Synthetic Cannabinoids: Information and Guidance for Clinicians

Clinician Outreach and Communication Activity (COCA) Call
March 31, 2016
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Objectives

At the conclusion of this session, the participant will be able to:

- Describe the epidemiology and clinical effects of synthetic cannabinoid use
- Discuss recent clusters of severe disease associated with synthetic cannabinoid use in the U.S.
- Identify opportunities for clinicians to support surveillance and response efforts
Amelia M. Kasper, MD, MHS
Epidemic Intelligence Service Office
National Center for Environmental Health
Centers for Disease Control and Prevention
TODAY’S PRESENTER

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Professor
Department of Emergency Medicine
University of Mississippi School of Medicine
Executive Director-TelEmergency
Synthetic Cannabinoids: Information and Guidance for Clinicians

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The findings and conclusions in this presentation are those of the author(s) and do not necessarily represent the views of the Centers for Disease Control and Prevention
Overview

• What are synthetic cannabinoids?
• Are they a threat to public health?
• What do we know?
• What don’t we know?
• What are our next steps?
What are They?

Source: http://wreg.com/2015/05/22/mississippi-spice-use-continues-to-skyrocket/
Synthetic Cannabinoid Timeline

1960s
• SCs first synthesized

1980s
• SCs developed to study human endocannabinoid system

1986
• Controlled Substance Analogue Enforcement Act signed
Synthetic Cannabinoid Timeline

2004
SCs appear on the internet, smoke shops in Western Europe

2008
First seizure of SC products in US

2009
Germany bans some SCs
Synthetic Cannabinoid Timeline

2011
- Five SCs placed on emergency Schedule I

2012
- 51 new SCs identified
- Synthetic Drug Abuse Prevention Act signed

2015
- Largest multistate outbreak of adverse events from SCs to date
An Emerging Public Health Threat

- Increasing use
- Health effects unpredictable, can be severe
  - More potent than cannabis
- Increasing severity of illness
- Widespread misperception of safety, legality
- Unknown contents
  - Not regulated
  - Blended with other substances
Recent Outbreaks

- **Multistate (WY, OR, NY, OK, RI, KS) – Feb 2012**
  - 16 patients with acute kidney injury after SC use
  - Flank pain, nausea, vomiting
  - 8 patients positive for XLR-11
Recent Outbreaks

• **Colorado – August 2013**
  - 263 people with agitated delirium linked to SC use
    - 10 admitted to ICU, no deaths
    - Patients positive for ADB-PINACA

• **Georgia – August-September 2013**
  - 22 patients seen in the ED for agitated delirium
    - 6 admitted to ICU, no deaths
    - Patients positive for ADB-PINACA
Recent Outbreaks

- Multistate (MS, AL, NY, VA, MD, TX) – Apr 2015
  - 721 suspected cases and 9 deaths in MS
  - Altered mental status
  - MAB-CHMINACA, blends of different SCs
What We Know: How?

- Usually smoked
- Can be vaped, ingested, insufflated (snorted)
What We Know: Why?

• Inexpensive
• Readily available
• Psychoactive effects
• Perceived safety
• Not detected by most routine drug screening
What We Know: Who?

- Residents of rural and urban areas
- Predominately young men aged 20–30 years
- Use of other substances (tobacco, alcohol, marijuana)
- Clusters of illness reported in adolescents, prison population, military, homeless
What Don’t We Know

• Baseline number of users and patterns of use
• Health effects of emerging compounds
• How to rapidly diagnose intoxication
• Specific treatments (antidotes)
• Long-term effects, dependence
  ▪ Treatment?
What Are Our Next Steps?

- Continue collaboration to reduce harm
- Develop understanding of baseline SC use
- Characterize health effects in more depth
- Encourage reporting of suspected SC clusters
- Develop diagnosis and treatment guidelines
- Targeted messaging
  - High-risk populations
  - Health care providers
References


Call from ED Nurse Manager!
3 psychotic patients in ED
One more in triage
Screaming “Spice”
Two Weeks Later

>400 Patients reported statewide
6 Potential Deaths
Also Heard

- Bath Salts
- MDMA Spice
- Take him down with a ketamine dart
- Synthetic marijuana
DANGEROUS
Spice or K2 is NOT Marijuana
Do Not Use!

