.

Bupropion-associated QRS prolongation unresponsive to sodium bicarbonate therapy

Brandon K Wills [1], Michele Zell-Kanter, Steven E Aks

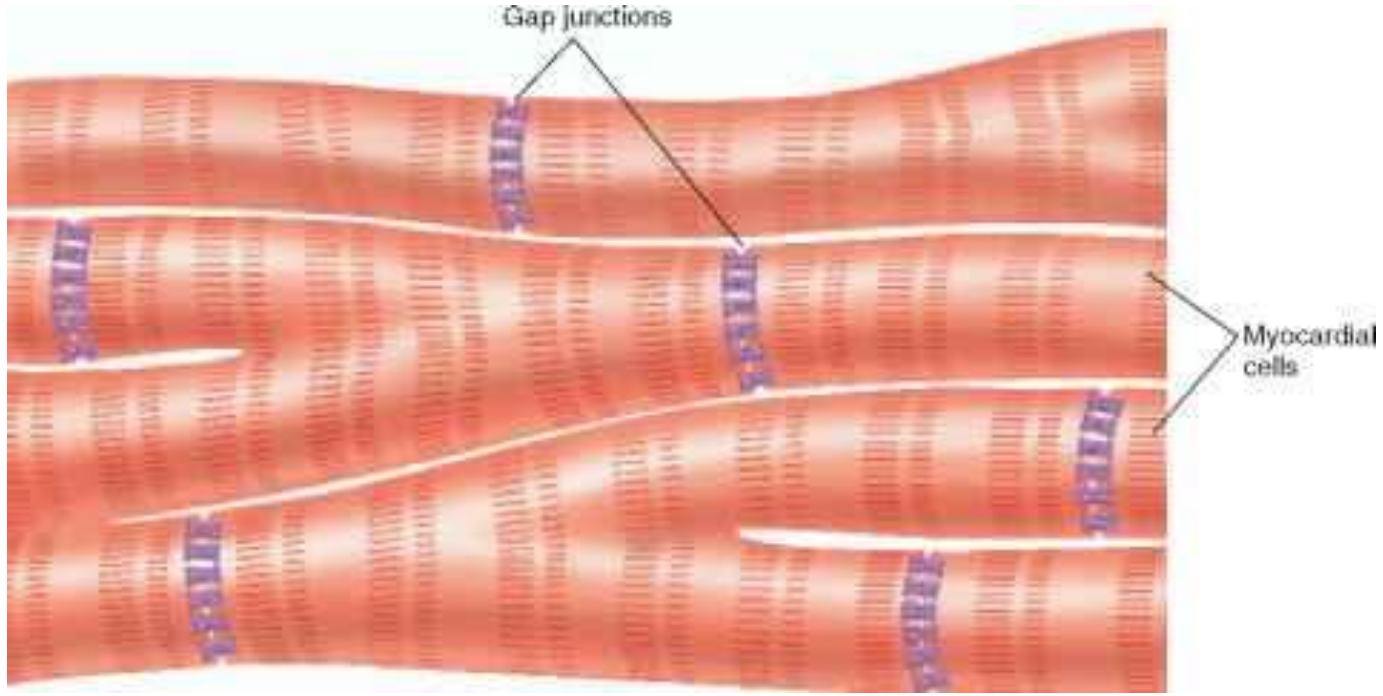
Comparative Study > Fundam Clin Pharmacol. 2012 Oct;26(5):599-608.
doi: 10.1111/j.1472-8206.2011.00953.x. Epub 2011 May 30.

QRS widening and QT prolongation under bupropion: a unique cardiac electrophysiological profile

Bertrand Caillier [1], Sylvie Pilote, Annie Castonguay, Dany Patoine, Verlaine Ménard-Desrosiers, Patrick Vigneault, Raymond Hreiche, Jacques Turgeon, Pascal Daleau, Yves De Koninck, Chantale Simard, Benoit Drolet

Gap Junctions

- Found in all cells
- Very important in heart



Decontamination:

CONTROVERSIAL:

Activated Charcoal

Whole Bowel Irrigation

Gastric Lavage????

Activated Charcoal

Bupropion binds to AC

When to give?

- After intubation
- Early without AMS(?)

Whole Bowel Irrigation

Also controversial

Large XL formulations

When to give?

- **After intubation**
- ~~**Early without AMS**~~

GASTRIC LAVAGE?

