

Emerging Drugs of Abuse

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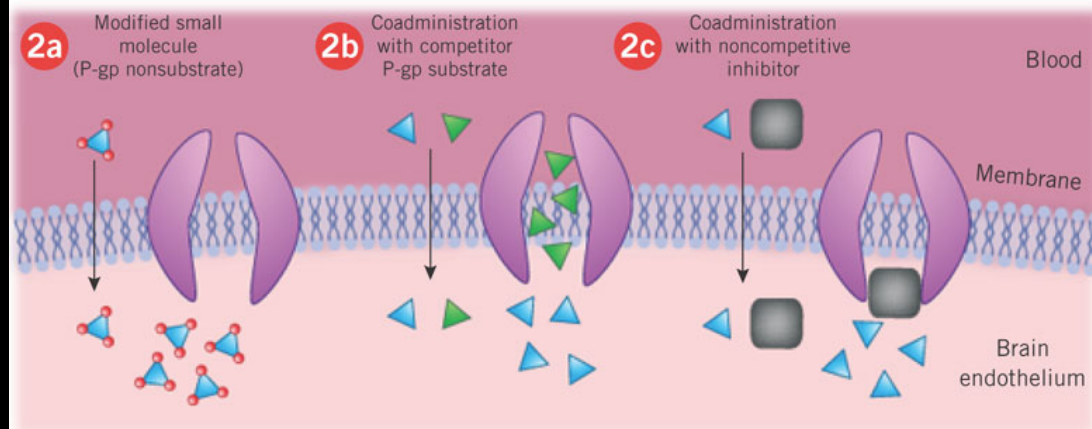
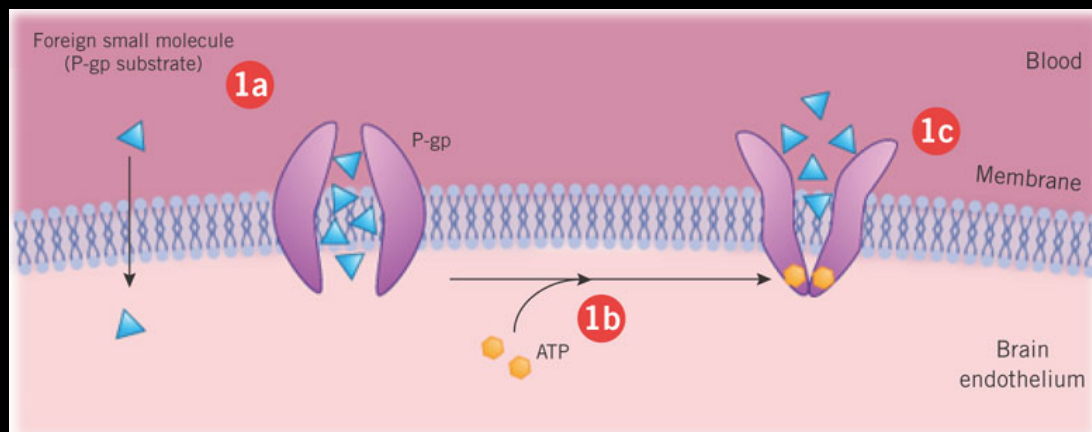
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Loperamide: An Emerging Opioid Substitute

