Will They Turn You into a Zombie? What Behavioral Health Clinicians Need to Know about Synthetic Drugs

Beth Rutkowski, MPH

July 16, 2014

AZ Summer Institute, Prescott, Arizona
Part 1 will review:

- Key terms
- Major classes of synthetic drugs
- Acute and chronic effects of synthetic drugs
- Extent of synthetic drug use (epidemiology)
What made you decide to select this workshop?

What do you hope to learn?
Training Collaborators

• South Southwest Addiction Technology Transfer Center
  – University of Texas at Austin, School of Social Work
• Pacific Southwest Addiction Technology Transfer Center
  – UCLA Integrated Substance Abuse Programs
• Centre for Addiction and Mental Health, Research Imaging Centre
Special Acknowledgements

• Dr. Volker Auwaerter, University Medical Center Freiburg, Germany
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• Dr. Paul Griffiths, EMCDDA
• James Hall, Nova Southeastern University
• Dr. Barry Logan, National Medical Services Labs, Inc.
• J. Randall Webber, JRW Behavioral Health Services
What are we talking about?
Have your heard these other media reports about “Bath Salts”?

- The man who slashed himself to remove the “wires” in his body
- The mother who left her demon-ridden 2-year-old in the middle of the highway
- The 21-year-old son of a family physician who, after snorting bath salts once, shot himself following 3 days of acute paranoia and psychosis, including hallucinations of police squad cars and helicopters lined up outside his house to take him away

“Tales of Bath Salts and Zombie Cannibalism”

- Bath Salts made headlines in summer 2012 when a story of possible cannibalism was reported in Miami, FL

- The Miami-Dade Medical Examiner found no traces of bath salts, LSD, or synthetic marijuana in the perpetrator's system

- The sole psychoactive substance detected was cannabis (marijuana)
Educational Objectives

At the end of this presentation, participants will be able to:

1. Identify the key characteristics and effects of synthetic drugs, most notably synthetic cannabinoids and synthetic cathinones.

2. Explain the neurobiology of synthetic drug use, and the differential impact of synthetic drugs vs. “classic” illicit drugs, such as marijuana and cocaine.

3. Describe the current information available on the availability and patterns of synthetic drug use in the United States.

4. List at least three strategies for communicating the dangers involved with synthetic drug use.
AN INTRODUCTION TO KEY TERMS AND DEFINITIONS
How Psychoactive Substances Work

• Because of their chemical structure, alcohol and drugs have **dramatic effects** on neurotransmitters in CNS

• Effects on:
  – Mental processes
  – Behavior
  – Perception
  – Alertness

## Commonly Used Psychoactive Substances

<table>
<thead>
<tr>
<th>SUBSTANCE</th>
<th>EFFECTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol (liquor, beer, wine)</td>
<td>euphoria, stimulation, relaxation, lower inhibitions, drowsiness</td>
</tr>
<tr>
<td>Cannabinoids (marijuana, hashish)</td>
<td>euphoria, relaxations, slowed reaction time, distorted perception</td>
</tr>
<tr>
<td>Opioids (heroin, opium, many pain meds)</td>
<td>euphoria, drowsiness, sedation</td>
</tr>
<tr>
<td>Stimulants (cocaine, methamphetamine)</td>
<td>exhilaration, energy</td>
</tr>
<tr>
<td>Club Drugs (MDMA/Ecstasy, GHB)</td>
<td>hallucinations, tactile sensitivity, lowered inhibition</td>
</tr>
<tr>
<td>Dissociative Drugs (Ketamine, PCP, DXM)</td>
<td>feel separated from body, delirium, impaired motor function</td>
</tr>
<tr>
<td>Hallucinogens (LSD, mushrooms, Mescaline)</td>
<td>hallucinations, altered perception</td>
</tr>
</tbody>
</table>
“Designer” Psychoactive Substances

A REVIEW OF SYNTHETIC DRUGS
User Report #1 (Drug not specified)

- “This is the worst experience I’ve ever had”
- “The most anxiogenic substance I’ve ever used”
- “Nausea, vomiting, heart pounding like I’m going to have a heart attack”
- “Not sure whether I just said that, thought it, or read it”
- 2 hours later: “Will never take this again”

User Report #2 (Synthetic Cannabinoid)

- 3 individual “hits” from a small pipe
- “Organic” taste/no chemical odor or taste
- 5 minutes: “Feels like cannabis”
- 10 minutes: “Like an intense cannabis high”
- “More than 3 puffs might be too much”

“Designer” Psychoactive Substances

Two classes:

1. **Stimulants**: mephedrone, MPDV, piperazines, “bath salts”
2. **Psychedelics**: 2C-B, mescaline, DMT, etc.

Differences in users:

1. Stimulant users *similar to* other ecstasy users; (shifting to mephedrone and MPDV due to shortage of Ecstasy?)
2. Psychedelic users *started ecstasy use earlier*; were more frequent users; *used multiple substances*; had more legal, mental health, and social problems.

Examples of Major Synthetic Psychedelics

<table>
<thead>
<tr>
<th>DRUG NAME</th>
<th>DESCRIPTION</th>
</tr>
</thead>
</table>
| 2C-I      | Phenethylamine, via PiHKAL; stimulant and hallucinogen  
Slow onset (1 hr); long duration of action (8-10 hr.) |
| 2C-B      | Phenethylamine, via PiHKAL; visuals  
Faster onset; shorter duration than 2C-I |
| 5-MeO-DMT | Tryptamine; naturally occurring (toad, shamantic brews)  
Smoked: almost immediate, very intense, short effect (<30 min) |
| DMT       | Tryptamine; naturally occurring  
Smoked: almost immediate, very intense, short effect (<20 min) |

# Examples of Major Synthetic Stimulants

<table>
<thead>
<tr>
<th>DRUG NAME</th>
<th>DESCRIPTION</th>
</tr>
</thead>
</table>
| Mephedrone | 4-methyl-methcathinone; “Miaow”  
Similar to cocaine and MDMA (ecstasy) |
| Methylone  | β-MDMA: 3,4-methylenedioxy-methcathinone; “Explosion”  
Similar to cocaine and MDMA (ecstasy) |
| MDPV       | 3,4-methylenedioxyprovalerone; MDPV;  
“NRG-1” (Brandt, 2010); “Ivory Wave”  
Stimulant with rapid onset; 2-4 hour duration of action |
| BZP        | 1-benzyl-piperazone  
Similar to amphetamine  
1/10 potency of d-methamphetamine |

From the term “Bath Salts” to...

