GENERAL DISCLOSURES

The University of Washington School of Medicine also gratefully acknowledges receipt of educational grant support for this activity from the Washington State Legislature through the Safety-Net Hospital Assessment, working to expand access to psychiatric services throughout Washington State.
CONFLICTS OF INTEREST?

• NONE!
OBJECTIVES

• Review some common drugs of abuse popular among young adults
• Introduce some “newer” drugs of abuse
• Understand psychiatric manifestations of these substances of abuse
• Learn resources to use in order to stay current with evolving drug trends and newly synthesized drugs of abuse
• Questions, discussion
DESIGNER DRUG

• Synthetic structural or function analogs of controlled substances designed to mimic the pharmacological effects of the original drug while avoiding illegality
REASONS FOR USE

• Often Legal
• Often Less expensive
• More readily available
• More desirable pharmacological effects
CHALLENGES TO THIS TOPIC

**Psychedelics**
- **5'-substituted tryptamines**
  - Related to: butotenin
  - 5-MeO-DMT 5-MeO-DALT 5-MeO-MIPT 5-MeO-MET 5-MeO-DPT 5-MeO-AMT
- **NBOMe series**
  - Related to: 2C-x series
  - 2C-B 2C-D 2C-I 2C-E 2C-T-7 2C-B-FLY
- **Ergolines**
  - Related to: LSD, LSA
  - ALD-52 LA-SS-AZ (LSZ) PRO-LAD ETH-LAD
- **4'-substituted tryptamines**
  - Related to: psilocin
  - 4-AcO-DMT 4-HO-DPT 4-AcO-DET 4-HO-DALT 4-HO-MIPT 4-HO-DPT 4-MES-DMT
- **Psychedelic amphetamines**
  - Related to: 2C-x, amphetamine
  - DOB DOM DOC DOET DOI TMA-2 Bromo-dragonFLY

**Stimulants**
- **Cathinones**
  - Related to: methcathinone, cathinone, amphetamine, MDMA
  - Methedrone Pentedrone Methylene Flophedrone Butylene bk.-PMMA, benzoedrone 4-MEC
- **Piperazines**
  - Related to: piperyazine
  - APB APB 6-ADP 4-methylaminorex 4-ethylaminorex
  - Desoxypipradrol
  - MDAI MDAT 2-AI 5-IAI Dimethocaine
- **Phenylalkylpyrrolidines**
  - Related to: Pyrovalerone, Prolintane
  - MDPV α-PVP MDPVP α-BPP MOPVP
  - Ethylphenidate

**Cannabinoids**
- Functionally related to naturally occurring cannabinoids including THC
- **Naphthoylindoles**
  - WIN-55,212-2 AB-001
  - JWH-018 JWH-019 JWH-073 JWH-081 JWH-122 JWH-200
  - AM-1221 AM-2201
- **Phenylacetylindoles**
  - CP-47,497 CP-47,497, CS homologue CP-55,940
  - JWH-250 JWH-251 JWH-203 RCS-6
  - CB25 CB52
- **Cyclopropanoylindoles**
  - UR-144 5F-UR-144 A-834,735 A-796,260
  - JWH-133 JWH-161
- **Naphthopyroles**
  - JWH-307 JWH-147 JWH-030
  - HU-210 HU-211 HU-331 O-1812
- **Benzoylindoles**
  - AM-694 AM-1241 AM-2233 RCS-4
  - JWH-175

**Dissociatives**
- Related to: ketamine, PCP
- Methoxetamine
- 3-MeO-PCP
- 4-MeO-PCP
- 3-MeO-PCP
- 2-MeO-ketamine

**Sedatives**
- Related to: morphine, fentanyl, heroin
- α-methylfentanyl 3-methylfentanyl MPPP
- O-desmethyltramadol 7-acetoxymorphone Metonidazole AIH-7921
- Phenazepam
SUBSTANCES COVERED TODAY

• Synthetic Marijuana (Spice)
• Synthetic Cathinones (Bath Salts)
• MDMA (Ecstasy)
• Others
  – Piperazines
  – 2C series
  – DXM (Dextromethorphan)
  – “Syrup”
  – GHB
  – Kratom
HOW DO I ASK MY PATIENTS ABOUT SUBSTANCES?

