SYNTHETIC DRUGS: BATH SALTS, HERBAL INCENSE AND MORE...

Alexander Garrard, PharmD
Clinical Toxicologist
Upstate New York Poison Center
Disclosure

- I have no possible financial or personal relationships with commercial entities (or their competitors and products) that may be referenced in this presentation.
Objectives

- Identify emerging trends in synthetic drugs of abuse
- Understand the history, development, and pharmacology of synthetic drugs
- Recognize the most common clinical manifestations of these drugs
- Apply appropriate management principles and modalities in intoxicated patients
One major caveat

- Very few street drugs are 100% pure
- Many are adulterated or contaminated
- Discussion will be over pure presentation
Shrub to Bath Salts?
Catha Edulis
Khat plant geography
What is khat?

- Cathinone active alkaloid in khat leaves
- Chewing popular in middle east
- Produces amphetamine-like sympathomimetic symptoms
What are bath salts?

- Synthetic cathinone derivatives
- Synthesized as early as 1928 and studied for medical use
  - Methcathinone
  - Mephedrone
- Bupropion only cathinone with medical indication
- MDPV, mephedrone, buphedrone, pentedrone, methylone, 4MEC, 4MePPP, α-PVP, etc
Structures!

Cathinone  
\[
\begin{align*}
\text{NH}_2 & \quad \text{NH}_2 \\
\text{CH}_3 & \quad \text{CH}_3 \\
\end{align*}
\]

Methcathinone  
\[
\begin{align*}
\text{NH} & \\
\text{H}_3 & 
\end{align*}
\]

Amphetamine  
\[
\begin{align*}
\text{NH}_2 & \\
\text{CH}_3 & 
\end{align*}
\]

Mephedrone  
\[
\begin{align*}
\text{H}_3 & \\
\text{H}_3 & 
\end{align*}
\]

Bupropion HCl  
\[
\begin{align*}
\text{CH}_3 & \\
\text{N} & \\
\text{H}_3 & \\
\text{H}_3 & \\
\end{align*}
\]

Source: EMCDDA (2009c).
Pharmacology

- Similar to amphetamines
  - Affect dopamine, serotonin, and norepinephrine
- Neuronal stimulation due to increased post-synaptic catecholamines
  - Increased release of catecholamines
  - Blockade of pre-synaptic uptake and storage
  - Reduced MAO activity
  - Indirect glutamate pathway stimulation
- End result: increased chemicals in the synapse causing increased effects
How supplied?

- Powder, capsules, and tablets
- Insufflation, ingestion, IV use, and rectal use
- Mephedrone: 100 – 200 mg
- MDPV: 10 – 15 mg
- Effects within 30 mins; lasts up to 7+ hours
Patient Case

- 30 yo male admits to using 1 – 2 grams of bath salts daily x 2 months
- VS: 187/93 P129 R12-16 T 98
- Presents to ED “shaky and anxious” and hallucinating

- Administered lorazepam
- Patient returns to baseline 24 hours later
Patient Case

- 26 yo male presents to ED after injecting bath salts
- Found agitated, altered, violent and combative and foaming at the mouth by EMS
- VS: 148/66 P 175 T 106.3 (rectally)
- Patient intubated with RSI and aggressive cooling measures instituted
- CK peaked at 235,377 U/L (normal < 170 U/L)
Patient Case

- 40 yo male injected unknown amount of “bath salts”
- Became aggressive, uncontrollable, delusional, removed all his clothing, and violent behavior
- Tazed by police and had be physically restrained by EMS
- VS: P 164 131/72 R24 rectal temp 105.4
- Declared brain dead 42 hours after presentation after complicated ICU stay
Clinical Manifestations

- Agitation (53.3%)
- Tachycardia (40%)
- Hypertension (20%)
- Seizures (20%)
- Palpitations (13.3%)
- Hallucinations/delusions
- Paranoia
- Renal failure?
- Cannibalism?
- Death
Clinical Manifestations

- 45% of patients experience symptoms beyond 24 hours post exposure
- 30% have symptoms > 48 hours post exposure
- Are there adulterants present or contaminants?
Management