**Synthetic Cathinones**
- Mephedrone, methylone, 4-MEC
- Stimulants related to methcathinone, MDMA, amphetamines

**2C-Phenethylamines**
- Psychedelics related to mescaline
- Some were created in the past to imitate MDMA

**Tryptamines**
- 5-MeO-DMT & 4-AcO-DMT
- Psychedelics related to psilocin & bufotenin

**Piperazines**
- BZP & TFMPP
- Stimulants

And **Dissociatives** related to ketamine and PCP and **Opioids** related to morphine, fentanyl, and heroin.
Synthetic Drugs

- Not really “Spice,” “Bath Salts,” “Incense,” or “Plant Food”
- Chemically-based; not plant derived
- Complex chemistry
- Constantly changing to “stay legal”
- Need to prove “intended to use” to convict in some areas
Synthetic Cannabinoids
Spice vs. “Spice”
Synthetic Cathinones
Bath Salts vs. “Bath Salts”
Marijuana (Cannabis)

- Often called pot, grass, reefer, MJ, weed,
- A mixture of the dried, shredded leaves, stems, seeds, and flowers of *Cannabis* sativa—the hemp plant
- Most commonly used drug in the U.S.
- Delta-9-tetrahydrocannabinol (THC) is the main active ingredient in marijuana
- Common effects include: euphoria, relaxation, heightened sensory perception, laughter, altered perception of time, and increased appetite
- May also produce anxiety, fear, distrust, or panic, and can lead to severe mental health problems for some users.

Synthetic Cannabinoids

- Wide variety of herbal mixtures
- Marketed as “safe” alternatives to marijuana
- Labeled “not for human consumption”
- Contain dried, shredded plant (inert) and chemical additives that are responsible for their psychoactive effects.

SOURCE: NIDA. (2012). *NIDA DrugFacts: Spice (Synthetic Marijuana).*
Synthetic Cannabinoids

- Mainly abused by **smoking** (alone or with marijuana); may also be prepared as an herbal infusion for **drinking**.
- Many of the active chemicals most frequently found in synthetic cannabis products have been classified by the DEA as Schedule I controlled substances, making them illegal to buy, sell, or possess.
- Multiple “generations” of drugs.

**SOURCE:** NIDA. (2012). *NIDA DrugFacts: Spice (Synthetic Marijuana).*
Cannabinoids by Generation*

- **Generation 1**
  - Includes: JWH-018, JWH-019, JWH-073
- **Generation 2**
  - Includes: AM2201, RCS-4, JWH-122
- **Generation 3**
  - Includes: AKB48, STS-135
- **Generation 4**
  - Includes: UR-144, 5-Fluoro-UR-144
- **Generation 5**
  - Includes: PB-22, 5-fluoro-PB-22, BB-22
- **Generation 6**
  - Includes: AB-PINACA, AB-FUBINACA, ADB-FUBINACA
- **Generation 7**
  - Includes: THJ-018, FUB-PB-22

*Might even be up to Generation 8??*

*Generations set by STRL*

SOURCE: Slide courtesy of Emily Dye, DEA Special Testing and Research Laboratory, Emerging Trends Program.
# Cannabinoids by Year

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<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td>JWH-018</td>
<td>JWH-019</td>
<td>JWH-203</td>
<td>MN-24 (NNE1)</td>
<td>AB-CHMINACA</td>
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<tr>
<td>JWH-073</td>
<td>JWH-081</td>
<td>JWH-203</td>
<td>AB-FUBINACA</td>
<td>FDU-PB-22</td>
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<tr>
<td>JWH-250</td>
<td>JWH-122</td>
<td>UR-144</td>
<td>ADB-FUBINACA</td>
<td>FAB-144</td>
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<tr>
<td>CP-47,497</td>
<td>JWH-200</td>
<td>5-Fluoro-UR-144</td>
<td>AB-PINACA</td>
<td>SDB-005</td>
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<tr>
<td></td>
<td>AM2201</td>
<td>2NE1</td>
<td>5-fluoro-AB-PINACA</td>
<td>5-Fluoro-AMB</td>
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<td></td>
<td>AM694</td>
<td>STS-135</td>
<td>PB-22</td>
<td>FUB-UR-144</td>
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<tr>
<td></td>
<td>RCS-4</td>
<td>AKB48</td>
<td>FUB-PB-22</td>
<td>UR-144 Indazole</td>
</tr>
<tr>
<td></td>
<td>RCS-8</td>
<td>AB-001</td>
<td>THJ-018</td>
<td>EG-018</td>
</tr>
</tbody>
</table>

*SOURCE: Slide courtesy of Emily Dye, DEA Special Testing and Research Laboratory, Emerging Trends Program.*
The Evolution of Cannabinoids

SOURCE: Slide courtesy of Emily Dye, DEA Special Testing and Research Laboratory, Emerging Trends Program.
Naming Conventions

Developer/institution
- JWH = John W. Huffman
- AM = Alexandros Makriyannis

Website
- RCS-4 (SR-19, BTM-4)
- RCS-8 (SR-18, BTM-8)

Pharmaceutical companies
- A = Abbott Laboratories
- WIN = Sterling Winthrop

Pop culture references
- 2NE1
- AKB48
- STS135
- XLR-11
- BB-22

Chemical names
- QUPIC (PB-22)
- AB-FUBINACA
- AB-PINACA
  - N-(1-Amino-3-methyl-1-oxoButan-2-yl)-1-(Pentyl-1H-INDazole-3-CarboxAmide)

SOURCE: Slide courtesy of Emily Dye, DEA Special Testing and Research Laboratory, Emerging Trends Program.
Factors Associated with Synthetic Cannabinoid Popularity

- They induce psychoactive effects
- They are readily available in retail stores and online
- The packaging is highly attractive
- They are perceived as safe drugs
- They are not easily detectable in urine and blood samples

Six States Report Cases of Kidney Damage Linked to Synthetic Cannabinoids

• Sixteen cases of kidney damage reported by CDC
  – All admitted to hospital
  – Five required hemodialysis

• Fifteen of the patients were male; ranged in age from 15 to 33, no history of kidney disease

• In early Feb 2013, UA-Birmingham reported 4 cases of previously healthy young men, whose acute kidney injury was associated with synthetic marijuana
  – Symptoms of nausea, vomiting, and abdominal pain
  – All four men recovered kidney function, and none required dialysis

Synthetic Cannabinoid Use Leads to Dangerous Symptoms in Pregnant Women

• Leads to symptoms similar to those caused by dangerous conditions known as preeclampsia and eclampsia
  – Preeclampsia is marked by high blood pressure and a high level of protein in the urine
  – Preeclampsia can lead to eclampsia, which can cause a pregnant woman to develop seizures or coma, and in rare cases is fatal

Case Example: Synthetic Cannabinoid Use among Pregnant Woman

• A woman (35 weeks pregnant) suffered a seizure and appeared agitated
  – High blood pressure and protein in urine, treated for eclampsia
  – An emergency C-section was performed (baby in distress)
• The woman screened negative for drugs, but an anonymous caller reported the woman regularly smoked “Spice Gold,” a synthetic cannabinoid.
  – Spice Gold cannot be detected with a standard urine test.
• The baby tested negative for drugs.
• The woman required psychiatric care for psychotic behavior the day after delivery.
  – “This was not a pregnancy problem but a drug problem. Eclampsia is cured with delivery of the baby, but she did not get better after delivery.” (Dr. Cindy Lee)
Khat

