What Happens When Adam, Molly, and Spice Walk into a Psych Ward?

A discussion on (some of the) the latest drugs of abuse
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Objectives:

1. Introduce a range of newer substances abused in the community and their corresponding terminologies.
2. Identify substances which are prevalent and more commonly abused in Oregon.
3. Recognize intoxication and withdrawal syndromes of select substances.
4. Evaluate the therapeutic potential of particular substances of abuse.

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Synthetics and Serotonin Phenylethylamines
The Ecstasy Revolution

Ecstasy, XTC, Adam, Molly, E, X
empathogens designer amphetamines
euphoria, heightened awareness of senses, stimulant
When intoxicated, known as “rolling”

MDMA: where it all began

- First produced by Merck in 1912
- 1965: chemist Alexander Shulgin synthesizes while working at Dow
- In 1960/70s, “Adam” gained popularity among the psychotherapy community
- DEA classified as Schedule I drug in 1985 (no therapeutic value)
- 1991, Shulgin published PiHKAL

MDMA Pharmacology

3,4 methylenedioxymethamphetamine

- 5-HT2a receptor agonist, also acts as stimulant, releasing NE
- Typical dose 1-2 mg/kg (60-120mg)
- Onset: 30 to 60 minutes
- Duration of Intoxication: 4 to 6 hours
- Formulation: Tabs, Capsules, Powder, Liquid
- Route: PO, insufflation
- UDS + for amphetamines and methamphetamines
- Common Adulterants: DXM, ephedrine, cocaine, caffeine

Recent use/trends:

- [https://www.drugabuse.gov/drugs-abuse/mdma-ecstasymolly](https://www.drugabuse.gov/drugs-abuse/mdma-ecstasymolly)
- More than 20 percent of U.S. respondents reported using MDMA in the past year (Global Drug Survey 2015)
- Oregon Student Wellness Survey 2014

Ecstasy, XTC, Adam, Molly, E, X
empathogens designer amphetamines
euphoria, heightened awareness of senses, stimulant
When intoxicated, known as “rolling”
The “2Cs”: phenethylamines 2.0

- One of many “designer drug” or “research chemical” classes
- 2C=acronym
- Methoxy groups at the 2 and 5 positions on the ring, and a hydrophobic substitute at position 4
- Currently considered “drugs of concern” by the DEA; schedule I or II under the CSA or being considered for such status.

Serotonin Syndrome

Treatment:
- Supportive care in hospital setting
- Benzodiazepines to address sympathomimetic symptoms
2C Series

Initial claim to fame

1974
Shulgin synthesized 2C-B
(4-bromo-2,5-dimethoxyphenethylamine)

Fast forward to 2003
Ralf Heim synthesized 25I NBOMe
(2C-I-NBOMe)

25I NBOMe

Intoxication: 0.5 mg to 0.75 mg PO
Toxicity: above 1.5 mg PO

2C-B
Intoxication: 12 to 60 mg PO

2011 internet drug forums began buzzing about N-Bombs
25I, Smiles, Solaris, Cimbi-5, Foxy methoxy
marketed and sold as “LSD”

2C-X-NBOMe

Pharmacology

25I-NBOMe; 25C-NBOMe; 25B-NBOMe
2-(4-Iodo-2,5-dimethoxyphenyl)-N-(2-methoxybenzyl) ethanamine

Desired effects:
- Visual Hallucinations
- Euphoria
- Aphrodisiac

Onset: 1 hr
Duration of intoxication: up to 15 hrs
Formulations: liquid, powder, capsules, blotter
Routes: IV, PO, insufflation, buccal
Bitter/metallic taste
Metabolites excreted through the kidney
N-BOMe Lives in Infamy

“Texas synthetic drug ringleader sentenced to 246 months for his role in the deaths of 2 North Dakota teens.”
-ICE Newsroom, 2014

“New LSD-like drug 25I, or N-bomb, caused seizures in Sherwood, deaths around nation.”
-Oregonian, 2014

Prevalence

Significant medical consequences:
Delirium
Seizures
Multi-organ failure

Everything old is new again:
Novel uses of cannabis and codeine
Old plant, new highs...

- Chinese Emperor Shen Nung: 2727 BC
- Used by ancient Greeks and Romans.
- 1840’s: Dr. W.B. O’Shaughnessy introduces to West
- 2014 survey: 22.2 million current users (NSDUH)
- A significant proportion of those who use regularly reported that their primary motive was medicinal.

Medical Cannabis:

- Marijuana plant: not approved by the FDA
- Dronabinol (Marinol) and Nabibolone (Cesamet): approved for chemo-associated nausea and AIDS-related cachexia.
- Primary conditions for current card-holders...
- Proliferation of medical dispensaries/recent legal changes regarding recreational use --> increased methods for the administration: vaporizers, edibles, tinctures, patches, and capsules are now common.