- Protect yourself!
  - Difficult to manage patients and unpredictable behavior
- ABCs
- No antidote
- GI decon?
- BZDs, BZDs, and more BZDs for agitation
  - DPH likely won’t be effective
  - Haloperidol could be problematic
Management

- All BZDs work the same
  - Increase frequency of chloride channel opening leading to hyperpolarization
  - Only works in conjunction with GABA

<table>
<thead>
<tr>
<th></th>
<th>Diazepam</th>
<th>Midazolam</th>
<th>Lorazepam</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Onset</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>Quick (min)</td>
<td>Quick (min)</td>
<td>5 – 20 min</td>
</tr>
<tr>
<td>IM</td>
<td>Unpredictable</td>
<td>5 – 10 min</td>
<td>20 – 30 min</td>
</tr>
<tr>
<td><strong>Duration</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single dose</td>
<td>Short</td>
<td>Short</td>
<td>Long</td>
</tr>
<tr>
<td>Repeated Doses</td>
<td>Long</td>
<td>Intermediate</td>
<td>Long</td>
</tr>
</tbody>
</table>
Management

- What if BZDs do not work?
  - No real ceiling to BZD doses
    - Respiratory depression
  - Haloperidol
    - Anticholinergic
    - QTc prolongation
    - Risk vs benefits
- Bring product into ED
Synthetic Cannabinoids
Where did it come from?

- 1960s: research into THC-like compounds
  - Analgesic and anti-inflammatory minus psychotropic effects
- Recognized as drugs of abuse in early 2000’s in Europe
- Dr. JW Huffman researched THC analogues for use in cancer and AIDS patients
  - Developer of JWH compounds
  - HU-210 from Hebrew University
What are they?

- Synthetic cannabinoids which work on the CB₁ and CB₂ receptor like THC
- Marketed as herbal incense, herbal smoking blends, potpourri, etc.
  - Spice, K₂, Mr. Nice Guy, Legal Funk, Tai Fun, Zen Ultra, Smoke, Chaos Mint, etc.
- Misleading packaging
  - Not for human consumption
- Commonly smoked
What’s in them?

\[\Delta^9\text{-tetrahydrocannabinol (THC)}\]
Pharmacology

- Effects likely from mixture of herbs and actual synthetic compounds
  - Baybean, Beach bean, Dwarf skullcap, red clover, vanilla, honey, wild dagga and more

- Affects CB1 and CB2 receptors found in CNS/PNS
  - Responsible for elevating mood, anxiety, cognition
  - Responsible for reducing inflammation induced pain

- HU-210 100-800x more potent than THC
Patient Case

- 21 yo male smoked some K2 earlier in evening
- Presents to ED tachycardic, dilated pupils and with myoclonic jerking
- Given BZDs and symptoms resolved over 8 hours
Patient Case

- 48 yo man had generalized seizure within 30 minutes of ingesting a synthetic marijuana-like product
- Initial vital signs were: pulse, 106/min; BP, 140/88 mmHg; respirations, 22/min
- GCMS confirmed substance to be JWH-018
Patient Case

- 35 yo male admits to smoking legal weed 90 minutes ago
- C/o chest pain and dizziness
- Supportive care instituted
- Patient leaves AMA
Clinical Manifestation

- Most information from case reports and case series
- Psychiatric effects predominate
  - Anxiety, paranoia, agitation, delusions, and psychosis
- Physical manifestations
  - Tachycardia, HTN, diaphoresis, seizures, and ????
Management

- Like bath salts, unpredictable
- ABCs
- GI decontamination
- No antidote
- Supportive care
  - BZDs for agitation and anxiety
- Bring product into the ED
Ecstacy-related Compounds
Ecstasy-related Compounds

- 1990s: surge in use of 3,4-methylenedioxy-N-methylamphetamine (MDMA)
- Many new derivatives available now
- Most contain little MDMA
  - Amphetamine, DXM, BZP, etc.
- Next generation includes:
  - Tryptamines
  - Phenylethylamines
  - Piperazines
Tryptamines

