Learning Objectives

• Participants will be able to describe the current cocaine/methamphetamine overdose death situation in the US.

• Participants will be able to understand how stimulants damage the body and the brain.

• Participants will be able to describe the most efficacious strategies for addressing stimulant intoxication, overdose and withdrawal.
Epidemiology of Methamphetamine and Cocaine Use
**Evolution of Drivers of Overdose Deaths, All Ages**

**Analgesics** → **Heroin** → **Fentanyl** → **Stimulants**

- **Synthetic Opioids other than Methadone (Primarily Fentanyl), 36,359**
- **Stimulants, 30,231**
- **Natural and Semi-synthetic Opioids and Methadone, 14,139**
- **Heroin, 14,019**

70,630 Deaths in 2019
49,860 from Opioids (Prescription and Illicit)

Source: The Multiple Cause of Death data are produced by the Division of Vital Statistics, National Center for Health Statistics (NCHS), Centers for Disease Control and Prevention (CDC), United States Department of Health and Human Services (US DHHS).
Stimulant Overdose Rates

From 2012 through 2018, the age-adjusted rate of drug overdose deaths involving cocaine more than tripled.

The rate of deaths involving psychostimulants (including methamphetamine) with abuse potential increased nearly 5-fold.

Stimulant Overdose Rates 1999-2018

Figure 4. Age-adjusted drug overdose death rates involving stimulants, by type of stimulant: United States, 1999–2018

1Significant increasing trend from 1999 through 2006, decreasing trend from 2006 through 2012, and increasing trend from 2012 through 2018 with different rates of change over time, p < 0.05.

2Significant increasing trend from 1999 through 2005, 2008 through 2012, and 2012 through 2018 with different rates of change over time, p < 0.05.

NOTES: Deaths are classified using the International Classification of Diseases, 10th Revision. Drug-poisoning (overdose) deaths are identified using underlying cause-of-death codes X40–X44, X60–X64, X85, and Y10–Y14. Drug overdose deaths involving selected drug categories are identified by specific multiple-cause-of-death codes: cocaine, T40.5, and psychostimulants, T43.6. Deaths may involve multiple drugs. The percentage of drug overdose deaths that identified the specific drugs involved varied by year, with ranges of 75%–79% from 1999 through 2013 and 81%–92% from 2014 through 2018. Access data table for Figure 4 at: https://www.cdc.gov/nchs/data/databriefs/db356_tables-508.pdf#4.

Increase in Drug Overdose Deaths Involving Cocaine: United States, 2009-2018 Hedegaard et al., 2020

- The rate of overdose deaths involving cocaine was stable from 2009-2013.
- The rate of overdose deaths nearly tripled from 2013-2018.
- From 2009-2018 the rate of OD deaths involving cocaine was highest in the non-Hispanic black population.
- In 2018 the rate in the non-Hispanic black population was nearly twice that of non-Hispanic whites, and three times that of Hispanics.
Age-adjusted rates of drug overdose deaths involving cocaine by race and Hispanic origin.
Increase in methamphetamine overdose deaths by sex, race, and ethnicity

- Data from the 2011-2018 Multiple Cause of Death records
- Looked at age group 25-54 years old (people who use methamphetamine are mostly in this range).
- More than a 5-fold increase from 2011-2018.
- In non-Hispanic American Indians and Alaska Natives deaths more than quadrupled.
- Non-Hispanic Blacks had the sharpest increase (10-fold); this group previously had very low rates of methamphetamine deaths.
- Rates in all groups were higher in men than women; each group increased 5-fold.
U.S. Overdose Deaths Involving Methamphetamine in People Ages 25 – 54*

*Recent national data show that most people who use methamphetamine are between 25 and 54 years old, so investigators limited analysis to this age group.
Methamphetamine SW Border Seizures

U.S. Customs and Border Protection Southwest Border Methamphetamine Seizures, 2013 – 2019

- 2013: 10,969
- 2014: 12,973
- 2015: 16,351
- 2016: 21,081
- 2017: 29,311
- 2018: 39,268
- 2019: 68,355

Kilograms Seized
Psychostimulant Drug Poisoning Deaths

Psychostimulant-involved Drug Poisoning Deaths, 2007 – 2018

Source: National Center for Health Statistics/Centers for Disease Control and Prevention

Vermont Center on Behavior & Health
The University of Vermont
Methamphetamine Purity 2000-2003 and 2016-2019

