2018 New Drugs on the Streets-Risks for Users

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Disclosure

- Anthony Dekker, DO has presented numerous programs on Chronic Pain Management and Addiction Medicine. The opinions of Dr Dekker are not necessarily the opinions of the VA, DoD, Indian Health Service or the USPHS. Dr. Dekker does not represent any federal agency. Dr. Dekker has no conflicts to report.
Objectives

• To be aware of the special considerations in American at risk substance users
• To be able to recognize opioid use in US users
• To be aware of changes in the opioid epidemic
• Overview of New Psychoactive Substances of abuse
Synthetic Psychoactive Substances

• Designer drugs derived from known herbals, stimulants, hallucinogens, opiates, sedatives
• “Legal highs” may be unregulated due to novel chemical structures
• Access via “head shops” and the Internet
• Most labs now test for over 20 SYNCANs, 9 Cathinones but not many others
Overview of Synthetic Psychoactive Substances

- Cannabinomimetic
  - Spice/K2
- Stimulant
  - Bath Salts
  - Piperazines
- Powder Alcohol
- Powder Caffeine

- Hallucinogen
  - Methoxetamine

- Salvia divinorum
- NBOMe

- Opioid
  - Kratom
  - Krokodil
  - Acetyl fentanyl
  - Carfentanil

- NBOMe
Synthetic Marijuana: Synthetic Cannabinoids (SC)

- Spice, Spice Gold, Spice Diamond
- K2, K2 Blonde
- Aroma
- Yucatan Fire
- XXX
- Black Box
- Zombie
- Skunk
- Moon Rocks
- Bizarro
Routes of Administration

• Smoked with a pipe, bowl, or cigarette paper
• E-cigarette device
• Ingested as an infusion
• Inhaled
Onset and Duration of Action

• Euphoria and calming effects within seconds to minutes of inhalation
• Intoxicating effects disappear within 30 to 60 minutes
• Repeat use is common to maintain effect
• Tolerance and Dependence
• Adverse reactions can accumulate and persist
# Synthetic Marijuana Data

American Association of Poison Control Centers

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011</td>
<td>6,968</td>
</tr>
<tr>
<td>2012</td>
<td>5,230</td>
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<tr>
<td>2013</td>
<td>2,668</td>
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<tr>
<td>2014 Through Oct. 31, 2014</td>
<td>2,996</td>
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Drug Enforcement Agency Bans the following SC (March 2011) for one year

- JWH-018
- JWH-073
- JWH-200
- CP-47,497
- CP-47,497-C8

Synthetic Drug Abuse Prevention Act of 2012 (July 10)

- Cannabimimetic Agents- Schedule I, as set forth in section 202(c) of the Controlled Substances Act is amended by adding at the end the following:
- Unless specifically exempted or unless listed in another schedule, any material, compound, mixture, or preparation which contains any quantity of cannabimimetic agents, or which contains their salts, isomers, and salts of isomers whenever the existence of such salts, isomers, and salts of isomers is possible within the specific chemical designation.
Aminoalkylindole

Cyclohexylphenol

μ-opioid agonist

O-Desmethytramadol

Fatty Acid Amide

Dibenzopyran (Classical Cannabinoid)

Synthetic Cannabinoids: Mechanism of Action

• Full and potent agonist of the CB1 receptor
• 4- to 5-fold higher affinity to CB1 receptor
• 10-fold higher affinity to CB2 receptor


Forrester MB, Kleinschmidt K, Schwarz E, Young A. Synthetic cannabinoids and marijuana exposures reported to poison centers. Hum Exp Toxicol 2012; 31:1006–11.
Medical Sequelae

- Hypertension
- Tachycardia
- Nausea and Vomiting
- Hypokalemia
- Acute Kidney Injury
- Seizures
- Coma
Psychiatric Sequelae

- Psychosis resembling schizophrenia with hallucinations, delusions and thought disorder
- Multiple case reports of exacerbations of psychosis in schizophrenia
- Longer term adverse effects to be determined

Every-Palmer S. Warning: Legal Synthetic Cannabinoid-Receptor Agonists such as JWH-018 May Precipitate Psychosis in Vulnerable Individuals. *Addiction.* 2011, Aug.
Management of SC Toxicity

• Supportive
  • Duration usually less than 8 hours
• Symptomatic
  • IV Fluids
• No antidote

Synthetic Cannabinoids: Withdrawal Syndrome

- Cravings
- Anxiety
- Insomnia
- Anorexia → Nausea and Vomiting
- Headaches
- Diaphoresis
- Tachycardia