• Pronounced “cot”
• Stimulant drug derived from a shrub (Catha edulis) native to East Africa and southern Arabia
• Use is considered illegal, because one of its chemical constituents, cathinone, is a Schedule I drug
• Khat found in the U.S. often comes in by mail from Africa

Synthetic Cathinones

- Could be MDPV, 4-MMC, mephedrone, or methylone
- Sold on-line with little info on ingredients, dosage, etc.
- Advertised as legal highs, legal meth, cocaine, or ecstasy
- Taken orally or by inhaling
- Serious side effects include tachycardia, hypertension, confusion or psychosis, nausea, convulsions
- Labeled “not for human consumption” to get around laws prohibiting sales or possession

Designer Cathinones

Three parts of the cathinone molecule can be modified:

- Aromatic ring
- Alkyl group
- Amine group

SOURCE: Slide courtesy of Emily Dye, DEA Special Testing and Research Laboratory, Emerging Trends Program.
Designing MDPV

Methcathinone  \rightarrow  3,4-MDPV

SOURCE: Slide courtesy of Emily Dye, DEA Special Testing and Research Laboratory, Emerging Trends Program.
Product Components

- Mephedrone
- Methylone
- MDPV
- Ethcathinones
- Methcathinones
- Fluoroamphetamineines
- Fluorocathinones
- MXE
- MPPP
- APBs
- APDBs
- Butylone
- Naphyrone
- Pentedrone
- Pentyrone
- Buphedrone
- alpha-PVP
- alpha-PBP
- alpha-PVT
- PV8
- 5-IAI
- MDAI

The use of adulterants/diluents such as inositol, benzocaine, lidocaine, caffeine, etc. is common.

SOURCE: Slide courtesy of Emily Dye, DEA Special Testing and Research Laboratory, Emerging Trends Program.
Synthetic Cathinones are $\beta$-keto (‘bk’) Analogs of Amphetamine

- Methamphetamine
- Methcathinone
- 4-Methylmethcathinone (Mephedrone)
- 3,4-Methylenedioxmethcathinone (Methyline)
- 3,4-Methylenedioxyppyrovalerone (MDPV)
Current Trends

- Methylone*
- Butylone
- DMMC
- Alpha-PVP

*China controlled methylone in January 2014

SOURCE: Slide courtesy of Emily Dye, DEA Special Testing and Research Laboratory, Emerging Trends Program.
Challenges with Chromatography Screening

- Lack of availability of the reference standard for new drugs
- Variable quality of reference standards
- Lack of purity and labeled internal standards
- Chemical similarity of new drugs within a class requires great care with identification
- Sensitivity (correctly IDs the drug)

Synthetic Drug Testing Protocol – What to Consider

• Questions to consider when selecting a toxicology laboratory:
  – For which synthetic drugs should you test?
  – How many derivatives/formulations can the laboratory detect with their test?
  – Are the newest generations (4th and above such as the AM, XLR, and UR versions) detected?
  – How much does the test cost?
Human Exposure Calls to U.S. Poison Centers on Synthetic Cannabinoids and Cathinones and the Effect of Federal Regulations

The Effect of Federal Controls on Synthetic Cannabis Calls to Poison Centers

The Effect of Federal Controls on Synthetic Cathinone Calls to Poison Centers

SOURCE: American Association of Poison Control Centers, 2010-2013 data.
“New Zealand’s Designer Drug Law Draws Global Interest”

• The law, enacted in July 2013, represents a U-turn from the traditional approach of retroactively banning synthetic drugs

• New Zealand will attempt to regulate designer drugs, allowing their sale if they go through rigorous safety testing similar to that for pharmaceuticals

• Giving users a high wouldn't be a reason to ban them

THE EPIDEMIOLOGY OF SYNTHETIC DRUG USE
Number of Emerging Drug Items Identified in U.S. NFLIS Forensic Labs: 2010-2013

**Synthetic Cannabinoids**
- 2010: 3,285
- 2011: 22,957
- 2012: 33,239
- 2013: 42,709

**Synthetic Cathinones**
- 2010: 6,766
- 2011: 14,604
- 2012: 15,284

**Source:** U.S. DEA, Office of Diversion Control, NFLIS data, 2012.
Number of Unique Types of Synthetic Drugs Identified Nationally: NFLIS (2010-2013)

![Bar chart showing the number of unique types of synthetic drugs identified from 2010 to 2013.](chart)

- Synthetic Cannabinoids:
  - 2010: 19
  - 2011: 44
  - 2012: 55
  - 2013: 47

- Synthetic Cathinones:
  - 2010: 10
  - 2011: 25
  - 2012: 37
  - 2013: 26

**SOURCE:** U.S. DEA, Office of Diversion Control, NFLIS data, 2010-2013.
Calls Received by U.S. Poison Control Centers for Human Exposure to Synthetic Marijuana, 2010 to July 2013

There was 1 cannabinoid death in 2010 and 4 in 2011

Past Year Drug Use (%) by 12th Grade Students: MTF, 2012 vs. 2013

- **Marijuana**: 36.4% (2012), 36.4% (2013)
- **Synthetic Marijuana**: 7.9% (2012), 11.3% (2013)
- **Synthetic Cathinones**: 0.9% (2013), 1.3% (2012)
- **MDMA**: 4% (2012), 3.8% (2013)
- **Hallucinogens**: 4.5% (2012), 4.8% (2013)
- **LSD**: 2.2% (2013), 2.4% (2012)

Attitudes That “Use of Synthetic Cannabis Once or Twice was Harmful” by Age Group and Prevalence of Use: Monitoring the Future, 2012-2013

Decreased Use by 18 Year Olds Between 2012 and 2013

Attitudes Towards Harm by Age Group

- 18
- 19-22
- 23-26
- 27-30
- Annual Use
Attitudes That “Use of Synthetic Cathinones Once or Twice was Harmful” by Age Group and Prevalence of Use: Monitoring the Future, 2012-2013

Decreased Use by 18 Year Olds Between 2012 and 2013

Attitudes Towards Harm by Age Group

- 18
- 19-22
- 23-26
- 27-30
- Annual Use
Percentage of U.S. Students (Grades 9 to 12) Reporting Past Year Alcohol and Other Drug Use, 2012 (N=3,884)

- Alcohol: 57%
- Marijuana: 39%
- Synthetic Marijuana: 12%
- Rx Pain Relievers: 10%
- Rx Stimulants: 9%
- Ecstasy: 8%
- Cocaine: 7%
- Inhalants: 7%
- OTC Cough Medicine: 7%
- Crack: 4%
- Methamphetamine: 4%
- Salvia: 4%
- Bath Salts: 3%

## Emergency Room Visits Related to Synthetic Cannabis and Cathinones: DAWN, 2011

<table>
<thead>
<tr>
<th></th>
<th>% Male</th>
<th>% Under Age 21</th>
<th>% Sent to ICU or Sub. Abuse Treatment</th>
<th>% Discharged Home</th>
</tr>
</thead>
<tbody>
<tr>
<td>Synthetic Cannabis</td>
<td>70%</td>
<td>55%</td>
<td>3%</td>
<td>78%</td>
</tr>
<tr>
<td>Synthetic Cathinones</td>
<td>76%</td>
<td>14%</td>
<td>12%</td>
<td>55%</td>
</tr>
</tbody>
</table>

Synthetic Cannabinoids Identified in U. S. NFLIS Forensic Labs

Source: U.S. DEA, Office of Diversion Control, NFLIS data, 2010-2013. Data not shown: ‘other/unknown’ 7% 2010; 15% all other years
Synthetic Cannabinoids Identified in U. S. NFLIS Forensic Labs

2010: 3,285 seizures, 18 subst.
2011: 22,957 seizures, 32 subst.