Sources: The National Threat Assessment, 2005, National Drug Intelligence Center, U.S. Dept. of Justice DEA Methamphetamine Profiling Program.
Increase in Fatal Drug Overdoses Across the United States Driven by Synthetic Opioids Before and During the COVID-19 Pandemic
Distributed via the CDC Health Alert Network
December 17, 2020, 8:00 AM ET
CDCHAN-00438

Designed by LM Rossen, A Lipphardt, FB Ahmad, JM Keralis, and Y Chong: National Center for Health Statistics.
Overdose Deaths for 12-months ending August 2020

Based on data available for analysis on: 3/8/2021

Figure 1a. 12 Month-ending Provisional Counts of Drug Overdose Deaths: United States

Figure 1b. Percent Change in Predicted 12 Month-ending Count of Drug Overdose Deaths, by Jurisdiction: August 2019 to August 2020
A lethal dose

30mg

HEROIN

3mg

FENTANYL
Results: Individual factors

• Participants found the methamphetamine (MA) high attractive (energy, focus, and confidence).
  – “…gave me the confidence and courage to do things I normally didn’t wanna do.”

• Participants used MA to treat health concerns including attention difficulties, mood disorders, emotional trauma.
  – “It was, you know, the best to me, the best thing ever. I got PTSD from my childhood, and when I sleep I have nightmares. So meth kept me awake, and I didn’t have them nightmares, and I was better. I thought I was better, I was numbing my pain.”
Results: Individual factors

• Was a way some treated chronic pain.
  – A 39-year-old male laborer with a history of chronic back pain said: “When we’ve got a big day at work, I’ll take me a couple hits that morning, work all day, daylight to dark or whatever we have to do.”

• Helped to suppress withdrawal symptoms and opioid cravings.
  – “Meth will stop withdrawal; did you know that? For anything. It stops it for any kind of drugs—Xanax, Neurontin, pain pills, Suboxone. So, a lot of people have used meth to get off Suboxone.”
Results: Interpersonal factors

• Initiation of MA was often facilitated by members of the participants drug network.
• Many were given MA without knowing what it was.
  – “I was 15 when I first tried meth. I seen one of my friends that I had not seen in a while and she tells me that she had ‘ice cream.’ I didn't know what it was. And my person that I got weed off was out, so I gave her $20. I was looking for weed, but as soon as I took my first hit of meth I was like, ‘Oh my god’ because I fell in love.”
• MA was increasingly available everywhere.
Results: Community factors

• Participants uniformly described how MA is now the easiest illicit substance to acquire.
  – “Meth already took over. Meth is every corner, every street, every straight stretch you see.”
  – “You don’t even hear about selling Lorcets or Percocets anymore. Opioids are gone except for people who that actually take them for real pain.”

• Participants consistently described how the ubiquity made MA affordable, especially compared to non-medical prescription opioids (NMPOs), marijuana, and benzodiazepines.
Co-use of Opioids and Stimulants
Introduction

• Rural residents initiate drug use at younger ages.
• They are more likely to use methamphetamine (MA).
• They are more likely to engage in riskier drug use behavior.
• This study explores perceptions of methamphetamine use among people who use opioids in rural communities impacted by high rates of opioid overdose.
Results

• Interview data resulted in 3 themes related to MA use:
  – Theme 1: Environmental characteristics support MA.
  – Theme 2: Perceived benefits of MA use.
  – Theme 3: Perceived consequences of MA use.
Theme 1: Environmental factors foster use.

• Early exposure: first use in early or mid-adolescence.
  – “I was 12 years old…I was at my friend’s house…he brought out white dope (meth) and gave it to all of us. I snorted it, and my life has never been the same ever since then.”

• Availability and low cost.
  – “The price of meth has gone down…It’s hard to even give it away because everybody wants to do heroin instead…I would prefer to do heroin, but people give meth away these days pretty much.”

• Lower stigma relative to heroin.
  – “Meth is very popular. Heroin isn’t as popular; people have this stigma that it’s the devil’s drug, a bad drug.”
Theme 2: Perceived benefits of MA

• Opioid withdrawal relief.
  – “If I couldn’t find opiates, then I found out that you could use meth and it would help (with opioid withdrawal) a little bit. So I started substituting that with meth.”
  – “It gives you more energy and you feel a little bit better. You don’t feel so sick.”

• Reducing opioid use and using MA to quit using opioids.
  – “We quit – me and my mom – doing heroin and started doing meth, pretty much. That’s how we came off it.”

