Drugs of Abuse: Update 2017

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Objectives

• Highlight new drugs of abuse
  – “Heroin”
  – “Spice/K2”
  – “Bath Salts”
  – Emerging Drugs

• And discuss their
  – Pharmacology
  – Clinical findings
  – Treatment
The New Normal!

- Synthesize novel drugs overseas
- Ship anywhere in the world!
New Psychoactive Substances (NPS)

- UN tracking NPS
  - Estimates 600 NPS’ over last few years
  - Extremely hard to track
  - Extremely hard to detect
  - Nearly impossible to police
### Synthetic Cannabinoids

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Cathinones

- 4-Methoxy-α-PV8: 1
- 4-F-α-PVP: 1
- 4-F-α-PHP: 1
- 4-FMC: 1
- 4-BMC: 1
- 3-MEC: 1
- PV8: 2
- 4-MEC: 2
- 3,4-Methylenedioxy-α-PBP: 2
- 3,4-MDPV: 2
- 3-CMC: 3
- N-Ethyl-4-methylnorpentedrone: 4
- 4-CEC: 4
- Dimethylene: 6
- 4-CMC: 6
- Methylene: 10
- 4-Cl-α-PPP: 11
- 4-Cl-α-PVP: 13
- TH-PVP: 16
- Pentyline: 18
- α-PVP: 44
- N-Ethylpentyline: 57
- Ethylene: 63
- Dibutylene: 78

FMC = Fluoromethcathinone
BMC = Bromomethcathinone
MEC = Methylethcathinone
CMC = Chloromethcathinone
CEC = Chloroethcathinone
PV8 = Pyrrolidinoheptanone
### Opioids

Of the 15 substances identified, nine of these substances (60%) were reported for the first time in 2016. The following compounds were seized and reported for the first time in 2016: furanyl fentanyl, U-47700, 4-fluoroisobutyrylfentanyl, acryl fentanyl, o-fluorofentanyl, benzylfentanyl, p-fluorobutyrylfentanyl, 3-methylnortyfentanyl, and acetyl norfentanyl.

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“Heroin”
National Overdose Deaths
Number of Deaths from Heroin

Source: National Center for Health Statistics, CDC Wonder
Drug poisoning death rates* by state: United States, 2013

- **Significantly higher than the U.S. rate**
- **No significant difference**
- **Significantly lower than the U.S. rate**

*The U.S. rate is 13.8 per 100,000 population.

NOTE: Drug poisoning death rates are age-adjusted deaths per 100,000 standard population.

What is heroin?

• Papaver somniferum (Poppy plant)
  – Indigenous to the Middle and Far East
  – Contains a natural mixture of morphine, codeine, and thebaine

• Opium
  – Dried latex or paste derived from immature poppy seeds

• Heroin
  – Diacetylmorphine
  – Greater potency
Not your father’s heroin…
Today’s Heroin

Acetyl fentanyl
Butyryl fentanyl
Fentanyl = Acryl fentanyl
Methyl fentanyl
Carfentanil

Potency
Fentanyl-mixed Heroin in Pittsburgh

- 1988: “China White”
- 2006: “Get High or Die Trying”
- January 2014: “Theraflu” and “Bud Ice”
- April, 2014: “Predator” and “Chocolate” were pure fentanyl
- September, 2015: “Hit and Run” contains fentanyl and cocaine
In **Adult** patients, options for titrating naloxone dosing every 2-4 minutes until adequate spontaneous respirations include:

- IV/IO: 0.4 mg, then 1.6 - 2 mg, then 2 mg (up to 4.4 mg total), or
- IM/IN: 2 mg, then 2 mg (4 mg total)

In **Pediatric** patients, naloxone should be dosed every 2-4 minutes until adequate spontaneous respiration using:

- IV/IO/IM/IN: 0.1 mg/kg (up to 0.4 mg initial dose), then 0.1 mg/kg (up to 2 mg), then 0.1 mg/kg (up to 2 mg)
Spice
Spice / K2
Synthetic Cannabinoids