- Re-emerged on drug scene
- Include DMT, 5-MeO-DIPT, 5-MeO-DMT, and more
  - Yakee plant, Foxy methoxy, alpha-O, O-DMS, alpha and bufo toad secretions
- Similar to psilocybin, psilocin, and bufotenine
- Derivatives of tryptamine contain stimulant and hallucinogenic effects
Tryptamines
Tryptamines

- DMT discovered in 1960s
- “Businessman’s lunch”
- DMT used in South America for spiritual and medicinal purposes
- Available in various formulations
Tryptamines

- Mechanism of action not fully elucidated
- Similar to classical hallucinogens like LSD
  - Agonists at 5-HT$_2$ and 5-HT$_{1C}$
- Presentation includes
  - Empathy
  - Euphoria
  - Visual/auditory hallucinations
  - Tachycardia/HTN
  - Confusion
  - Seizures
Tryptamines

- Management essentially supportive
- No specific antidote
- Benzodiazepines used for sympathomimetics symptoms
Phenylethylamines

- Newer designer analogues designated “2C” series
  - DOM: STP (Serenity, Tranquility, & Peace)
  - Mescaline: Mesc, Buttons, Cactus
  - 2C-B: Nexus, Bromo, Bees, Venus
  - 2C-T-2: Triptasy or Beautiful
  - 2C-E: Europa, Eternity
  - 2C-T-7: Blue Mystic and 7th Heaven
- Magical half-dozen
Phenylethylamines

- Exact mechanism uncertain but...
  - Direct and indirect sympathetic receptor stimulation
  - Inhibition of monoamine oxidase
  - Inhibition of reuptake by presynaptic neurons
  - Biotransformation to indolamines related to 5-HT
  - $5\text{-HT}_{2A}$ agonism

- Net result: hallucinogenic and stimulant activity
Phenylethylamines

- Phenylethylamine
- Amphetamine
- Methamphetamine

2,5-dimethoxy-4-(n)-propylthiophenethylamine (2C-T-7)
4-Bromo-2,5-methoxyphenyl-ethylamine (2CB)

3,4-Methylenedioxyethylamphetamine (MDMA)
Phenylethylamines

- Hallucinations
  - Visual and auditory
- Euphoria
- Entactogen
- Tachycardia
- Paranoia
- Delirium
- Violent behavior

- Several fatalities reported with 2C-T-7
- Recently in Oklahoma
  - Death in young adult secondary to 2-CE exposure
- MAOI activity coupled with polysubstance ingestion?
Management

- Management largely supportive
- Gut decontamination indicated depending on route of administration
- Benzodiazepines as indicated for sympathomimetic symptoms
http://www.erowid.org/library/books_online/pihkal/pihkal033.shtml
Piperazines

- Popular drugs of abuse marketed as “Party Pills” and “Legal Ecstacy”
- Street names include Benzo Fury, A2, Molly, MDAI, XXX Strong as Hell, and Exotic Super Strong
- Piperazines used as antihelminthic agents
Piperazines

- 1970s: potential antidepressant due to active metabolite
  - Serotonin reuptake inhibition and receptor agonism

- Due to adverse side effect profile, not pursued
  - BZP increased DA more than 5-HT → increased motor activity

- BZP schedule I drug as of 2004
  - TFMPP currently unscheduled
Pharmacology

- Increases sympathomimetic activity
  - Increased release of serotonin, norepinephrine, and dopamine
  - Inhibition of serotonin reuptake

- Net result: increased excitatory neurotransmitters in synapse
Piperazines

- BZP and TFMPP often combined due to synergistic and MDMA-like effects

- Presentation mix of stimulant and hallucinatory effects

- Deaths reported with BZP
  - 23-year-old woman developed massive brain edema and subsequent tonsillar herniation
Management

- Management largely supportive

- Benzodiazepines as indicated

- TFMPP and BZP known to be skin irritants
  - Skin decontamination

- Piperazines known to cause QTc prolongation in about a third of patients
  - EKG
Poison Control

- 24/7/365
- RNs, PharmDs, MDs
- On-call toxicologists
- Public and professional education
- 1-800-222-1222
Questions?