Treatment:
Neurotoxicity

Agitation

- BZD

Seizures

- BZD (Early use?)
- Phenobarb
- Propofol
- NO phenytoin
- EEG

Treatment: Cardiotoxity

Tachycardia

- Suportive

QRS Prolongation

- Can try NaBicarb

Hypotension

- Pressors (Levo)

Cardiogenic Shock/Arrest

- Lipid emulsion/ Intralipid?
- VA ECMO

Note on Lipids

Controversial (again)

Case Report Evidence only

Maybe as a bridge to ECMO

Clin Toxicol (Phila). 2018 Jan;56(1):51-54. doi: 10.1080/15563650.2017.1337909. Epub 2017 Jun 23.

Management of severe bupropion poisoning with intravenous lipid emulsion

Neeraj Chhabra [1], Carol DesLauriers [2], Michael Wahl [2], Sean M Bryant [1] [2]

Summary of Treatment Recommendations

Supportive care for most

Decontamination→ AC (airway protected)

- **Peds: 1 gm/kg; Adult: 50-100 gm**

Tachycardia→ fluids

Seizures→ BZD

QRS prolongation→ Try NaBicarb

- **Peds: 1-2 mEq/kg; Adult: 2-3 amps**

CV Instability: Intralipid vs ECMO

If that's not enough....

World J Emerg Med. 2018;9(1):67-69. doi: 10.5847/wjem.j.1920-8642.2018.01.011.

A Lazarus effect: A case report of Bupropion overdose mimicking brain death

Douglas Stranges [1], Alan Lucerna [2], James Espinosa [2], Neveen Malik [3], Marc Mongeau [4], Kelly Schiers [3], Syed Omar Shah [5], Joan Wiley [3], Philip Willsie [3]

Affiliations + expand

PMID: 29290899 PMCID: PMC5717380 DOI: 10.5847/wjem.j.1920-8642.2018.01.011

Free PMC article

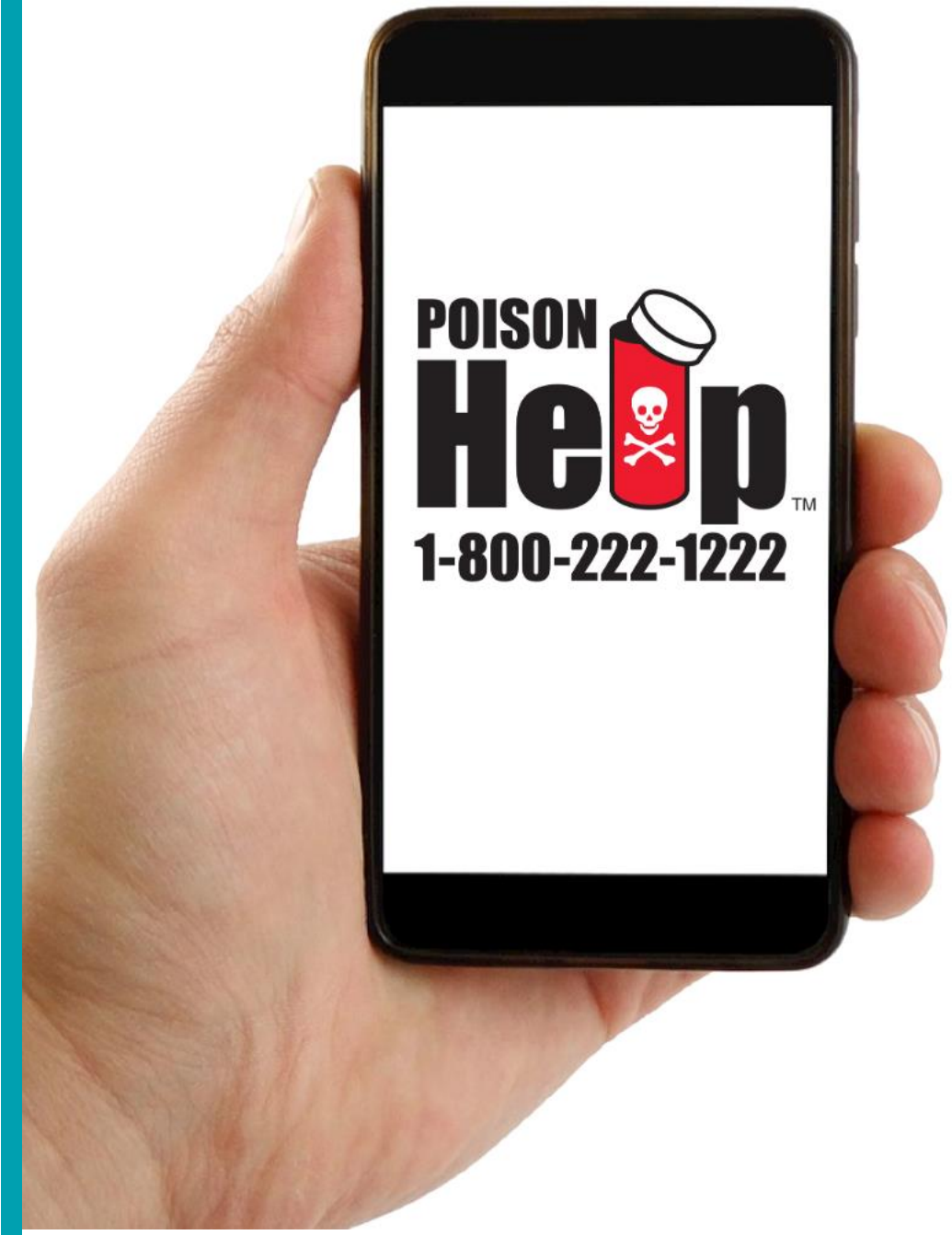
Bupropion commonly causes seizures in overdose.