Message by UBlueE2
Photo by Scharlie
Marijuana Vs. Synthetic Cannabinoids
C & C
Now Larger Modifications

Drugs deadlier than marijuana, 2011

<table>
<thead>
<tr>
<th>Drug Type</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tobacco deaths</td>
<td>480,000</td>
</tr>
<tr>
<td>Alcohol deaths*</td>
<td>26,654</td>
</tr>
<tr>
<td>Prescription painkiller deaths**</td>
<td>16,917</td>
</tr>
<tr>
<td>Cocaine deaths**</td>
<td>4,681</td>
</tr>
<tr>
<td>Heroin deaths**</td>
<td>4,397</td>
</tr>
<tr>
<td>Marijuana deaths**</td>
<td>0</td>
</tr>
</tbody>
</table>

SOURCE: Centers for Disease Control and Prevention
*Listed alcohol deaths do not include indirect causes like fetal alcohol syndrome, traffic accidents, and homicide.
**Only counts overdose deaths, because no better federal data is available.
Officials: Man choked to death on a bag of weed

COLUMBIA, SC (WIS) - A Richland County man died after Richland County sheriff's investigators, hospital officials, and a review of the Fifth Circuit Solicitor's Office say he choked to death on a bag of marijuana.

Zachary McDaniel was pronounced dead at Palmetto Health Baptist on Sept. 6, 2014 after he was pulled off life support by his family, according to the sheriff's department.

McDaniel, according to a review from the Fifth Circuit Solicitor's Office, died due to "subsequent cardiac arrest which resulted in diffuse anoxic brain injury" because the bag of marijuana became lodged in his throat, cutting off vital air supply to his brain.

Sheriff's Investigators say McDaniel and a second man stole a car from the Widewater Square Shopping Center on Broad River Road before deputies attempted to pull the pair over on Metzer Road.

McDaniel and his partner, however, jumped out of the car and fled on foot, officials said.

Deputies chased the pair and eventually caught up with McDaniel, who became "combative" and resisted arrest, authorities said. Once in custody, investigators said McDaniel began having trouble breathing.

EMS workers were called and McDaniel became unresponsive, investigators said. Those EMS workers also attempted to intubate McDaniel, but his airway was blocked with the bag that he had apparently tried to ingest.

Hospital workers attempted to remove the bag from McDaniel's airway, but were ultimately unsuccessful. McDaniel's condition drastically deteriorated and he was pronounced brain dead before his family removed life support.

An autopsy at the hospital revealed McDaniel actually managed to ingest four other bags of marijuana before the fifth became stuck.

"The Sheriff's Department takes all necessary steps to ensure the safety and well being of anyone in our custody. In this instance Mr. McDaniel swallowed packages that unfortunately took his life," a statement from the sheriff's department said.

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Cannabinoid Receptor Agonists

• Full agonist Vs Partial
• CB1-CNS
  - Applications-Analgesia, Anxiolytic
• CB2 - Peripheral neuro and immune syst
  - Applications-Suppress of neurodegerative disorders
    ▪ EG-Alzheimer’s
Synthetic Cannabinoids

- Developed beginning in 1980’s
- Several Series
  - JWH- XXX  John William Huffman
  - AM-XXX  Alexandros Makriyannis
  - HU-XXX  Hebrew University
  - CP-XXX  Pfizer

Designed for Pharmaceutical use
Analgesics, MS, HIV/AIDS, Chemo
Spice K2

JWH-018
341.1780

AM-2201
359.1685
Spice

Nature of Herbals for Incense

“Not for human consumption”

Lab Analysis 2008

- Cannabicyclohexanol (CP 47,497)
- JWH-018
- JWH-073
- HU-210
Not Synthetic Marijuana!

Relating to Synthetic Marijuana, 2010-2011

The number of calls in the first 10 months of 2011 are almost double that in 2010.

In 2011, calls have been steadily rising for the past 10 months so far.

Past-Year Use of Illicit Drugs by High School Seniors (percent)

- Marijuana/Hashish: 36.4%
- Synthetic Marijuana: 11.4%
- MDMA (Ecstasy): 5.3%
- Hallucinogens: 5.2%
- Cocaine: 2.9%

SOURCE: University of Michigan, 2011 Monitoring the Future Study
Physical Reactions

MARIJUANA
PHYSICAL EFFECTS

- Elevated blood pressure
- Red eyes
- Dry mouth
- Increased breathing rate
- Faster heart rate
- Increased appetite
- Relaxed muscles

SYNTHETIC CANNABINOIDS
PHYSICAL EFFECTS

- Extremely high blood pressure (stroke range)
- Dilated pupils, red eyes
- Glazed expression
- Inability to speak
- Rapid heart rate (possible heart attack)
- Nausea and vomiting
- Kidney failure
- Muscle cramps, seizures and temporary paralysis