Source: U.S. DEA, Office of Diversion Control, NFLIS data, 2010-2013. Data not shown: ‘other/unknown’ 7% 2010; 15% all other years
### Synthetic Cannabinoids Identified in U. S. NFLIS Forensic Labs

<table>
<thead>
<tr>
<th>Compound</th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
<th>2013</th>
</tr>
</thead>
<tbody>
<tr>
<td>JWH-018</td>
<td>3%</td>
<td>2%</td>
<td>1%</td>
<td>4%</td>
</tr>
<tr>
<td>JWH-250</td>
<td>3%</td>
<td>2%</td>
<td>1%</td>
<td>4%</td>
</tr>
<tr>
<td>JWH-073</td>
<td>3%</td>
<td>2%</td>
<td>1%</td>
<td>4%</td>
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<td>JWH-081</td>
<td>3%</td>
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<td>4%</td>
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<td>AM-2201</td>
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<td>21%</td>
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<tr>
<td>UR-144</td>
<td>14%</td>
<td>6%</td>
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<td>6%</td>
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<tr>
<td>AB-FUBINACA</td>
<td>14%</td>
<td>6%</td>
<td>6%</td>
<td>6%</td>
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<tr>
<td>(5F)-PB-22</td>
<td>14%</td>
<td>6%</td>
<td>6%</td>
<td>6%</td>
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</table>

#### Data
- **2010:** 3,285 seizures, 18 subst.
- **2011:** 22,957 seizures, 32 subst.
- **2012:** 42,709 seizures, 46 subst.

#### Source
U.S. DEA, Office of Diversion Control, NFLIS data, 2010-2013. Data not shown: ‘other/unknown’ 7% 2010; 15% all other years.
Synthetic Cannabinoids Identified in U. S. NFLIS Forensic Labs

Source: U.S. DEA, Office of Diversion Control, NFLIS data, 2010-2013. Data not shown: ‘other/unknown’ 7% 2010; 15% all other years
Calls Received by U.S. Poison Control Centers for Human Exposure to Synthetic Cathinones, 2010 to July 2013

There were no synthetic cathinone fatalities in 2010 but there were 18 in 2011

Synthetic Cathinones Identified in U.S. NFLIS Forensic Labs


2010: 729 seizures, 10 subst.
Synthetic Cathinones Identified in U.S. NFLIS Forensic Labs

Synthetic Cathinones Identified in U.S. NFLIS Forensic Labs

2010: 729 seizures, 10 subst.
2011: 6,766 seizures, 21 subst.
2012: 14,604 seizures, 31 subst.

Synthetic Cathinones Identified in U.S. NFLIS Forensic Labs

THE EFFECTS OF SYNTHETIC DRUGS
“People high on these drugs can get very agitated and violent, exhibit psychosis, and severe behavior changes...some have been admitted to psychiatric hospitals and have experienced continued neurological and psychological effects.”

(Dr. Rick Dart, AAPCC President)
Short-Term Effects of Synthetic Cannabinoids

- Loss of control
- Lack of pain response
- Increased agitation
- Pale skin
- Seizures
- Vomiting
- Profuse sweating
- Uncontrolled spastic body movements
- Elevated blood pressure
- Elevated heart rate
- Heart palpitations

*In addition to physical signs of use, users may experience severe paranoia, delusions, and hallucinations.*

Cannabis vs. Synthetic Cannabinoids: Effects Seen in Clinical Cases

- **Most symptoms are similar to** cannabis intoxication:
  - Tachycardia
  - Reddened eyes
  - Anxiousness
  - Mild sedation
  - Hallucinations
  - Acute psychosis
  - Memory deficits

- **Symptoms not typically seen** after cannabis intoxication:
  - Seizures
  - Hypokalemia
  - Hypertension
  - Nausea/vomiting
  - Agitation
  - Violent behavior
  - Coma

Synthetic Cannabinoids: Other Considerations

- Unlike cannabis, synthetic cannabinoids have **no therapeutic effects**
  - *Example: no cannabidiol (anti-anxiety), so mood effects unpredictable*

- Packets can contain other psychoactive substances: opioids, oleamide, harmine/harmaline (MAO-Is) that can interact with the synthetic cannabinoid

- Cancer-causing potential of inhaling smoke from these compounds unknown

SOURCE: Doris Payer, #CHSF2013.
“A Tale of Two Cases” – Case #1

- 33 year-old male
- Employed as an imaging technician
- Stable 8-year marriage
- Previous drug use: marijuana, alcohol, tobacco
- Used “herbal incense” daily
- After 3 months of use, suddenly experienced a panic attack
- Immediately discontinued all alcohol/drug use
- Repeated episodes of anxiety still occurring after 18 months of abstinence

“A Tale of Two Cases” – Case #2

- 16 year-old female
- In treatment for alcohol dependency
- History of bi-polar disorder
- Smoked 3 “hits” of “herbal incense”
- 10 minutes later (8:00 p.m.), experienced psychotic episode
- Following observation at hospital, returned to normal (12:00 a.m.)
- Next day, no apparent after-effects

Group Discussion: Why the Discrepancy in Reported Effects?

What factors do you think played a role in the differential effects of “herbal incense” on these two users?

# Clinical Symptoms of Synthetic Cathinone Use in Patients Admitted to the Emergency Department (N=236)

<table>
<thead>
<tr>
<th>Clinical Symptoms</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>

*Source: Spiller et al. (2011). Clinical Toxicology, 49, 499-505.*
Effects of Mephedrone

**Intended Effects:**
- Euphoria
- Stimulation
- Enhanced music appreciation
- Decreased hostility
- Improved mental function
- Mild sexual stimulation

**Unintended (Adverse) Effects:**
- Bruxism (teeth grinding)
- Dilated pupils
- Poor concentration
- Problems focusing visually
- Poor short-term memory
- Hallucinations
- Delusions