Oregon Stats: Cannabis

- “Current” use (in past 30 days) is highests in 18-25 year olds, followed by 12-17 year olds.
- The 2013 Oregon Healthy Teens survey found current use among 8th graders to be 10% and among 11th graders 20%.
- Oregon’s Medical Marijuana Program is administered by the Public Health Division; 77,000+ people hold an Oregon medical marijuana card as of January 1, 2016.
- As of January 9, there are 368 registered dispensaries in Oregon (Oregon.gov).
Pharmacology, in (very) brief:

- Two psychoactive species: *c. indica* and *c. sativa*
- More than 460 compounds, 80 of which are cannabinoids.
- THC, or tetrahydrocannabinol (delta-9-tetrahydrocannabinol) is the most psychoactive, and associated with some of the pharmacological effects.
- Other cannabinoids include delta-8-tetrahydrocannabinol, cannabidiol (CBD), cannabinol (CBN), cannabicyclol (CBL), cannabichromene (CBC) and cannabigerol (CBG); they have less psychotropic effects than THC, but may play a role in the medically beneficial effects of cannabis.

THC intoxication/overdose:

- THC can reduce anxiety, produce relaxation, and induce euphoria.
- It can alter sensory perception, decrease coordination, and slow reaction time.
- In some people, and in overdose, it can cause acute dysphoria, paranoia, and hallucinations.
- Use is associated with short-term memory loss.
- Withdrawal syndrome is possible.
Not your grandma’s Pot Brownies...

- A wide variety of edible, marijuana-infused food and drink products
- There has been a spike in ED visits from people who have eaten too many edibles, with syndromes including tachycardia, hallucinations, vomiting, paranoia
- Several studies have found an increase in pediatric MJ exposure since decriminalization/legalization laws have passed, often related to edibles.

Dabs, a rapid emergence:

- February, 2013 issue of High Times: “we didn’t really talk about it or cover it, because it was so rare.”
- 5 months later, the July 2013 issue features “Dabs!” as the cover story.

Dabs, the dangers...

- Butane, used to extract it, is highly flammable and prone to explosion.
- Blowtorch is used in the process of “dabbing”
- Very high concentrations of THC can lead to intoxication/overdose syndromes.
- Novel and more rapid administration method.
- ED visits

Deliciously dangerous....

- Different pharmacokinetics
- Edible products often are made with pure THC
- Products can contain from 6-10 dose equivalents of THC per individual serving.
- Packaging/products are visually appealing and familiar to young consumers.
**Old meds, new mixers...**

A brief history of codeine...
- Codeine is extracted from the opium poppy
- The name is derived from the Greek word κοδεία, for “poppy head.”
- Medicinal and recreational use of opium peaked in the 1830s and spurred the Opium Wars.
- Codeine was first isolated by French chemist Pierre-Jean Robiquet in 1832, paving the way for the proliferation of “less addictive” and “safer” codeine-based preparations.
- Codeine is now the most widely used opiate in the world. (WHO)

**Intoxication/Overdose:**
- Similar to other opiates
- Overdose—respiratory depression, extreme somnolence progressing to stupor or coma, bradycardia and hypotension
- Promethazine intoxication/overdose
- Possible anticholinergic toxidrome may also be seen; other reported reactions include hyperreflexia, hypertonia, ataxia, atheiosis
- Convulsions are rare but possible with both

**Pharmacology, in brief...**
- 3-methylmorphine, a natural isomer of methylated morphine.
- It acts on the mu opioid receptor
- Promethazine: primarily H1 receptor antagonism and moderate muscarinic, D2-receptor blocking activity
- It is used in cough syrups for its antihistamine, antiemetic, and sedative effects
- Enzymatic induction

**Sippin’ on some sizzurp...**
- Abuse of codeine-based cough preparations known for decades
- Prescription and OTC anti-tussives present a world-wide public health issue
- In 2006, over 3 million people in the US aged 12-25 reported using OTC cough and cold medicine to “get high”
- Since the late ‘90s, abuse of codeine-promethazine hydrochloride cough syrup (CPHCS) has become increasingly popular
Abuse in popular culture:

- DJ Screw
- Jamarcus Russell
- ESPN did a special report on codeine abuse gaining popularity amongst professional athletes
- 'Lil Wayne's “sizzurp” overdose
- Justin Bieber was reportedly addicted to lean.