Severe: QRS prolongation + shock sometimes refractory to treatment.

Decon is controversial, but reasonable in select circumstances.

There is NO antidote, supportive care is mainstay.

Bupropion is capable of *mimicking* brain death, days to metabolize.



Give your friendly local poison center a call.

THEY'RE ALWAYS AVAILABLE TO HELP

Questions?

Notes:

References:

- Riccoboni S, Darracq M. Does the U Stand for Useless? The Urine Drug Screen and Emergency Department Psychiatric Patients. J Emerg Med. 2018;54(4):500-506. https://www.ncbi.nlm.nih.gov/pubmed/29500048.
- Belson MG, Simon HK. Utility of comprehensive toxicologic screens in children. Am J Emerg Med. 1999;17(3):221-224. https://doi.org/ 10.1016/s0735-6757(99)90109-2
- Sugarman JM, Rodgers GC, Paul RI. Utility of toxicology screening in a pediatric emergency department. Pediatr Emerg Care. 1997;13(3):194- 197. https://doi.org/10.1097/00006565-199706000-00005
- Karen E Moeller Pharmd B, Kelly C Lee Pharmd B, Julie C Kissack Pharmd B. Urine Drug Screening: Practical Guide for Clinicians. Mayo Clinic Proceedings. Mayo Foundation for Medical Education and Research; 2007 Dec 18;83(1):66–76.
- Karen E Moeller Pharmd B, Kelly C Lee Pharmd B, Julie C Kissack Pharmd B. Urine Drug Screening: Practical Guide for Clinicians. Mayo Clinic Proceedings. Mayo Foundation for Medical Education and Research; 2007 Dec 18;83(1):66–76.
- Valentine JL, Middleton R, Sparks C. Identification of urinary benzodiazepines and their metabolites: comparison of automated HPLC and GC-MS after immunoassay screening of clinical specimens. J Anal Toxicol. 1996 Oct;20(6):416–24.
- Tyndall JA, Gerona R, De Portu G, Trecki J, Elie M-C, Lucas J, et al. An outbreak of acute delirium from exposure to the synthetic cannabinoid AB-CHMINACA. Clinical Toxicology. 2015 Oct 28;53(10):950–6.
- Waugh J, Najafi J, Hawkins L, Hill SL, Eddleston M, Vale JA, et al. Epidemiology and clinical features of toxicity following recreational use of synthetic cannabinoid receptor agonists: a report from the United Kingdom National Poisons Information Service. Clinical Toxicology. 2016 Apr 6;54(6):512–8.
- Reichman OS, Otto RA. Effect of Intranasal Cocaine on the Urine Drug Screen for Benzoylecgonine. *Otolaryngol Head Neck Surg*. 1992;106(3):223-225.
- Pitt JJ. Principles and applications of liquid chromatography-mass spectrometry in clinical biochemistry. Clin Biochem Rev. 2009 Feb;30(1):19–34.
- Domanski K, Kleinschmidt KC, Schulte JM, Fleming S, Frazee C, Menendez A, et al. Two cases of intoxication with new synthetic opioid, U-47700. Clinical Toxicology. 2016 Jul 19;:1–5.