- Do you use any substance to change the way you feel or enhance your experiences?
- What is it? What does it do for you?
- What’s the newest thing?
PAST YEAR DRUG USE BY 12TH GRADE STUDENTS

- Prescription opioids: 5.40%
- LSD: 2.90%
- Hallucinogens: 4.2%
- MDMA: 4.2%
- Synthetic Cathinones: 1.0%
- Synthetic Marijuana: 5.2%
- Marijuana: 35%
- Alcohol: 58.20%

Monitoring the Future Survey, 2015 results.
SPICE = SYNTHETIC CANNABINOIDs

• Herbal mixtures sprayed with chemical additives
  – “Spice”
  – “K2”
  – “Yucatan Fire”
  – “Skunk”
  – “Moon Rocks”
  – “Crazy Clown”
  – “Herbal Madness”

• Sold as
  – Potpourri
  – Incense
  – Air Fresheners
  – Obtained online, head shops, or gas stations/convenience stores

• Route of administration similar to marijuana

Why People Use It?

• The expectation of a more intense high
• Easy access
• Belief it is safe
• Avoid detection
Tetrahydrocannabinol
Binding affinity for CB1 K: 40.7 nM

JWH-018
Binding affinity CB1: 9 nM

AM-2201
Binding Affinity for CB1: 1.0 nM

All lipid soluble and highly volatized
Synthetic Cannabinoids

• Psychoactive effects – within minutes lasting up to 8 hours
  – Euphoria
  – Psychosis (9.4%-38%)
    • Visual
    • Altered perception of time
  – Anxiety
    • Panic
  – Agitation (23.4%)
  – Memory changes
  – Sedation (13.6%)
  – Confusion (12%)
Medical Consequences

- **Cardiovascular**
  - Chest pain
  - Tachyarrhythmia
  - Cardiotoxicity
  - Tachycardia (40%)
  - Hypertension (8.1%)
  - Dizziness (7.3%)

- **Gastrointestinal**
  - Nausea
  - Vomiting
  - Hyposalivation
  - Xerostomia

- **Renal**
  - Acute kidney injury

- **Other**
  - Seizures-status epilepticus
  - Somnolence, dilated pupils, brisk reflexes
  - Appetite changes
  - Stroke

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Tolerance, Withdrawal and Dependence

- Cravings, restlessness, NMs, sweating headache, nausea, and tremor
Diagnosis and Treatment

• Gas chromatography-mass spectrometry at selected labs

• Treatment is supportive
  – IVF
  – Calm setting
  – Benzodiazepines
  – Antipsychotic drugs prn
SYNTHETIC CATHINONES (BATH SALTS)
COMMON BATH SALT NAMES

- Meow meow
- Bubbles
- Cat
- Jeff
- Bliss
- Blue silk
- Cloud nine
- Drone
- Ivory wave
- Lunar wave
- Ocean burst
- Pure ivory
- Purple waves
- Red dove
- Snow leapard
- Stardust
- Vanilla sky
- White night
BATH SALTS = SYNTHETIC CATHINONES

- Similar to other stimulants
  - Increase synaptic concentration of amines: NE, DA, 5HT

Why People Use It?
- Easy access – Internet
- Avoid detection
- Potential for more intense high

Khat
BATH SALTS = SYNTHETIC CATHINONES

• Typically white powder in small packets of 500mg-1gm for about $25
• Average dose: few milligrams to >1gm
• Duration 2-3 hours
• Frequency 2-10+ per day
• Use
  – Nasal snorting
  – “Bombing”
  – “Keying”
  – Other: rectal, IV, IM, gingival, inhale
EMERGING DRUG ITEMS IDENTIFIED IN U.S. NFLIS FORENSIC LABS: 2010-2012

U.S. DEA, Office of Diversion Control, NFLIS data, 2012. SAMHSA lecture*
### Clinical Symptoms of Synthetic Cathinone Use in Patients Admitted to the Emergency Department (N=236)