"Lean", the basics:

- Sprite + Jolly Ranchers + CPHCS.
- Some preparations include alcohol.
- AKA purple drank, purple stuff, syrup, sizzurp, barre
- Named for the posture users assume when intoxicated
- Gained popularity in the Southern Rap culture
- Especially popular in youth <21

Lean, the dangers

- Overdose, as described in previous slides.
- A 2011 study by Hou et al
- The ingredients are often found around the home.
- Codeine is addictive, though less so than other opiates.
- Codeine is often obtained by doctor-shopping, forged Rx, or pharmacy theft.
"Natural" Drugs

Herbal Marijuana Alternatives (HMAs)
- Herbal ingredients + synthetic cannabinoids
- Popular in Europe since the early 2000s
  - EMCDDA monitoring Spice products since 2008
  - Banned in Russia and Europe in 2010, appeared in USA around the same time
- 2011 - US DEA made many synthetic cannabinoids schedule I
  - they remain available on the internet and in head shops
- Detection:
  - Plant material used is too varied to reliably detect
  - Synthetic cannabinoids do not cross-react with standard lab tests for THC

Variety of brand names, including K2 and Spice
- Marketed as incense, potpourri, fertilizer, etc
  - labelled “not for human consumption”
- Compositions altered slightly
- Deliberate misrepresentation?
  - Many listed ingredients not present
  - Synthetic ingredients not listed
  - Additives
  - Amanita muscaria

Synthetic cannabinoids:
- Starting in the 1960s - pharmaceutical and research efforts to develop compounds with the analgesic and anti-inflammatory effects of THC without the psychoactive effects
  - led to a better understanding of the endocannabinoid system
- Similar clinical effects as marijuana but not detectable by traditional screening methods
- Adolescents and young adults
**Toxicity and additional risks**
- AKI (particularly related to use of XLR-11)
- Seizures
- JWH-018 – suspected carcinogenic potential
- Possible heavy metal residues in some mixtures
- Accidental overdose:
  - Variable compositions

**Composition**
- Synthetic cannabinoids - 4 major groups:
  - Classical cannabinoids, eg HU-210
    - Dronabinol, Nabilone
  - Cyclohexylphenols, or “non-classical cannabinoids”
    - CP-47,497 – more potent than THC
  - JWH series
    - JWH-018: psychoactive compound in many Spice products; also more potent than THC
  - Miscellaneous compounds

**Pharmacology**
- Synthetic cannabinoids:
  - Lack structural similarity to THC but bind to CB1 and CB2 receptors
  - higher affinity for receptors
  - higher potency
  - some significantly longer half-lives -> greater potential for overdose and/or prolonged psychoactive effects
- May also exert activity on other receptor families
- Rapid onset, brief duration of action
  - significant variability
Potential therapeutic uses

- Immune
- Neuroprotective
- Analgesia

Kratom

- Derived from *Mitragyna speciosa* Korth tree
- Used to treat opioid withdrawal and pain for centuries
  Also called *Ketum, Kakuam, Ithang and Thom*
- Legal and available on the internet without a prescription
  - powder
  - leaves
  - gum
- Smoked or brewed in tea
- Undetectable by available drug screens

Pharmacology

- >25 alkaloids that vary based on location
- *Mitragynine*: most abundant alkaloid
  - Thought primarily responsible for opioid-like effects
  - Structurally similar to yohimbine and different from opiates
  - Acts at supraspinal μ and δ opioid receptors
- Additionally:
  - Serotonergic and noradrenergic pathways in the spinal cord
  - May stimulate post-synaptic α2 receptors
  - May block stimulation of 5-HT2A receptors

Clinical effects

Onset 5-15 minutes, duration of action up to 5 hours
Dose-dependent effects

- Analgesia, anti-inflammatory, antipyretic, antitussive, antimalarial, antihypertensive, local anesthetic, hypoglycemic, antidiarrheal
- Prolonging sexual intercourse
- Mild visual effects
- Chronic use:
  - Anorexia, weight loss, hyperpigmentation, and psychosis
- Tolerance, dependence, and withdrawal
Toxicity and Management

- Seizures not responsive to benzos
- No reported cases of death in the US
- **Krypton--contained tramadol and caffeine**
- Seek immediate medical attention for suspected toxicity
- Increased risk of opioid-related death
- Hypoventilation: airway management + opioid antagonism
- Seizures: airway management + benzo titration

I SWEAR IT HELPS, DOC:

JCP September 2015: MJ Use Is Associated With Worse Outcomes in Symptom Severity and Violent Behavior in Patients with PTSD.

- at least 9 states have approved medical MJ for use in PTSD.
- lots of our patients claim that it helps them in a variety of ways, but the study suggests it may actually worsen symptoms and violent behavior.

In this observational study, n=2,276 vets, mostly male, white. Prevalent comorbid disorders. Admitted to specialized VA treatment programs over a 20 year period.

- 4 groups: never used, stopped upon entering study, started after entering study, and continued to use during study.
- assessed at intake and 4 months after d/c.
- MJ use, especially when initiated after the study was significantly associated with worse outcomes in PTSD symptom severity, violent behavior, and measures of etoh and drug use.

MDMA vs. PTSD:

- A very “hot topic” in research right now.
- [http://www.mdmaptsd.org/research-category.html](http://www.mdmaptsd.org/research-category.html)

References

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