Bath Salts

• Synthetic analogs of cathinone
  • Psychostimulant found in leaves of khat plant
  • Native to East Africa
• Leaves chewed for centuries due to their euphoric effects
• Mephedrone, Methylone, MDPV
• Flakka
Bath Salts

- Snorted or ingested
- Not detected by standard drug screens
- Brand names
  - Charge Plus
  - Hurricane Charlie
  - Ivory Wave
Bath Salts

- Associated with violence in news reports
- Frequently agitated and aggressive in ER
- Intense cravings similar to methamphetamine
  - Encourages repeated doses
  - Increased risk of medical complications
  - Seizures, MI, Death – all reported
- Flakka
Bath Salts - Mechanism

- Augment effects of monoamines
- Inhibit reuptake of NE, DA, 5-HT
- Lesser extent – stimulate presynaptic release of monoamines
- Onset after ingestion: 15-30 minutes
- Duration of effects: 2-7 hours
Bath Salts – Effects & Physical Signs

• **Desired effects**
  - Euphoria
  - Heightened alertness
  - Elevated energy
  - Increased sexual arousal

• **Undesired effects**
  - Severe agitation
  - Psychosis – snorted
  - Self mutilation
  - Suicide attempts

**Physical Signs – stimulant toxicity**
- Tachycardia
- Hypertension
- Hyperthermia
- Dehydration
- Psychomotor agitation
- Arrhythmias
Piperazine Derivatives (Legal Ecstasy)

- Originally developed to expel parasitic worms
- Found to have amphetamine-like effects
- Derivatives developed to augment these effects
  - Benzylpiperazine (BZP) – most popular
  - Many other unregulated forms exist
Piperazine Derivatives

- Sold as pills and powders
- Usually ingested or snorted
- Common names:
  - Benzo Fury
  - Party Pills
  - MDAI
  - Head Rush
  - XXX Strong as Hell
Piperazine Derivatives - Mechanism

- Augment neurotransmission of serotonin
  - Stimulate 5-HT receptors
  - Inhibit 5-HT reuptake
  - Stimulate release of 5-HT endogenous stores
- Delayed onset of action after ingestion: 2 hours
  - More likely to overdose
- Duration of effects: 6-8 hours
Piperazines – Effects & Physical Signs

- **Desired effects**
  - Low doses – stimulant
    - Euphoria
    - Increased energy
  - High doses – hallucinogen

- **Undesired effects**
  - Palpitations
  - Anxiety
  - Headache
  - Vomiting

**Physical Signs**
- Tachycardia
- Hyperthermia
- QT prolongation
- Dilated pupils
- Seizures – up to 8 hours after last dose
Methoxetamine (Legal Ketamine)

- Synthetic analog of ketamine
- Unregulated in US
- Sold online as research chemical
- MXE, M-Ket, Kmax, Mexxy
Methoxetamine

- White powder
- Usually snorted or ingested
- Very little is known about toxicity
Methoxetamine - Mechanism

• Similar to ketamine
  • Inhibits NMDA receptors
  • Inhibits DA reuptake
• Onset of action within 10 minutes
• Effects wear off quickly within 1-2 hours
MXE – Effects & Physical Signs

**Desired effects**
- Euphoria
- Hallucinations
- Perceptual distortions – feeling detached

**Undesired effects**
- Nausea
- Vomiting
- Diarrhea
- Paranoia
- Anxiety

**Physical Signs**
- Tachycardia
- Nystagmus

Not associated with hypertension, laryngospasm, pulmonary edema – reported with ketamine
Salvia divinorum

• Mint herb native to Mexico
• Contains psychoactive compound salvinorin A
• Used for centuries as hallucinogen
• Surge over past decade in teens & young adults
Salvia divinorum

• Currently unregulated
• Sold as crushed leaves or salvinorin A extract
• Usually smoked or chewed
• Diviners Sage, Magic Mint, Purple Sticky, Sally D
Salvia – Mechanism

• Highly selective kappa opioid receptor agonist
• Vivid hallucinations occur within seconds
• Resolve within 30 minutes
• Users rarely present for medical evaluation
  • Short duration of action
  • Minimal side effects
Salvia – Effects & Physical Signs

- **Desired effects**
  - Heightened sensations
  - Distorted visual perceptions
  - Synesthesia (hear colors, smell sound)

- **Undesired effects**
  - Intense anxiety
  - Fractured reality sense
  - Headache
  - Drowsiness
  - Persistent psychosis