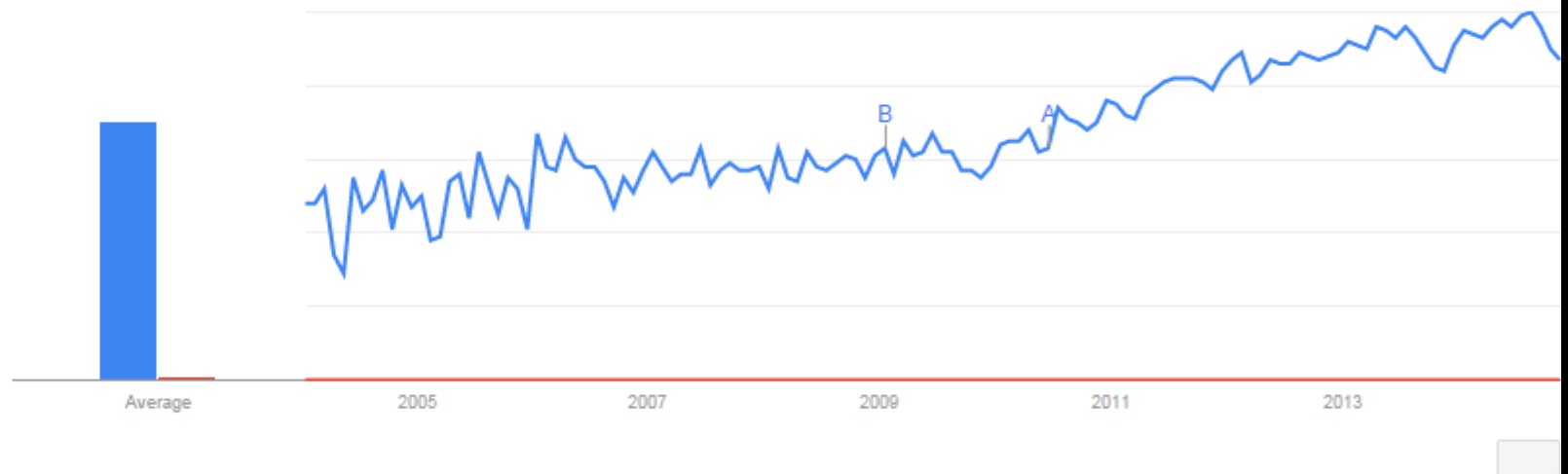
Loperamide

- Inexpensive, widely available
- Peripheral mu-opioid receptor agonist
- Therapeutic doses:
 - No CNS penetration due to P-glycoprotein
- Supratherapeutic doses/with P-Gp inhibitor
 - CNS penetration
 - Euphoria described with users



Interest over time

☐ ☐ News headlines ☐ ☐ Forecast



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CRITICAL CARE

Cardiac conduction disturbance after loperamide abuse

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Our Observations

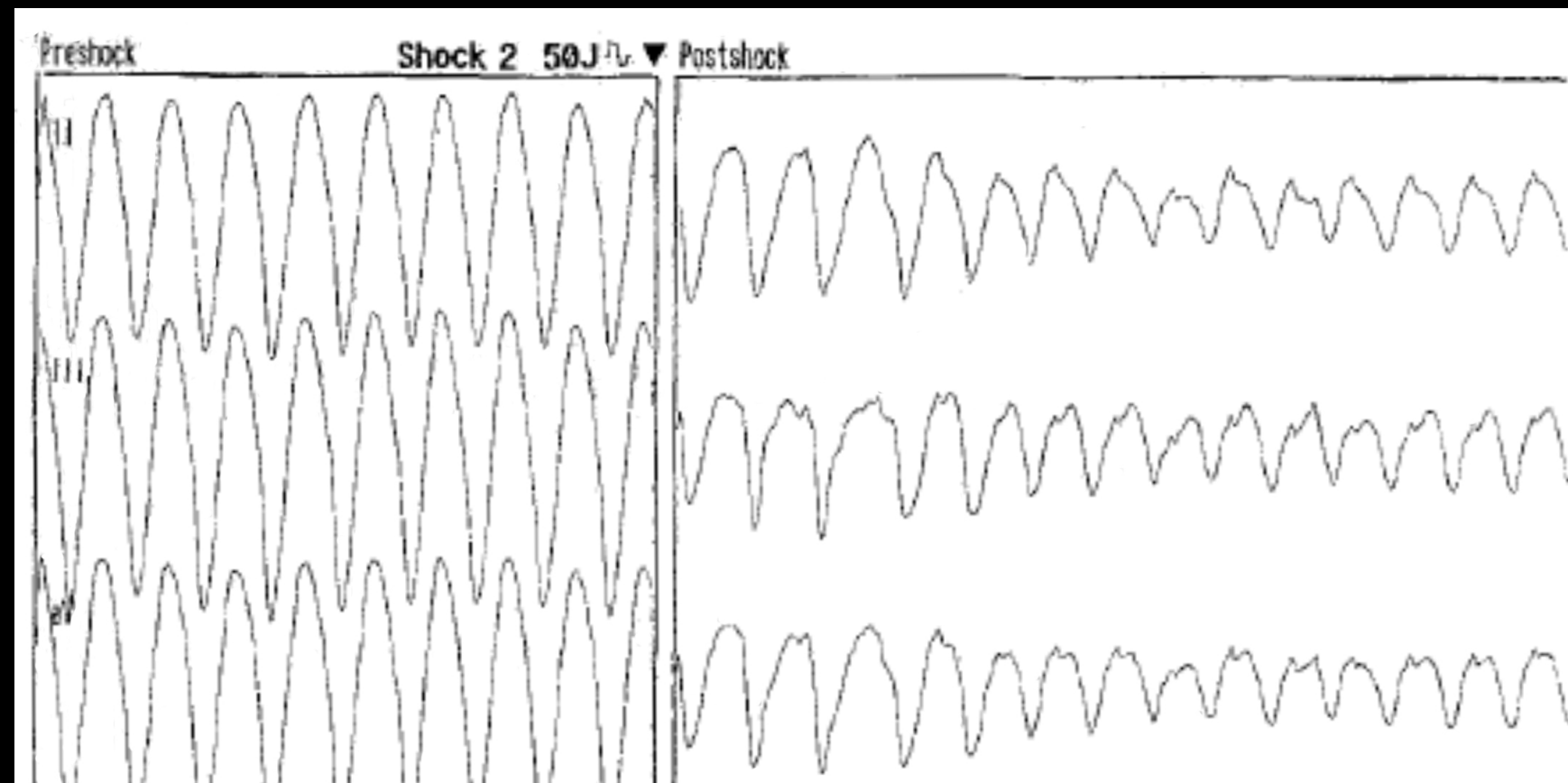
- Multiple patients with history of loperamide abuse
- Describe anywhere from 200-700 tablets ingested per day
- None used concurrent P-gp inhibitors
- 2 had severe cardiac toxicity
 - 1 patient has had at least 5 episodes of cardiac arrest