• How prevalent is it?
  – July 2016: ‘Why synthetic marijuana is more dangerous than ever’
  – March – May 2015:
    • Mississippi Dept Health
      – 1200 ED related visits
      – 17 deaths
    • Alabama Dept Health
      – 1000 ED related visits
      – 5 deaths
Synthetic Cannabinoids

• What’s the appeal??
  – 91% = experimentation
  – 89% = ‘feel good’
  – 71% = to relax
  – 71% = get high w/o a positive drug test

NEJM 373:2 July 2015
Marijuana
Cannabinoids

• 3 Types
  – Phytocannabinoids
    • Marijuana
  – Endocannabinoids
    • Produced by the human body (i.e, anandamide)
  – Synthetic cannabinoids
    • “Spice”
    • INACA
Marijuana

• *Cannabis sativa*

• 3 major cannabinoids (out of approx 60 total)
  – Cannabinol
  – Cannabidiol
  – Tetrahydrocannabinol (THC)
Marijuana

- **THC**
  - First use dates to Chinese in 4000 B.C.
  - First isolated in 1964

- **CB1 Receptor**
  - Cannabinoid receptor first isolated in 1988
  - THC initially not thought to bind receptors
Marijuana

• CB1 Receptor
  – Largely in CNS (hippocampus, basal ganglia, cerebral cortex and cerebellum)
  – Modulates
    • Memory
    • Cognition
    • Nausea/Vomiting
    • Vasodilation
    • Arterial tone
Marijuana

• CB2 Receptor
  – Found in immune cells (thymus, spleen, tonsils)
  – Modulates
    • Immune responses
    • Inflammation
Marijuana

- Used/Abused
  - Normally by smoking
    - Onset of clinical effects w/i minutes
    - Peak effects on average 8 minutes
  - Can be eaten
    - More unpredictable onset (1-2 hours)
    - Peak effects on average 2-4 hours
Marijuana

• Clinically (not so bad)
  – Relaxation
  – Euphoria
  – Perceptual alterations
  – Reduced coordination
  – Decreased memory processing
  – Increased appetite
  – Decreased vascular resistance
    • (red eyes)
    • Orthostatic hypotension
Marijuana

• Clinically (not so good)
  – In young children
    • Apnea
    • Bradycardia
  – In anyone
    • Dysphoria
    • Panic
    • Paranoia (psychotic reactions)
Marijuana

• Clinically (chronic use)
  – Increased risk of psychiatric illness
  – Decreased attention
  – Decreased verbal learning
  – Decreased memory
Medicinal Marijuana

- Used as antiemetic, appetite stimulant, and pain control:
  - Nabilone = Cesamet®
  - Dronabinol = Marinol®
  - THC/Cannabidiol = Sativex®
Synthetic Cannabinoids

• The Great Hope!! Possible Uses:
  – Epilepsy
  – Pain
  – Inflammation
  – Anxiety
  – Depression
  – Etc. . .
Synthetic Cannabinoids

- Developed in the 1960’s
- Synthesized for treatment of pain/nausea
- Hard to separate psychoactive effects
- Many have been developed
  - HU-210
  - CP series (i.e., CP-47,497)
  - J.W. Huffman (i.e., JWH 018)
Where Did INACA Come From?

- Big Pharma…of course
- Mid-2000s Pfizer patented the base structure for INACA-class compounds
- Were being studied as analgesics
- None have made it to phase I trials

Structure depicted in the Pfizer patent
Synthetic Cannabinoids

• Since 2010 (in USA)
  – Made available as “legal” high
  – Plant material coated with synthetic cannabinoids
  – Often used by adolescents and young adults
Synthetic Cannabinoids

- Sold under many names (usually as an incense or potpourri):
  - Spice
  - K2
  - Red X Dawn
  - Blase
  - Sense
  - Zohai
Synthetic Cannabinoids

• Pharmacology
  – Not much is known
  – However...