## Effects of Methylone

<table>
<thead>
<tr>
<th>Central Nervous System stimulation</th>
<th>Tachycardia (rapid pulse)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Euphoria or dysphoria</td>
<td>Hypertension (high BP)</td>
</tr>
<tr>
<td>Anxiolysis/Anxiogenesis</td>
<td>Hyperthermia</td>
</tr>
<tr>
<td>Increase in sociability</td>
<td>Sweating</td>
</tr>
<tr>
<td>Insomnia</td>
<td>Dilated pupils</td>
</tr>
<tr>
<td>Restlessness</td>
<td>Nystagmus</td>
</tr>
<tr>
<td>De-realization/De-personalization</td>
<td>Trismus (inability to open the mouth)</td>
</tr>
<tr>
<td>Hallucinations</td>
<td>Bruxism (teeth grinding)</td>
</tr>
<tr>
<td>Psychosis</td>
<td>Anorexia</td>
</tr>
<tr>
<td></td>
<td>Nausea and vomiting</td>
</tr>
</tbody>
</table>

Synthetic Stimulants: Cognition

• Same changes in mental state as classic stimulants: impulsive acts, decision-making, judgment → can lead to risky behavior in nightlife context

• Single human study: 20 mephedrone users snorting in own homes (vs. drug-free visit, vs. controls)
  – Regardless of high vs. not: worse memory than controls, some personality differences (schizotypy, depression)
  – High caused drug-wanting, “speedy” effects, increased speed of movement, worse working memory

SOURCE: Doris Payer, #CHSF2013.
Bath Salts in Michigan Case Report – MMWR, May 2011

- First report to summarize epidemiology of bath salt ED cases
- Based on 35 people who had ingested, inhaled, or injected bath salts and subsequently visited a Michigan Emergency Department (ED) between 11/13/10 and 3/31/11
- Patients presented with hypertension, tachycardia, tremors, motor automatisms, mydriasis, delusions, and paranoia
- No relationship found between route of administration and severity of illness

Maine Reports Serious Infections Linked with Injection of Bath Salts

- Four cases of invasive Group A streptococcal infections
- Dangerous because it can cause infections of heart and bloodstream
- Two patients developed Streptococcal Toxic Shock Syndrome
  - Can cause rapid drop in blood pressure and organ failure
- One patient developed necrotizing fasciitis, a disease that progresses quickly, destroying muscles, fat, and skin tissue

Conclusion of Part 1

• Any questions?
• What’s to come in Part 2:
  – Neurobiology of synthetic drug use
  – Case studies
  – Other notable drugs (“new and old”)
  – Strategies to identify and assess synthetic drug users
  – Clinical implications of synthetic drug use
Will They Turn You into a Zombie?
What Behavioral Health Clinicians Need to Know about Synthetic Drugs

Beth Rutkowski, MPH
July 16, 2014
AZ Summer Institute, Prescott, Arizona
Part 2 will review:

• Neurobiology of synthetic drug use
• Case studies
• Other notable drugs ("new and old")
• Strategies to identify and assess synthetic drug users
• Clinical implications of synthetic drug use
Recap of Part 1

Any questions?
THE NEUROBIOLOGY OF SYNTHETIC DRUG USE
Normal Dopamine Transmission
Cannabinoids

• Neurobiological Concerns:
  – Shown to induce dopamine release (although less directly than stimulants) → brain reward signal → potential for compulsive use/addiction
  – Shown to impact regions of the brain responsible for coordination, problem-solving, sense of time, motivation, etc. → impaired when high
  – Effects on regions underlying learning and memory → possible long-term effects
  – Possible link to psychosis and schizophrenia

SOURCE: Doris Payer, #CHSF2013.
“Classic” Cannabinoids

- Endocannabinoid system ("endo" = within)
  - Only recently discovered, unusual, not well understood
  - Receptors: CB1 (brain), CB2 (immune system)
  - Transmitters: Anandamide, 2-AG

- THC: binds to CB1 receptor
  - But not very well (low affinity) and not very good at inducing effects (partial agonist)
  - But unlike endocannabinoid transmitters, not degraded immediately, so CB1 activation is extended/exaggerated compared to anandamide

SOURCE: Doris Payer, #CHSF2013.
Synthetic Cannabinoids

- No structural similarity to THC, but same effects profile
  - Bind to CB1 and CB2 receptors
  - Same types of physical effects & impairments
  - In animals: signs of “high” similar, but at 2-14x lower dose

- The problem: Stronger & longer-lasting than THC
  - Better binding to receptors (high affinity/potency) AND each binding event has greater effect (full agonist)
    - 4x higher affinity for CB1, 10x for CB2
    - Longer half-life so effects longer lasting
  - Products of break-down (metabolites) also psychoactive
  - Together: More, more-likely, and longer-lasting adverse effects (especially if dosing is based on cannabis)

SOURCE: Doris Payer, #CHSF2013.
Synthetic Cannabinoids: “The Next Generation”

• New compound, URB-754: Does NOT bind to CB receptors itself, but inhibits enzyme that breaks down endocannabinoids
  – More endocannabinoid around ➔ more binding to receptors

• AND, one “spice” sample was found to contain URB + a cathinone, which reacted with one another and together created a whole new psychoactive compound

SOURCE: Doris Payer, #CHSF2013.
Stimulants

• Neurobiological Concerns
  – Addiction
    • Compulsive chase and use
  – Physical health
    • Cardio-vascular (heart rate, blood pressure, etc.)
    • Body temperature
    • Long-term brain changes
  – Mental state
    • Risky decisions, impaired judgment, impulsive acts, etc.

SOURCE: Doris Payer, #CHSF2013.
“Classic” Stimulants

Direct action on synapse

• Amphetamine, cathinone: induce dopamine release
• Cocaine, methylphenidate (Ritalin): block dopamine removal
• MDMA: additional effects on serotonin
  – Dopamine effects less strong, so less “reward,” so animals do not self-administer as much
  – Synthetic stimulants are variations on this theme, BUT: “Very subtle structural modifications can yield profoundly different behavioural, neurochemical, and neurotoxicological effects.”

SOURCE: Doris Payer, #CHSF2013.
Synthetic Stimulants

- In general: dopamine ↑ and animals like/want/work for drug
  - Sign of high abuse potential
  - Recreational use can progress easily to compulsive use

SOURCE: Doris Payer, #CHSF2013.