A. Hausloher and P. Hermann - Washington Post

University of Mississippi Medical Center

Department of Emergency Medicine
Psychological Reactions

**Marijuana**
- Paranoia
- Anxiety
- Depression
- Slow reaction time
- Distorted sense of time
- Short-term memory loss
- Feeling of relaxation
- Strange feelings or “random” thinking

**Synthetic Cannabinoids**
- Paranoid delusions
- Anxiety
- Depression
- Suicidal thoughts
- Psychosis
- Severe agitation
- Inability to feel pain
- Hallucinations
- Total memory loss
Desired Effect is the same as THC
- Teen from Indianola, Iowa
- June 6, 2010- self-inflicted GSW to head
- Friends admit he smoked K-2 one hour before
Legislation

- Introduced by Senator Chuck Grassley (R-IA)
- Passed June, 2011
- Synthetic Drug Abuse Prevention Act of 2012
  - Places SCs as Schedule 1, Controlled Substances Act
- Several States Also Enact Legislation
Next Generation

- New Drugs Developed
- Rogue Chemists
- Mild Modifications
- Law Changed to Cover Analogues
MOLECULAR EVOLUTION OF SYNTHETIC CANNABINOIDs

JWH-018  AM-2201  XLR-11  PB-22  ADB-PINACA  AB-CHMINACA MAB-CHMINACA or ADB-CHMINACA

1st Generation  2nd Generation  3rd Generation  4th Generation  5th Generation  6th Generation  7th Generation
2010-Q2 2011  Q2 2011- Q3 2012  Q2 2012- Q2 2013  Q2 2013-  Q3 2013-  Q2 2014-  Q3 2014-
AB-CHMINACA & MAB-CHMINACA
<table>
<thead>
<tr>
<th>SC Clinical Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Meant to be Same as Previous</td>
</tr>
<tr>
<td>• Instead Adverse Reactions More Severe</td>
</tr>
<tr>
<td>Hypertension</td>
</tr>
<tr>
<td>Tachycardia</td>
</tr>
<tr>
<td>Dysrhythmias</td>
</tr>
<tr>
<td>MI</td>
</tr>
<tr>
<td>Death</td>
</tr>
</tbody>
</table>
WOMAN AWAY IN HANDCUFFS EARLIER
Fumure acid
500g
Of 273 cases

• 216 analyzed
• 101 confirmed MAB-CHMINACA
• 113 predicted metabolites
• 138 either MAB-CHMINACA or metabolite
• 73 both MAB-CHMINACA and metabolite
### Other Synthetic Cannabinoids Detected

<table>
<thead>
<tr>
<th>Drug</th>
<th>Confirmed</th>
<th>Possible Formula Match</th>
</tr>
</thead>
<tbody>
<tr>
<td>AB-CHMINACA</td>
<td>36</td>
<td></td>
</tr>
<tr>
<td>AB-FUBINACA</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>AB-PINACA</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>UR-144</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>AKB-48</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>AM-2201 N-(3-chloropentyl) isomer</td>
<td>3</td>
<td>(8)</td>
</tr>
<tr>
<td>5-Fluoro-AB-PINACA</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>5-Fluoro-ADBICA, 5-Fluoro-AMB, XLR-11, JWH-018</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>5-Fluoro-THJ</td>
<td>0</td>
<td>25</td>
</tr>
<tr>
<td>JWH-210</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>FUB-AMB</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>MAM 2201</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>AM-1248</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>MDMB-CHMINACA, 5-CI-NNEI</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>
Treatment

- Agitation
  - Ativan
  - Zyprexa
  - Geodon
- Elevated Creatinine
  - Fluids
- Rhabdo
  - fluids
• Various Presentations
  - Mild - Reassurance
  - Moderate - Zyprexa, Geodon
  - Severe - Paralysis, Intubation
Current numbers in MS

- ED Visits - 1263
- Hospitalizations -
  - ED 14%
  - ED and 23 Hour Obs 59%
  - Admissions 22%
  - ICU Admissions 5%
- Suspicious Deaths - 17
What next?