Notes:

References:

- "Bupropion (Wellbutrin)". eMedExpert.com. 31 March 2008. Retrieved 20 August 2013.
- Berigan TR. The Many Uses of Bupropion and Bupropion Sustained Release (SR) in Adults. Prim Care Companion J Clin Psychiatry. 2002 Feb;4(1):30-32. doi: 10.4088/pcc.v04n0110a. PMID: 15014734; PMCID: PMC314381.
- "Bupropion HYDROCHLORIDE Extended-Release Tablets, USP (XL)." Package insert. Sun Pharmaceuticals. Goregaon, Mumbai. Accessed April 10, 2021.
- Tox & Hound. Tox & Hound – Illbutrin. *EMCrit Blog*. Published on April 16, 2018. Accessed on April 10th 2021. Available at [https://emcrit.org/toxhound/illbutrin/].
- Internet book of critical care (IBCC). Bupropion intoxication. Published Nov 14, 2019. Accessed on April 10, 2021. Available at [https://emcrit.org/ibcc/bupropion/].
- Ascher JA, Cole JO, Colin JN, Feighner JP, Ferris RM, Fibiger HC, Golden RN, Martin P, Potter WZ, Richelson E, et al. Bupropion: a review of its mechanism of antidepressant activity. J Clin Psychiatry. 1995 Sep;56(9):395-401. PMID: 7665537.
- Wander TJ, Nelson A, Okazaki H, Richelson E. Antagonism by antidepressants of serotonin S1 and S2 receptors of normal human brain in vitro. Eur J Pharmacol. 1986 Dec 16;132(2-3):115-21. doi: 10.1016/0014-2999(86)90596-0. PMID: 3816971.

- "Bupropion (Wellbutrin)". eMedExpert.com. 31 March 2008. Retrieved 20 August 2013.
- Berigan TR. The Many Uses of Bupropion and Bupropion Sustained Release (SR) in Adults. Prim Care Companion J Clin Psychiatry. 2002 Feb;4(1):30-32. doi: 10.4088/pcc.v04n0110a. PMID: 15014734; PMCID: PMC314381.
- "Bupropion HYDROCHLORIDE Extended-Release Tablets, USP (XL)." Package insert. Sun Pharmaceuticals. Goregaon, Mumbai. Accessed April 10, 2021.
- Tox & Hound. Tox & Hound – Illbutrin. *EMCrit Blog*. Published on April 16, 2018. Accessed on April 10th 2021. Available at [https://emcrit.org/toxhound/illbutrin/].
- Internet book of critical care (IBCC). Bupropion intoxication. Published Nov 14, 2019. Accessed on April 10, 2021. Available at [https://emcrit.org/ibcc/bupropion/].
- Ascher JA, Cole JO, Colin JN, Feighner JP, Ferris RM, Fibiger HC, Golden RN, Martin P, Potter WZ, Richelson E, et al. Bupropion: a review of its mechanism of antidepressant activity. J Clin Psychiatry. 1995 Sep;56(9):395-401. PMID: 7665537.
- Wander TJ, Nelson A, Okazaki H, Richelson E. Antagonism by antidepressants of serotonin S1 and S2 receptors of normal human brain in vitro. Eur J Pharmacol. 1986 Dec 16;132(2-3):115-21. doi: 10.1016/0014-2999(86)90596-0. PMID: 3816971.

Notes:

Additional Resources:

Tox and Hound – U(ds) and I

- *https://emcrit.org/toxhound/uds-and-i/*

A Test of Limitations - Urine Drug Screens

- *http://www.tamingthesru.com/blog/diagnostics/urine-drug-screens*

TOXCard: Urine Drug Screens

- *http://www.emdocs.net/toxcard-urine-drug-screens/*

Clinical Policy: Critical Issues in the Diagnosis and Management of the Adult Psychiatric Patient in the Emergency Department from *Annals of Emergency Medicine*

- *https://www.annemergmed.com/article/S0196-0644(05)01789-0/fulltext*