Synthetic Cathinones

• Block transporters (removal)
  – Rank at **DAT**: MDPV/pyrovalerone >> cocaine, amphetamine/MA, methcathinone, naphyrone > mephedrone, butylone, methylone, etylone, flephedrone, MDEA > cathinone, MDMA, MBDB
  – Rank at **SERT**: MDEA, MDMA, naphyrone > MBDB, cocaine, ethylone, mephedrone, butylone >> rest
  – Rank at **NET** (fight/flight): MDPV, pyrovalerone > amph/MA, methcathinone > cathinone, mephedrone, flephedrone, naphyrone > MDMA, cocaine, methylone > MDEA, butylone, ethylone, MBDB

SOURCE: Doris Payer, #CHSF2013.
Synthetic Cathinones

• Also **release**
  – **Dopamine**: Amph/MA, cathinone, methcathinone, mephedrone*, flephedrone > MDMA (potency low)
  – **Serotonin**: MDMA, MDEA, MBDB, methylone, ethylone, butylone, mephedrone
    • Amph/MA, methcathinone, flephedrone only at very high concentrations
• Pyrovalerone, naphyrone, MDPV: **NO** dopamine or serotonin release, but still extremely good at blocking removal – 10x cocaine

SOURCE: Doris Payer, #CHSF2013.
Synthetic Cathinones vs. “Classic” Stimulants

• Mephedrone originally thought to be more like MDMA than amphetamine b/c of serotonin effects, but dopamine release more like amphetamine → greater abuse liability

• In and out of brain faster than MDMA → greater potential for repeated binge use

• Effects on body temperature regulation different from MDMA: “Adverse effects cannot be extrapolated from previous observations on MDMA” (Shortall)

• MDPV: greater self-administration than even MA

SOURCE: Doris Payer, #CHSF2013.
Synthetic Stimulants: Physical Concerns

• Norepinephrine (fight/flight) system: hyper-active movement, body temperature regulation, cardio-vascular effects

• Especially MDPV
  – Better than cocaine (x10) at producing hyper-active movement, increased heart rate & blood pressure
  – Itself does not disrupt body temperature regulation (like MA or MDMA do), but heart rate/blood pressure interact with room temperature (Fantegrossi)

• Neurotoxicity (“brain damage”): some evidence for serotonin and dopamine depletion in animals
  – Mephedrone NOT toxic to dopamine cells (several reports)
  – **BUT: Mephedrone enhances toxic effects of amph/MA and MDMA! (Angoa-Perez) → co-administration frequent, even if accidental

SOURCE: Doris Payer, #CHSF2013.
MDPV Addiction Potential

- August 2013 journal *Neuropharmacology*
- Animal self-administration
- Found to be more rewarding than methamphetamine and poses a substantial threat for compulsive use that is potentially greater than that for methamphetamine

Piperazines

- **BZP, TFMPP**: Release dopamine and serotonin, but less than MDMA or MA
- **mCPP**: serotonin release; human study: no reinforcing or stimulant-like effects (unlike MA/MDMA) (Tancer)
- **BZP + TFMPP** sometimes taken together because
  - Roughly adds up to to low-dose MDMA → but combination induces seizures (Baumann)

SOURCE: Doris Payer, #CHSF2013.
PMA/PMMA

- Serotonin effects different from MDMA: delayed peak (risk of redose/overdose while waiting), effects last longer, serotonin syndrome
- Evidence for long-term serotonin depletion (but not as pronounced as MDMA)
- Dopamine not affected long-term
- **Can interact with MAO-I$s and temperature to produce unexpected effects (Stanley)

SOURCE: Doris Payer, #CHSF2013.
Dissociative Anesthetics

**Neurobiological Concerns**
- Addiction/dependence
- Dissociation
- Mental state that mimics psychosis
- Interaction with other sedative drugs (e.g., alcohol)

**“Classic” dissociatives** (PCP, Ketamine)
- Block receptor in the glutamate system (NMDA)
  → **Slows everything down**
- Bind to brain opiate receptors
- Block removal of dopamine, serotonin, norepinephrine from the synapse (“reward”)

**SOURCE:** Doris Payer, #CHSF2013.
Synthetic Dissociatives

Methoxetamine

Same as classics, but additionally:

- Higher likelihood of abuse
  - Blocks more dopamine and serotonin removal from synapse (also 3-MeO-PCE)
  - Binds to & activates receptors: dopamine, serotonin, opiate systems

- Similar effects profile as ketamine, **BUT**
  - Takes longer to come on → risk of redosing
  - Side effects more severe
    - Mood disturbance/suicide attempts
    - Possibly toxic to cerebellum
  - Lasts longer → unwanted side effects

SOURCE: Doris Payer, #CHSF2013.
Psychedelics

Neurobiological Concerns

– Long-term psychosis
– Unpredictable effects while high
– Low abuse potential (no “reward circuitry” dopamine component, animals won’t self-administer)

“Classic” Hallucinogens
(LSD, psilocybin, 2-cx, mescaline)

– Very few human studies, have to rely on animal “head twitch” models
– 5-HT$_{2A}$ (sub-type of serotonin receptor) main site of action; correlation between binding and hallucinogenic properties \(\Rightarrow\) necessary & sufficient.

SOURCE: Doris Payer, #CHSF2013.
Synthetic Psychedelics

- Potency at 5-HT$_2$ receptors:
  LSD $\sim$ DOI > DOB >> DOM > 5-MeO-DMT > DMT
- Can roughly rank hallucinogenic properties
- But also have additional action on serotonin system

**5-MeO-DIPT (Foxy)**

- Blocks SERT (serotonin removal from synapse, like cocaine, SSRIs)
- Rats find it “like LSD, but not exactly”
  - Same for 2C-T-7
  - May be less intense: also activates 5-HT$_{1A}$, which inhibits 5-HT$_{2A}$
- Potential long-term effects
  - Toxic to petri-dish serotonin system (Nakagawa, Sogawa)
  - Giving it to adolescent rats $\rightarrow$ worse cognitive function as adults $\rightarrow$ serotonin system damage? (Compton)

SOURCE: Doris Payer, #CHSF2013.
Synthetic Psychedelics: Other Considerations

- 5-MeO-DMT interacts with MAO-I
  - (unlike classics)
  - DMT and bufotenine (active metabolite) stay in system longer (Jiang et al.)

SOURCE: Doris Payer, #CHSF2013.
Case Study #1

You work to educate people about the negative impact of alcohol and drug use and abuse. Unlike most drugs, many synthetic drugs are relatively new to the drug scene. Youth have been misinformed about the dangers, and their parents often have never heard of the drugs, as they were not the drugs that they were exposed to when growing up.

1. How would you design a public information campaign that does not scare people?
2. What messages would you want to communicate?
3. What strategies would you use to develop and publicize the campaign?
4. How would you educate youth and their parents about the risks of using synthetic drugs?
OTHER NOTABLE SYNTHETIC DRUGS – “NEW AND OLD”
What will be Covered in this Section?

- MDMA/ecstasy, and Molly
- Piperazines
- 2C-Phenethlyamines
- Psilocybin/Psilocin
- Dextromethorphan
- PCP
- Kratom
- Krokodil
- Benzo Fury
- Syrup/Sizzurp/Drank
- Dabs/Vapor Pens
Changes in Psychoactive Substances Identified in Forensic Laboratories in US: 2004-2013

MDMA (Ecstasy)

- 3, 4-methylenedioxy-methamphetamine
- Street terms: Adam, E, X, XTC, love drug, Molly
- A synthetic, psychoactive drug with both stimulant and hallucinogenic properties similar to methamphetamine and mescaline
- Adverse effects: enhanced physical activity, sweating, lack of coordination, mental confusion, jaw clenching, hyperthermia, and agitation

Glimpses of MDMA Situation in U.S.: 1999-2013

Results of Pill Tests Containing MDMA*

MDMA Items Identified in DEA’s NFLIS Tox Labs: 2004-2013


What is “Molly”?  