Potency =
FUBINACA < THC < PINACAC < CHMINACAC
Synthetic Cannabinoids

Remember:
Classical cannabinoids are *partial* agonists

BUT

Synthetic cannabinoids are *full* agonists
Synthetic Cannabinoids

• Clinically
  – Hypertensive
  – Tachycardia or Bradycardia
  – Agitation
  – Nausea/Vomiting
  – Hallucinating/psychotic
  – Seizures
Adverse Reactions

- Excited delirium
- Acute kidney injury
- Seizures
- Psychosis
- Hallucinations
- Cardiac dysrhythmias
- Coma
Synthetic Cannabinoids

• Deaths
  – From drug??
    • Myocardial Infarction
  – From behavior
    • Suicide from anxiety
    • Invincibility
    • Attempting to fly
  – From other stuff
    • Pneumonitis
Synthetic Cannabinoids

• Treatment
  – Restraints
  – Benzodiazepines
  – IV fluids
  – Monitor for rhabdo

• Symptoms usually resolve w/i hours
Synthetic Cannabinoids

• Testing
  – Urine drug tests cannot detect!
Recent Synthetic Cannabinoid “Data”

- From UPMC Hamot ED (Erie, PA)
  - 10/2015 – 12/2015
  - 105 patients with alleged “K2” use
    - 55 admitted
    - 16 intubated

- ADB-CHMINACA
  - Called “K2” or “Deuce Death”
  - Identified in several patients sent to us.
  - All adolescents
Bath Salts
Bath Salts

• Synthetic Cathinones
Bath Salts

- Alpha Pyrrolidinopentiophenone (Alpha-PVP)
- AKA
  - Flakka
  - Gravel
“Crystal” Meth
MDMA / Methamphetamine

• Methamphetamine
  – Stimulates neuronal release. . .
    • Serotonin
    • Dopamine
    • Norepinephrine
    • Epinephrine

• MethylenedioxyMethamphetamine
  – Additionally, causes hallucinations
Methamphetamine

- Easily made from store bought ephedrine (Herbal supplement) or pseudoephedrine (Sudafed)
MDMA / Methamphetamine

• Very similar to cocaine EXCEPT
  – Longer lasting (up to 24 hrs)
  – Less seizures but more psychosis
  – Less cardiac dysrhythmias

• MDMA
  – Hallucinogenic
MDMA / Methamphetamine

- **Adverse effects**
  - Life-long psychosis (even after discontinuation)
  - Bruxism
  - Choreoathetosis
  - Pulmonary hypertension
  - Valvular heart disease

- **Mortality is directly proportional to core temp**
MDMA / Methamphetamine

• Treatment
  – Benzos
    • For HTN, tachycardia, agitation
  – Nitro or phentolamine
    • For HTN
  – Haldol
    • For psychosis (large doses)
  – Active cooling
    • For hyperthermia
Bath Salts

- Since 2010 (in USA)
  - Made available as “legal” high
  - Marketed much like “Spice”
  - Synthetic substitute for Cocaine/Meth
Bath Salts

• Sold under many names (usually as a bath salt):
  – Red Dove
  – Blue Silk
  – Zoom
  – Bloom
  – Cloud Nine
  – Ivory Wave
  – Vanilla Sky
Bath Salts

- Usually contains combinations of:
  - Ephedrone
    - AKA
      - Methcathinone
      - “Jeff”
  - Mephedrone
    - AKA
      - Methylmethcathinone
      - “meow meow”
  - Methylenedioxypyrovalerone (MDPV)
Alpha PVP

• How prevalent is it?
  – July 13, 2015 USA Today
    • Powerful street drug “flakka” shakes Kentucky county
  – May 26, 2015
    • Why is flakka more dangerous than cocaine?
Khat \((\textit{Catha edulis})\)
Khat

Khat/Cathinone

Ephedrine/Methcathinone

Alpha PVP
“Medicinal Khat”

Bupropion

Khat/Cathinone
Bath Salts

• Pharmacology
  – Currently no published studies!