DEA
MS Bureau of Narcotics
CDC/Public Health
   Epidemiology
   Education
Blasphemy: CO, OR, AK, DC
Practitioners, Poison Centers & Public Health Collaborations

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The findings and conclusions in this presentation are those of the author(s) and do not necessarily represent the views of the Centers for Disease Control and Prevention/the Agency for Toxic Substances and Disease Registry.
Poison Centers – History

**U.S. Poison Centers** originated in Chicago in 1953

- Within 10 years, expanded services to public
- 1970s saw number of centers expand to more than 600 centers
- 1978 American Association of Poison Control Centers (AAPCC) regionalized services
- 1980s and 1990s saw consolidation of centers and more consistent services
- 2003 saw amendment of Title XII of the Public Health Services Act to include Poison Centers
- 2006 saw the implementation of a web-based electronic reporting system for all Poison Centers
U.S. Based Poison Centers Today

55 Poison Centers (2014)
- 2,165,142 human exposures
- 56,265 animal exposures
- 663,305 information calls
- 2,617,346 calls originated from Poison Centers

1-800-222-1222
U.S. Based Poison Centers Today

Available 24-hours a day, every day of the year
Free of charge to users
Confidential

Manage user calls:
◦ Exposure calls
◦ Information calls

Provide follow-up calls to monitor progress and outcome
Poison Center Services

Lay public
- Accidental poisonings, intentional poisonings, & envenomations
- Pill identification
- Education, prevention, and outreach
- Pet calls*

Medical professionals
- Accidental poisonings, intentional poisonings, & envenomations
- Pill identification
- Consultation with Medical Toxicologists
Established Public Health Benefits of Poison Centers

Key roles:

1) Accessible & Affordable
   - Free, 800-222-1222
   - No direct cost to the user

2) Reduction in Health-Care Costs
   - Reduced ED Visits
   - Reduced Length of Stay

3) Toxico & Public Health Surveillance

4) Public & Professional Education

5) Research (Toxicity & Drug Monitoring)
   - CDC, FDA, Consumer Product Safety Commission, EPA, State/L
Poison Center Organization

Staffed by:

- **Managing Director** (Pharmacist or RN with ABAT certification)
- **Medical Director** (Physician board-certified in medical toxicology)

- **Specialists in Poison Information (SPIs)**
  - Often Pharmacists or RNs
  - Front-line
  - Have received specialized training in toxicology

- **Certified Specialists in Poison Information (CSPIs)**
  - Minimum 2,000 calls
  - Minimum 2,000 hours at Poison Center
  - Pass certification examination
Both linear and second order (quadratic) terms were statistically significant for least-squares second order regressions of Human Exposures ($R^2 = 0.377$). Smoothing spline fit with $\lambda = 1200$ was used for Information Calls ($R^2 = 0.768$) and Animal Exposures ($R^2 = 0.882$).

Figure 1. Human Exposure Cases, Information Calls and Animal Exposure Cases by Day since 1 January 2000.
<table>
<thead>
<tr>
<th>Site</th>
<th>Site of caller</th>
<th>Site of exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
</tr>
<tr>
<td>Residence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Own</td>
<td>1,506,125</td>
<td>69.56</td>
</tr>
<tr>
<td>Other</td>
<td>30,229</td>
<td>1.40</td>
</tr>
<tr>
<td>Workplace</td>
<td>22,688</td>
<td>1.05</td>
</tr>
<tr>
<td>Health care facility</td>
<td>458,938</td>
<td>21.20</td>
</tr>
<tr>
<td>School</td>
<td>9,878</td>
<td>0.46</td>
</tr>
<tr>
<td>Restaurant/food service</td>
<td>441</td>
<td>0.02</td>
</tr>
<tr>
<td>Public area</td>
<td>6,871</td>
<td>0.32</td>
</tr>
<tr>
<td>Other</td>
<td>124,255</td>
<td>5.74</td>
</tr>
<tr>
<td>Unknown</td>
<td>5,717</td>
<td>0.26</td>
</tr>
</tbody>
</table>
National Poison Data System (NPDS)

Introduced in April 12, 2006

• Serves as the only near real-time public health surveillance tool in the U.S.
  • Actively monitored by AAPCC & CDC for anomalies of public health significance
  • Utilized by some Poison Centers and Health Departments to monitor other locally relevant events*

• Repository for all data obtained by U.S. Poison Centers
  • Incorporated into research (public health, industry, individual health practitioners)
  • Incorporated into annual report published by AAPCC

All AAPCC member poison centers upload data to NPDS every 8 minutes providing a near real-time snapshot of poison call conditions nationwide.
Figure 2. Illustration of data flow for NPDS users.
National Poison Data System Surveillance

Data is continuously monitored using surveillance algorithms

Surveillance algorithms monitor:
- Total and human call volume
- Clinical effects volume (signs, symptoms, lab abnormalities, etc)
- Case-based specific volume (substances, clinical effects, outcomes, etc)