1. Ecstasy pills with little MDMA and lots of caffeine, meth, assorted drugs?  
2. A pure crystalline form of MDMA, often sold as a powder filled capsule?  
3. Methylone? Bath salts?  

• Reports of symptoms reported: euphoria, hallucinations, paranoia, agitated episodes, violent or destructive self-harm behavior, including death  
• Bottom line - Molly usually is not a pure form of MDMA, but may be a drug that can be very dangerous since its contents are unknown

New MDMA Warning

• European Monitoring Centre for Drugs and Drug Addiction issued warned in February 2014 that “dangerously high” levels of MDMA are appearing in Europe.

• MDMA tablets in the EU typically contain between about 60 and 100 mg of MDMA (2012 figures), however, tablets containing between 150 and 200 mg of MDMA are currently available and some have been found to contain even higher amounts, e.g. 240 mg.
Piperazines

- Frenzy, Bliss, Charge, Herbal ecstasy, A2, Legal Z, Legal E.
- Mainly available over internet and sold as ecstasy pills that are “safe.”
- Two classes: (1) benzylpiperazines (BZP) and (2) phenylpiperazines (TFMPP).
- Mimics effects of ecstasy (MDMA); dangerous with seizure disorders, psychiatric illness, or coronary disease.
- Adverse events included hypertension, reduced consciousness, psychotic episode, hallucinations, tachycardia, hyperthermia, coma. Could be toxic if combined with MDMA or amphetamines.

Piperazines

TFMPP is not controlled at the federal level but is controlled by at least 10 states.

Levels of use peaked in 2009 and have declined since.

Piperazine Reports by NFLIS Labs: 2005-2012

Hallucinogens

- 2C Family
- DOX Family
- NBOMe Family
  - Active at very low doses (similar to LSD)

SOURCE: Slide courtesy of Emily Dye, DEA Special Testing and Research Laboratory, Emerging Trends Program.
2C-Phenethylamine

- A broad range of compounds that share a common phenylethan-2-amine structure.
- Some are naturally occurring neurotransmitters (Dopamine and Epinephrine), while others are psychoactive stimulants (Amphetamine), entactogens (MDMA), or hallucinogens (the 2C-X series of compounds).
- 2 C-X can be snorted or dissolved into a liquid and placed on blotter paper under the tongue.
- May last 6-10 hours; onset takes 15 min to 2 hours.
- Reports of seizures and renal failure.

2C-Phenethylamines

- Almost all of the 2C-phenethylamines are produced in Asia, principally China, but some small labs in the U.S. are capable of producing 2C (usually 2C-B).

- In 2011, DEA offices throughout the country began noting the increasing availability and abuse of 2C at raves and in nightclubs, particularly by teenagers and young adults.

- NFLIS labs nationwide identified **193 reports of phenethylamines in 2010**, 340 in 2011, 1,097 in 2012, and **1,876 in 2013**.
Spread of 2C-Phenethylamine throughout the United States

**Figure 5.1** 2C-Phenethylamine Reports to NFLIS, by State, 2006

**Figure 5.2** 2C-Phenethylamine Reports to NFLIS, by State, 2010

2C-C-NBOMe, 2C-I-NBOMe, Mescaline-NBOMe

• Analogs of the 2C-X family of phenethylamines
• Strongly active at the sub-milligram (microgram) dose (a Super Potent drug)
• Most 25I and 25C is sold as pure powder
  – Weighing and handling pure high-potency chemicals such as LSD or 25I-NBOMe should be performed wearing eye protection, gloves, and a filter mask
• Perhaps the greatest risk of the wide availability of pure NBOMe powders is confusing one white powder for another, or simply misunderstanding the difference between one psychedelic or stimulant drug and another
• In 2011, 10 items of the NBOMe family were seized and identified in NFLIS forensic laboratories, as compared to 447 in 2012.

Psilocybin vs. Psilocin

• Psilocybin and psilocin are naturally occurring psychedelics with a long history of human use. Both are present in 'psychedelic' or 'magic' mushrooms.

• Psilocybin, the better known of these two chemicals, is metabolized after ingestion into psilocin, which is the primary active chemical.
Opioids

• **AH-7921**
  – Reported as 80% potency of morphine
  – Found on plant material and in “bath salts”

• **MT-45**
  – Reported as 80% potency of morphine
  – Possible ODs in NY and VT

• **W-15**
  – Reported as 5.4x potency of morphine

• **W-18**
  – Reported as 10,000x potency of morphine

Kronstrand, R; Thelander, G. AH7921 Case Study (2013). www.soft-tox.org

SOURCE: Slide courtesy of Emily Dye, DEA Special Testing and Research Laboratory, Emerging Trends Program.
What is **DXM**? Dextromethorphan is a psychoactive drug found in common over-the-counter cough medicines.

Dextromethorphan (DXM)

- Dextromethorphan’s slang names include “Robo;” people refer to using DXM as “robo-tripping.”
- At high doses, may produce dissociative hallucinations (distance from reality, visual effects with eyes open and closed; perceptual changes, drug liking, mystical-type experiences similar to use of psilocybin.
- Can also produce tachycardia, hypertension, agitation, ataxia, and psychosis at high doses.
- Users of DXM engage in “dose dependent” behaviors in which they try to gauge the amount of the drug they take to produce the desired effects, which they call “plateaus”. Plateau is the mildest effect and the 5th plateau will guarantee a trip to the hospital.

Enter your weight in pounds: 150

Strength: 2 mg/mL

You must drink between 85mL and 256mL of cough syrup to achieve your desired high!
Phencyclidine

- PCP, Angel Dust, Killer Weed
- Dissolved in embalming fluid ("Fry," "Amp," "Water, Water")
- Swallowed, sniffed, smoked on joints dipped in "Fry"
- Users report out-of-body strength

A Few Other Substances to Throw in the Mix...

- **Kratom** – opioid-like effects
- **Krokodil** – cheap heroin replacement
- **Salvia divinorum** – hallucinogenic effects
- **Methoxetamine** – “legal ketamine”
- **Benzofury (5-APB)** – stimulant and hallucinogenic effects

Kratom

- Structurally similar to some hallucinogens but **no hallucinogenic activity or effects**
- Acts on **opioid receptors**
- Not scheduled in U.S.
- Seems to be a **stimulant in lower doses**
  - Mitragynine
- Seems to be a **sedative at higher doses**
  - 7 hydroxymitragynine
- Often produces a **mixed effect**
- Onset of effects within 5 to 10 minutes of ingestion; effects last for several hours

SOURCE: Ken Dickenson, MS, RPh, Hon DSc, July 2013 (Emerging Drug Trends 2013: Beyond Synthetics and Bath Salts).
Kratom: Dependence, Withdrawal Symptoms, and Craving in Regular Users

• Kratom preparations have been traditionally used in Southeast Asia for its medicinal properties.
• First study to measure dependence, withdrawal symptoms, and drug craving in regular Kratom users in Malaysia (n=293).
• Physical withdrawal symptoms: muscle spasms and pain, sleeping difficulty, watery eyes/nose, hot flashes, fever, decreased appetite, and diarrhea.
• Psychological withdrawal symptoms: restlessness, tension, anger, sadness, and nervousness.
• Regular users who consumed ≥3 glasses Kratom per day, had higher odds of developing severe Kratom dependence, withdrawal symptoms, and inability to control Kratom craving.