• Based on knowledge of “amphetamines”
  – Sympathomimetic
    Plus
  – Hallucinogenic
Bath Salts

• Used/Abused
  – Normally by snorting or eating
    • Mephedrone or Ephedrone
      – Onset w/i minutes
      – Peak 30 minutes
      – Duration 2-4 hours
    • MDPV
      – Onset 5-30 minutes
      – Peak 0.5-3 hours
      – Duration as long as 48 hours
  – Rarely smoked
IV Use
Bath Salts

• Clinically
  – Tachycardia
  – Hypertension
  – Vomiting
  – Agitation
  – Hallucinations/psychosis
Bath Salts

• Treatment
  – Restraints
  – Benzodiazepines
  – PLUS...Haldol
  – IV fluids
  – Cooling
  – Monitor for rhabdo
  – Monitor lytes, creatinine

• Symptoms may last for days.
Bath Salts

• Some report treatment success with . . .
  – Ketamine
  – Versed

• Many may require intubation to control agitation!!
Bath Salts

• Testing
  – MAY trigger positive ‘amphetamine’ screen on urine drug.
A Few New Emerging Drugs
Kratom

- Tropical evergreen native to Thailand
- Use goes back to the 1800’s
- Related to coffee family
Kratom

- Used anecdotally in Asia to treat:
  - Coughs
  - Diarrhea
  - Muscle aches
Kratom

• Contains 40ish compounds

• Mechanisms
  – Mitragynine main compound
    • Mu agonist = similar opioids
    • Serotonin agonist = similar to LSD
    • \( \text{Alpha}_2 \) agonist = similar to clonidine
  – Rhynchophylline
    • NMDA antagonist = similar to ketamine/PCP
Kratom

• How is it used?
  – Chew leaves
  – Smoked
  – Swallow crushed dried leaves
  – Make tea
  – Etc.
Kratom

- Clinical Effects (Low Dose)
  - Increased sociability
  - Increase attentiveness

- Clinical Effects (High Dose)
  - Sedation
  - Respiratory depression
  - Hallucinations
  - Psychosis
  - Seizures
  - N/V

When eaten, onset of effects 30-45 minutes and last 2-5 hours
Kratom

• Treatment?
2C-x Compounds

• In the news...
  – March 12, 2012 – “New LSD-Like drug under investigation”
  – Dec 2, 2014 – “Deadly High: How synthetic drugs are killing kids.”
  – Jan 20, 2016 – “Designer drug puts 6 people in hospital”
2C-x Compounds

• Developed in 1970’s as aid to psych therapy
• Marketed in the 1980s as a legal alternative to MDMA (Ecstasy)
• Commonly street names:
  – “ACID”
  – “B-25”
  – “Bromo Dragon Fly”
2C-x Compounds

25B-NBOMe

2C-B

MDMA

Dopamine
2C-x Compounds

• No academic research on these!
• Used/Abused
  • 2C-B (Eating)
    – Onset 45-75 minutes
    – Duration 4-12 hours
  • 2C-E (Snorting)
    – Onset w/i minutes
    – Duration 3-6 hours
  • 2C-I (Eating)
    – Onset 45-60 minutes
    – Duration 5-8 hours
2C-x Compounds

- Mechanism
  - Serotonergic
  - Dopaminergic

- Likely, similar mechanism to the amphetamines
2C-x Compounds

• Clinical Effects (Low Dose)
  – Giddiness
  – Hallucinations
  – Increase attentiveness

• Clinical Effects (High Dose)
  – Restless / agitated
  – Hypertension / tachycardia
  – Hyperthermia
  – Paranoia
  – N / V
2C-x Compounds

Anecdotally... we have treated “Acid” cases, but no LSD is detected!!

I think this is out there!
Pearls

Welcome to the new normal!
Questions?
Call 412-647-7000