**Physical Signs**
- No significant physical signs reported
- More research needed to explore safety
N-BOMe Derivatives

• What is it?
  • 25I-NBOMe, 25C-NBOMe, and 25B-NBOMe
  • Synthetic phenethylamines with effects similar to LSD
    • Powders, liquids, edibles, blotter papers

• Desired Effects
  • Potent hallucinogenic activity
  • Euphoria, loving feelings, enhanced awareness, sexual sensations/desires

• Dangers
  • Psychosis, agitation, erratic behavior, depression, anxiety, paranoia
  • Seizures, cardiac arrest, respiratory arrest, death
Kratom

• Derived from leaves of Mitragyna speciosa plant
• Native to Southeast Asia
• Leaves contain mitragynine
• Used for centuries to treat opiate withdrawal
Kratom

• Currently unregulated in US
• FDA-proposed this Schedule I on 30SEP2016
• mitragynine and 7-hydroxymitragynine
• Sold as crushed leaves, green powder, pills
• Usually smoked, brewed into tea, ingested
• Ithang, Ketum, Krypton, Thom
Kratom – Mechanism

- Mitragynine stimulates mu opioid receptors
- Onset: 5-10 minutes after ingestion
- Duration: 2-5 hours
- Low doses – stimulant
  - Increased alertness
  - Elevated energy
- High doses – opiate
  - Sedation
  - Euphoria
Kratom – Undesired Effects

- Respiratory depression
  - Especially if combined with other opiates
  - May lead to death

- Tolerance & Withdrawal – similar to opiates
  - Nausea
  - Vomiting
  - Sweating
  - Piloerection
  - Hypertension
  - Tachycardia
  - Enlarged pupils
  - Muscle pain
  - Anxiety
  - Insomnia
Krokodil

• Desomorphine: home-cooked from codeine using toxic household products including paint thinner, gasoline, red phosphorus and iodine

• When injected it is supposedly 8-10 times more potent than heroin, faster-acting, but shorter-lasting
Krokodil

- Vasculitis
- Necrosis
- Infection with resistance
- Analgesia
Acetyl Fentanyl

- Schedule I
- Russian Mafia
- Enhanced mu receptor affinity
- Enhancement for heroin when cut
- Largest contributor of OD deaths currently in US but difficult to test.

- Philadelphia and Pittsburgh had over 50 deaths each in 2013
- 19 deaths in Providence RI NYE 2014
- Appears to contribute to the 400% rise in Heroin ODs in many areas
- 85% heroin in Maricopa Co contaminated with fentanyl
Officials at the Nogales Port of Entry arrest a woman transporting 5 pounds of fentanyl inside a baby stroller WITH the infant in the stroller.
Law Enforcement Exposure
U-47700

- Synthetic Opioid Commonly Referred to as Pink
- Scheduled by DEA in November 2016
- Maricopa County Medical Examiner’s Office- U-47700 Contributed to Deaths in 2016
U-47700 a.k.a. “Pink”
Fentanyl related heroin deaths

• 2014 over 700 deaths
• Apache, China girl, China white, dance fever, friend, goodfella, jackpot, murder 8, TNT, as well as Tango and Cash
• 2017 Fentanyl major cause of increase in deaths
Prescriptions to Heroin

Memorial tattoo

- Reconsiderations of opioid use
- Addition of agonist therapies
- Naloxone injector availability
- Non pharmacologic therapies
Powdered Alcohol

• Freeze-dried powder formulation of alcohol
• Most notably marketed in the US under the name Palcohol
  • Labeling originally approved by the Alcohol and Tobacco Tax and Trade Bureau, but withdrawn days later

• Desired Effects
  • Discreet means of intoxication
  • Use on food products for “an extra kick”
  • Snorting powder as a means of immediate intoxication

• Dangers
  • Over-consumption of alcohol
  • Addictive potential
  • Attractiveness to young children

http://time.com/71664/powdered-alcohol-palcohol-error/
Powdered Caffeine

• What is it?
  • Powdered form of pure caffeine
  • One teaspoon is equivalent to approximately 25 cups of coffee
  • Marketed as a dietary supplement

• Desired Effects
  • Energy boost, weight loss

• Dangers
  • Vomiting, diarrhea, stupor, disorientation
  • Rapid and abnormal heartbeat, seizures, death

http://www.fda.gov/Food/RecallsOutbreaksEmergencies/SafetyAlertsAdvice/ucm405787.htm
http://nypost.com/2014/07/19/powdered-caffeine-scrutinized-after-prom-knight-dies/