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agitation</td>
<td>82%</td>
</tr>
<tr>
<td>Combative/Violent behavior</td>
<td>57%</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>56%</td>
</tr>
<tr>
<td>Hallucinations</td>
<td>40%</td>
</tr>
<tr>
<td>Paranoia</td>
<td>36%</td>
</tr>
<tr>
<td>Confusion</td>
<td>34%</td>
</tr>
<tr>
<td>Myoclonus/Movement disorders</td>
<td>19%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>17%</td>
</tr>
<tr>
<td>Chest pain</td>
<td>17%</td>
</tr>
<tr>
<td>CPK elevations</td>
<td>9%</td>
</tr>
</tbody>
</table>

Spiller et al. (2011). *Clinical Toxicology*, 49, 499-505.
CATHINONE: DIAGNOSIS

• Clinical presentation

• Urine drug screen is not reliable
  – Even with specific screening most labs test only for Methylenedioxypyrrovalerone (MDPV)
  – Sometimes false positive for methamphetamine

• History from patient and collateral sources
CATHINONE: TREATMENT

• Supportive
  – Cardiac, Renal, Hyponatremia may necessitate hospitalization
  – Psychiatric may necessitate hospitalization for safety
    • Agitation: Benzodiazepines
    • Hallucinations: low-dose antipsychotics for hallucinations (Risperidone 1mg)
      – Avoid aggressive use of antipsychotics due to increased morbidity

• Monitor for vitals/lab abnormalities
  – Hyperthermia, dehydration, Renal function
MDMA – Ecstasy
MDMA (ECSTASY)

- 3, 4-methylenedioxy-methamphetamine
- Street terms: Adam, E, X, XTC, love drug, Molly
- Cost per pill ranged from $3-$30
- Synthetic psychoactive drug
  - Both stimulant and hallucinogenic properties similar to methamphetamine and mescaline
- INCREASES DA, 5-HT, and NE
  - Inhibits 5-HT, DA, and NE reuptake, reverses transporters, decreases MAO activity
  - Releases 1.5 times more 5-HT than DA, more potent as 5-HT transporter inhibitor
- Releases oxytocin via directly and indirectly agonizing 5-HT entactogenic

WHAT IS “MOLLY”

1. Ecstasy pills with little MDMA and lots of caffeine, meth, assorted drugs?  OR
2. A pure crystalline form of MDMA, most often sold as a powder filled capsule?  OR
3. Methylone/Bath salts?
   - Reports of desired effects of euphoria, but also increased paranoia, agitated delirium, scary hallucinations, psychotic episodes, violent or destructive self-harm behavior, including death
   - Molly usually is not a pure form of MDMA, but may be a drug that can be very dangerous since its contents are unknown

Source - Will They Turn You into a Zombie? What Clinicians Need to Know about Synthetic Drugs (2nd Edition), SAMHSA
MDMA (ECSTASY)

• Adverse effects:
  – *Serotonin Syndrome*
  – Sweating, hyponatremia
  – Decreased coordination
  – Jaw clenching
  – Agitation
  – Hyperthermia
  – Rhabdomyolysis
  – hepatotoxicity

Mortality

• 1997-2007 in the UK there were 605 deaths related to MDMA
• Polydrug use a large factor
• Hyperthermia related: 40-43°C (104-109), multiple organ failure
  • Induces apoptosis in cultured liver cells, acute liver failure
• Cardiac arrest
• Seizure
• Rhabdomyolysis

NIDA. (2010). *NIDA InfoFacts: MDMA (Ecstasy). SAMHSA lecture*
MDMA Diagnosis & Treatment

- Serum and urine assays for MDMA
  - Negative test cannot confirm symptoms are result of MDMA toxicity
- Treatment for toxicity
  - ED Referral
  - Symptomatic care
    - IVFs, Oxygen
    - HTN-benzos 1st line and usually sufficient
    - Agitation-benzos
    - Psychosis-
  - Monitor
    - Serial neurological checks
    - Telemetry
    - Labs-Glucose, Renal/Liver
    - Urine output
  - Cool core temperature
  - Seizure treatment with benzodiazepines
  - Activated charcoal for ingestion within 1 hour
PIPERAZINES

• Street Names:
  – “Frenzy”
  – “Charge”
  – “Herbal ecstasy” or “Legal X”
  – “A2”