Krokodil

• Russian cheap replacement drug for heroin made from cooking down desomorphine with gasoline, paint thinner, alcohol, iodine, red phosphorous (match heads), etc.

• In Russia, lack of clean needles and methadone, high cost of heroin, poverty, high numbers of HIV+ individuals, etc.

• No confirmed cases of desomorphine in the U.S. since 2 were identified in 2004.

• Injuries that look like krokodil can be due to shared dirty needles, bacteria, toxic adulterants, gangrene, staph infection, MRSA.
Benzo Fury

• Active ingredient is 5-APB
• Stimulant and hallucinogenic properties
• Fairly easy to buy via the Internet, at music festivals, and in clubs - priced at around $15 per pill.
• User-reported effects include:
  – Increased happiness, euphoria, extreme mood lift, increased self-acceptance, increased intimacy, closed-eye hallucinations, increased sexual interest

SOURCE: Ken Dickenson, MS, RPh, Hon DSc, July 2013 (Emerging Drug Trends 2013: Beyond Synthetics and Bath Salts).
“Syrup” in Texas

- Codeine cough syrup continues to be abused.
- Cut with Karo syrup, jolly ranchers, and soft drink.
- Hip-Hop/Rap music on syrup continues to drive this phenomenon.
- Also available as a non-alcoholic soft drink pre-packaged to introduce to youth or ready to add the syrup.
New “Relaxation” Drinks: Drank and Lean

Valerian Roots
Melatonin
Rose Hips
“Slow Your Roll”
“Slow Motion Potion”

In Colorado retail marijuana shops, there is a purple drink being sold that includes high potency THC instead of codeine.
“Sizzurp”
Cognac, Vodka, and Fruit Flavor
Dabs, BHO, Honey, Budder

• Dabs, shatter wax and vaporizer pens contain hash oil (“wax”). Supposedly 80%-90% THC. Different methods available on the Internet.

• Butane Honey Oil or Butane Hash Oil is a golden resin created by placing dried and ground marijuana into a special pvc filter. Butane gas is shot in through one end of the filter while the other end is placed in a bowl full of water. The filter spews out the fresh oil into the cold water where it sinks to the bottom. The bottom is scraped and the oil is ready to use.

• Users touch the heated knife point or the pin to the Budder on the end of a pin and inhale fumes (and sit down).
Vapor Pens

- Advertised for “patients”
- Cost $100-$200
- Potency varies
- Higher percentage of THC
- No odor. Similar to electronic cigarettes
- Pen-style vaporizers contain 100-150 hits
- Some can be recharged and refilled
- 3 types of e-cigarettes:
  - Pre-filled cartridge
  - Liquid used to fill reusable e-cigarette
  - Disposable e-cigarette

CASE STUDY, SAMPLE
TREATMENT PROTOCOLS, AND
CONCLUDING THOUGHTS
Case Study #2

A nineteen year old male reports using “spice” 7-8 times along with marijuana. He stopped using spice about 45 days ago, and stopped marijuana about 30 days ago. While on these drugs, his thoughts became disorganized, and he was having grandiose ideas. Since he discontinued his use of drugs, his behavior can best be described as manic. He sleeps 4-5 hours over a two-day period, and then sleeps 22 hours straight. He is constantly moving around, sings loudly, and has delusions about becoming a rap star. He has been hospitalized three times, and the psychiatrists keep saying “he is mentally ill and his drug use probably caused the onset.”
Case Study #2, continued

1. What additional information do you need to know before figuring out a treatment plan?
2. What kind of intervention does this young man need?
3. Do you believe he has stopped using spice and marijuana altogether?
4. Where do you go from here?
Synthetic Cannabinoids – Clinical Presentation

• Persistent depression
• Memory problems (can last for several weeks)
• Blunted affect
• Difficulty focusing
• Difficulty participating in clinical until stabilized
• Users also report elevated mood, relaxation, and altered perception
• Psychotic effects, such as extreme anxiety, paranoia, and hallucinations

Sample Clinical Treatment Protocol for Synthetic Cannabinoid Users

• Direct individual to emergency room via ambulance
• Consult a regional Poison Control Center
• Acute management consists of:
  – Supportive care with the use of benzodiazepines, if needed, to control agitation and anxiety
  – Observe until resolution of abnormal vital signs, vomiting, and psychiatric symptoms

Recognizing Synthetic Cathinone Intoxication

• Present with severe sympathetic stimulation:
  – Tachycardia
  – Hypertension
  – Hyperthermia
  – Seizures

• Present with profoundly altered mental status:
  – Severe panic attacks
  – Agitation
  – Paranoia
  – Hallucinations
  – Suicidal behavior

Sample Clinical Treatment Protocol for Synthetic Cathinone Users

• Supportive care
• Aggressive sedation with benzodiazepines (for agitation, seizures, tachycardia, and hypertension)
• Significant hyperthemia may require passive or active cooling
• Lab studies including electrolytes, renal and liver function tests, cardiac markers, and creatine kinase should be considered

What do you do if someone has taken a Synthetic 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

In Summary: Key Points

• Lack of information on the chemical contents, dosage levels, and consistent quality of the products is a major problem since users are taking drugs about which they know little, which makes provision of health care for adverse events more difficult.

• Despite widespread Internet availability and use among certain populations, health care providers remain largely unfamiliar with synthetic drugs and the multiple variations which have appeared recently.
In Summary: Key Points

• Research is needed to better understand the side effects and long-term consequences associated with the use of synthetic cannabinoids and synthetic cathinones.

• More toxicological identification of these new drugs, more information on the sources of them, as well as their distribution and patterns of use is needed to curtail future increases in use.
In Summary: Key Points

• We do not have human neurobiological data or long-term data, but we can extrapolate a few key points from the existing literature:
  – Synthetics vs. Classics: Neurobiological concerns hold up, plus more
  – In all cases, neurobiology predicts abuse potential
  – In general, synthetic versions are not a simple substitute for “classics” – effects tend to be more intense (including side effects), some unexpected, and some new interactions that were not a concern before

SOURCE: Doris Payer, #CHSF2013.
Resources for Continued Learning

• American Association of Poison Control Centers, www.aapcc.org
• Drug Enforcement Administration, www.dea.usdoj.gov
• European Monitoring Centre for Drugs and Drug Addiction, www.emcdda.europa.eu
• Office of National Drug Control Policy, www.ondcp.org
• Pacific Southwest ATTC, www.psattc.org
• Refer to the Synthetic Drugs Reference List**
Thank you for your time!

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Pacific Southwest ATTC and South Southwest ATTC:
http://www.psattc.org
http://www.attcnetwork.org/regcenters/index_southsouthwest.aspt