Case Series

- **Patient 1:**
- 43 year old female presented to the ED with syncope.
- On arrival to the ED, her initial ECG showed a sinus rhythm with a QRS complex duration of 130 milliseconds and QTc interval of 684 milliseconds with frequent PVCs. She rapidly deteriorated and had recurrent episodes of PMVT/ Torsades de Pointes (TdP). She required at least 15 defibrillations.
- She was awake and able to communicate between the arrhythmias and provide information. She reported that her use of loperamide had escalated to 140 tablets of the 2 mg tablets (280 mg) daily.
- Transvenous pacemaker with overdrive pacing was the only effective therapy for suppressing ventricular arrhythmias.
- The transvenous pacer was continued until hospital day (HD) 3.

Preshock

Shock 2 50J ∇ Postshock



- **Patient 2a:**
- 28 yo male transferred to our facility with recurrent wide complex tachycardia and collapse.
- Past medical history included Crohn's disease and substance abuse.
- He had a similar episode one year prior although at that time the etiology remained unclear.
- Medications: amitriptyline and loperamide; He reported that his use of loperamide had escalated to more than 396 tablets of the 2 mg tablets (792 mg) daily.

- Transvenous pacemaker with overdrive pacing was effective at suppressing ventricular arrhythmias.
- The transvenous pacer was continued for 2 days and isoproterenol infusion was subsequently started and continued for 5 additional days.
- His QTc remained greater than 500 msec until HD 10. Follow up ECG one month later off loperamide showed a sinus rhythm with QRS of 102 ms and QT/QTc of 360/435 ms.
- 5 hours post-presentation blood: Loperamide : 130 ng/mL; Amitriptyline 100 ng/ mL; Nortriptyline 82 ng/mL (therapeutic, total TCA: 100-250 ng/mL); Quinine negative