- Utilizes historical averages for the same location and time period using previous NPDS data.
- Anomaly reports are generated automatically and alert:
  - AAPCC Surveillance Team
  - CDC’s Health Studies Branch
  - Designated Poison Center Staff
  - Designated Public Health Agency Staff
<table>
<thead>
<tr>
<th>Definition Name</th>
<th>Definition Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute radiation syndrome</td>
<td>Human exposure to nonradiopharmaceutical isotopes or caller reporting symptoms of cytopenia and vomiting or diarrhea or coma or confusion; excluding anyone reporting disseminated intravascular coagulation, suspected suicide, intentional misuse, or exposure to radon or radon gas</td>
</tr>
<tr>
<td>Arsenic</td>
<td>Human exposure to arsenic or caller reporting symptoms of hypotension and abdominal pain and diarrhea and nausea or vomiting; excluding any dermal or malicious exposures</td>
</tr>
<tr>
<td>Botulism</td>
<td>Human exposure to botulism or caller reporting symptoms of dysphagia or muscle weakness and blurred vision or photophobia or visual defect; excluding any callers with ocular irritation</td>
</tr>
<tr>
<td>Ciguatera</td>
<td>Human exposure to ciguatera</td>
</tr>
<tr>
<td>Cyanide</td>
<td>Human exposure with caller reporting symptoms of acidosis and agitation or coma or confusion or drowsiness and hypotension; excluding any suspected suicide or exposure to ethylene glycol, methanol, aspirin, lithium, acetaminophen</td>
</tr>
<tr>
<td>Nerve agents/organophosphates/carbamates</td>
<td>Human exposure with caller reporting symptoms of excess secretions or diaphoresis or lacrimation and diarrhea or fecal incontinence</td>
</tr>
<tr>
<td>Paralytic shellfish</td>
<td>Human exposure to paralytic shellfish</td>
</tr>
<tr>
<td>Puffer fish</td>
<td>Human exposure with caller reporting ingestion of tetrodotoxin; excluding any exposure to a bite/sting or exposure to salamanders</td>
</tr>
<tr>
<td>Radiation injury</td>
<td>Human exposure with nonradiopharmaceutical isotopes or radiopharmaceuticals and caller reporting symptoms of cytopenia or vomiting or coma or burns; excluding any exposure to radon or radon gas</td>
</tr>
<tr>
<td>Ricin</td>
<td>Human exposure with caller reporting vomiting and diarrhea and abdominal pain or elevated liver enzyme levels and hypotension or hematemesis or renal failure or oliguria/anuria or increased creatinine level or cytopenia or rhabdomyolysis; excluding any exposure involving mushrooms or known formulations</td>
</tr>
<tr>
<td>Smallpox</td>
<td>Human exposure to smallpox or other biological weapon</td>
</tr>
</tbody>
</table>
Figure 2. Illustration of data flow for NPDS users.
Poison Center’s Expanded Role

**Augmenting** local public health response to emergencies
- Customize surveillance definitions
- Access & share their regional & national aggregate data
- Share NPDS real-time surveillance with external organizations (e.g. public health & regulatory agencies)

Serving as an “always staffed” public health resource
- Assist with public-health after hours lines (Rabies)
- Assist with outbreak information and messaging and monitoring (Ebola, Flu)
- Assist as a centralized data repository (Synthetic Cannabinoids)
Key Collaborations

Rapid data collection, interpretation, and integration into a public health response can only occur with coordination and collaboration between various local, state, and federal agencies.

- **Local practitioners** play a key role in accurately reporting cases and symptoms to rapidly identify and describe public health emergencies.

- **State and local health departments** are poised to aid in both data collection and monitoring as well as in implementing public health interventions.

- **Poison Centers** and NPDS must maintain flexibility to be able to adapt and respond to public health emergencies.
Great example of collaboration of both contributors and end-users of poison center data

- Initially, MSDH reached out to practitioners using a data collection tool
- Data was collected by MDOH and Mississippi Poison Control Center
- Data was entered into NPDS
- Data was used during the event to monitor:
  - Identification of new cases
  - Demographics
  - Clinical features
  - Severity of cases

Additionally, cases from adjacent states and national trends were monitored by CDC and shared with MSDH on a daily basis.

MSDH was able to provide public health interventions, resources, and tools to front line practitioners.
Practitioners

Poison Centers

Health Departments
References


To Ask a Question

- **Using the Webinar System**
  - “Click” the Q&A tab at the top left of the webinar tool bar
  - “Click” in the white space
  - “Type” your question
  - “Click” ask

- **On the Phone**
  - Press Star (*) 1 to enter the queue
  - State your name
  - Listen for the operator to call your name
  - State your organization and then ask your question
Thank you for joining!
Please email us questions at coca@cdc.gov

Centers for Disease Control and Prevention
Atlanta, Georgia
http://emergency.cdc.gov/coca
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