• Two classes:
  – benzylpiperazines (BZP) and phenylpiperazines (TFMPP)

• Mimics effects of ecstasy (MDMA): ↑5-HT, DA, NE
  – Particularly dangerous if mixed: seizures and coronary syndromes

Adverse Events

• HTN/Tachycardia
• Reduced consciousness
• Psychosis
• Hyperthermia/coma

Dextromethorphan - DXM
DEXTROMETHORPHAN (DXM)

- Dissociative hallucinations
  - distance from reality
  - visual effects
  - perceptual changes
  - mystical-type experiences similar to psilocybin.
- Tachycardia, hypertension, agitation, ataxia, and psychosis at high doses; need to be careful of serotonin syndrome
- OTC often found in combination
  - Acetaminophen
  - Diphenhydramine
  - Phenylephrine or pseudoephedrine
  - Alcohol
- Monitoring the Future survey 2011
  - 5% of 12 graders used in the past 12 months

Reissig et al. (2012). *Psychopharmacology, 223*(1), 1-15
DEXTROMETHORPHAN (DXM)

• Street names include
  – “Robo” or act of using “Robo-tripping”
  – Triple Cs

• “Plateaus”
  – Darkridge.com – street lore regarding different levels of high
    • “1st plateau (100-250mg): Great for conversation, yet can be a powerful trip. It all depends on the mindset. Usually one is very empathetic, and has great insights to everything”
    • “2nd plateau (250-450mg): All the effects of the 1st plateau are present, with the addition of more euphoria, a decreased sense of time and a decreased sense of surroundings.”
    • “3rd plateau (450-800mg): Many of the effects of the first two plateaus are present + Visual (closed-eye-visual, mostly) hallucinations. Insights are extraordinary. “
    • “4th plateau (800-1800mg): The highway can be crossed at this plateau. What is on the other side of the highway could be anything. Alien encounters, out of body experiences, etc. are not uncommon.”
“SYRUP” OR SIZZURP

- Codeine + Promethazine cough syrup
- Cut with jolly ranchers/flavoring, and soft drink
- Sedation, pain relief, euphoria
  - Promethazine potentiates the codeine
- Hip-Hop/Rap music phenomenon
  - Pimp C – death 2008 associated
  - Lil Wayne - continues to struggle
GAMMA HYDROXYBUTYRATE (GHB)

• 2 types of users
  – Body builders, self-med: depression, anxiety, insomnia
  – Recreationally: clubs, socially - enhancement of sexual experience/aphrodisiac
  – Will use concurrently with MDMA, cocaine, alcohol, methamphetamine
  – Higher use among young club goers
GAMMA HYDROXYBUTYRATE (GHB)

• **Acute Intoxication**
  – Unpredictable product, steep dose-response curve $\Rightarrow$ difficult to titrate dose and overdose is common
  – Vitals: hypotension, bradycardia, decreased respiratory rate, hypothermia
  – CNS: Coma (within 15 minutes)
    • Agitation: including self-injurious behaviors
    • Amnesia
    • Seizure/seizure-like: myoclonus,
    • Ataxia, disconjugate gaze
  – Respiratory depression
  – CV: brady and hypotension, arrhythmias
  – GI: vomiting, incontinence
WHAT DO YOU DO IF SOMEONE HAS TAKEN AN UNKNOWN DRUG?

• Call your local poison center at 1-800-222-1222
  – 57 poison centers around the country have experts waiting to answer your call.
  – The experts at the Center can help you decide whether someone can be treated at home, or whether he or she must go to a hospital.
• Dial 9-1-1 immediately if they:
  – Stop breathing
  – Collapse
  – Have a seizure

...or if they have taken one of these and are having physical symptoms or behaving in a way that is concerning to you

For More Information

http://www.teens.drugabuse.gov/

http://www.drugabuse.gov/drugs-abuse/club-drugs

http://drugpubs.drugabuse.gov/promotions/back-to-school

http://www.samhsa.gov/
SPECIAL THANKS – MARK DUNCAN, MD
1. Will they Turn You into a Zombie? What Clinicians Need to Know about Synthetic Drugs (2nd Edition). Substance abuse and Mental Health Services Association (SAMHSA)