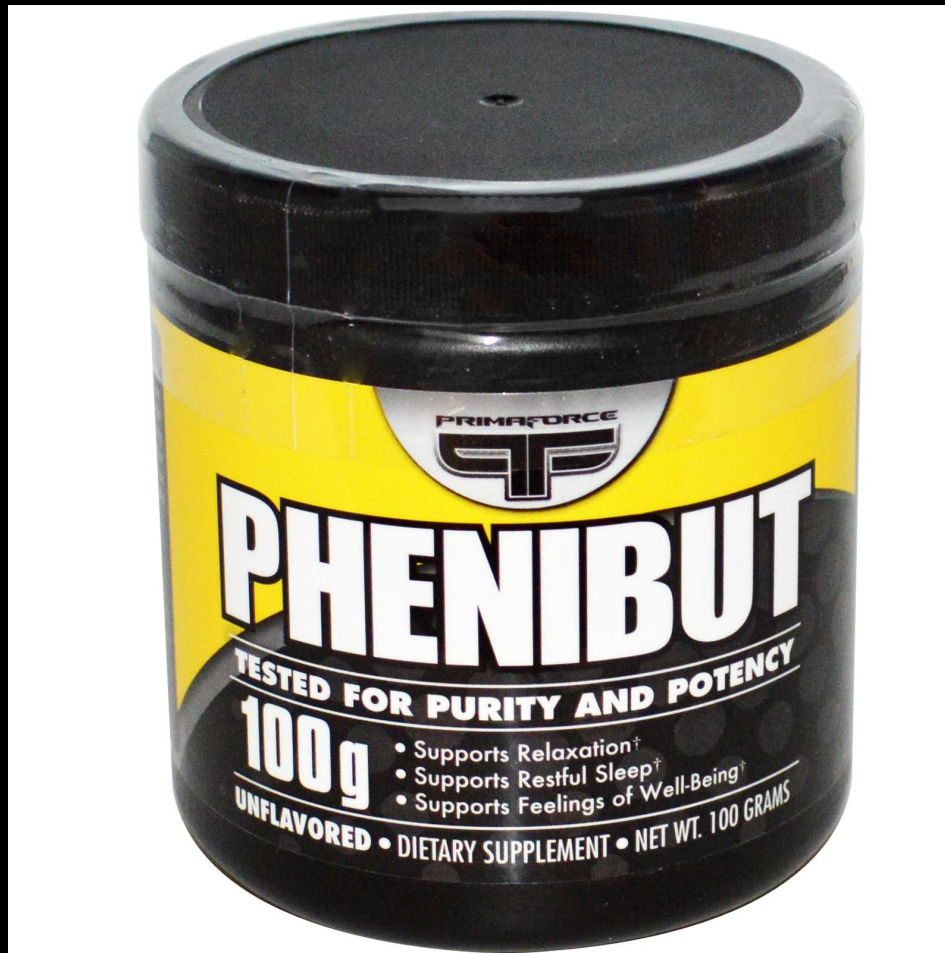


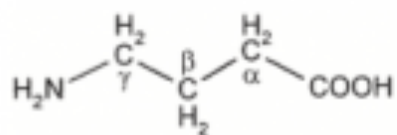
- Patient 2b:
 - Since that admission
 - At least 3 more hospitalizations for syncope
 - Had TdP during 2 of those hospitalizations
 - Reports up to 700 tablets daily
 - Last hospitalization:
 - Received buprenorphine nearly 36 hours later and went into acute precipitated withdrawal

Additional Observations

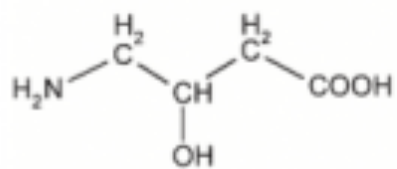
- Patients describe euphoria
- Both QRS and QTc prolongation have occurred
- Prolonged duration of effect
- Increased number of case reports in the literature describing cardiotoxicity
- Deaths reported

Phenibut

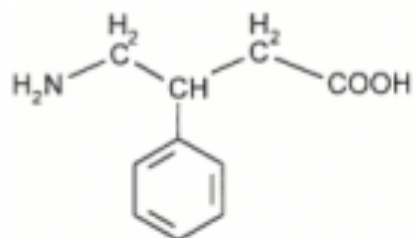




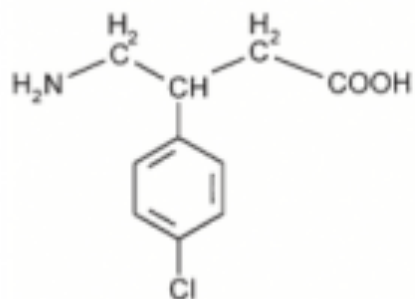
GABA – γ -amino-butyric acid



GABA-OH – β -hydroxy- γ -amino-butyric acid



Phenibut (PB) – β -phenyl- γ -amino-butyric acid



Baclofen (BAC) – β -p-Cl-phenyl- γ -amino-butyric acid,
Cl-PB

Fig. 1

Our Experience

- Several Cases Since 2014
 - Altered, depressed mental status
 - Myoclonic jerking
 - Tonic clonic seizure activity (N=2)
 - Prolonged duration of toxicity
- 1 gram phenibut = 10 mg baclofen

Kratom



Kratom

- *Mitragynina speciosa* Korth
- Used for opioid withdrawal
- Stimulant properties

Our Experience

- Several cases
- Seems to be increasing recently
- \$\$\$
- Altered mental status
- Seizures
 - ?Liver dysfunction

Conclusions

- As regulations become tighter, there will be an increase in alternative drugs for abuse
- Internet offers a unique alternative for access
- www.erowid.org
- www.bluelight.com