• Opioid overdose reversal.
  – “In our eyes, we all think that if you have meth in your shot of heroin, you’re not going to die just because it’s that helper that’s going to keep your heart going…”
Theme 2 (cont.)

• Enhancement of functioning.
  – “I don’t shoot MA to get high...I use it as a tool so that I can work my 10 ½ hour day with it and go home and still be a husband and do what I need to do…”

• Pleasurable effects.
  – Using heroin and MA sequentially or simultaneously produced a more enjoyable high.
  – “It’s a yin and yang kind of thing...they go well together.”
Theme 3: Perceived consequences of MA

• Discharge from treatment.
  – “I like the people at the methadone clinic but...some of the new policies about if you use meth then you get kicked out. After a couple UAs you get kicked out.”
  – “My wife got kicked out of the methadone clinic...she started getting sick...opioid withdrawal...I went out and started buying heroin...then we both started using the heroin, and here we are...”

• Fentanyl adulteration risk.
  – “Because of the opioids that are mixed in with the MA now, it’s more of a draw to it.”
**Discussion**

- Use of MA to cope with opioid withdrawal is concerning and reflects a need for education on MA overdose risk.
- 29.8% of rural residents compared to 2.2% of urban residents live in a county without a buprenorphine provider.
- Treatment services including Medications for Opioid Use Disorder (MOUD) should not base enrollment on abstinence.
- There is a need for evidence-based treatment for polysubstance use.
- Factors that need to be addressed include transportation barriers, community stigma, and social norms around drug use.
Stimulant Effects
Neurotoxicity

- Excessive dopamine resulting in damaged cell structures
- Cell death
- Activation of dopamine D3 receptors resulting in hyperthermia
- Disruption of the blood-brain barrier
- Overall, the altered brain state is consistent with degenerative central nervous system diseases.
Behavioral Effects of Neurotransmitters

FIG. 1  Behavioural effects mediated by the three main neurotransmitters

- Norepinephrine
  - Alertness
  - Concentration
  - Energy
  - Fight or flight stimulation

- Dopamine
  - Reward
  - Pleasure
  - Motivation
  - Drive

- Serotonin
  - Anxiety
  - Impulse
  - Irritability

- Memory
- Compulsion

Mood
- Cognitive function
- Appetite
- Aggression
- Sex
Cognitive Effects

Soon after cessation of methamphetamine use:
– Poor performance on motor and processing tasks
– Poor performance on verbal fluency and attention

After prolonged abstinence:
– Poor learning efficiency and comprehension
– Poor visual-spatial processing
– Slow processing and psychomotor speed
Cognitive Effects

It is estimated the more than 2/3 of those with methamphetamine use disorder show cognitive impairment.

Impairment is associated with older age, longer duration of use, injection route of administration and greater frequency of use.

Impairment may limit ability to follow through with treatment, comprehend advice and direction in treatment as well as generally achieve good treatment outcomes.
Cerebrovascular and Cardiovascular Disease

Leading causes of death with methamphetamine use disorder
Strokes on rise, most often with young men
Strokes are primarily hemorrhagic

Cardiovascular Disease associated with methamphetamine use:
- Pulmonary hypertension
- Cardiac arrhythmia
- Cardiomyopathy
Stroke and Methamphetamine use in Young Adults: a Review  Lappin et al., 2017

- 77 articles reviewed reporting stroke in young adult (<45) methamphetamine users.
- 81 hemorrhagic, 17 ischemic strokes reported.
- Hemorrhagic associated with oral or injection route of administration.
- Ischemic associated with inhalation.
- Following hemorrhagic stroke, 1/3 died.
- Following ischemic stroke, 1/5 died.
Stimulant Use in Pregnancy
Smid et al., 2019

Meta-analysis of 31 studies found cocaine use during pregnancy increased risk of:

• pre-term delivery,
• low birth weight,
• small for gestational age, (Gouin, 2011).

Meta-analysis of 8 studies found methamphetamine use during pregnancy was associated with:

• earlier gestational age at delivery,
• lower birth weight,
• smaller head circumference (Kalaitzopoulou, 2018).

Infants with prenatal exposure to methamphetamine exhibit jitteriness, drowsiness, and respiratory distress suggesting withdrawal.

Cocaine and methamphetamine are excreted in breastmilk and contraindicate breastfeeding.
Stimulant Use in Pregnancy
Smid et al., 2019

• Long-term follow-up of 204 methamphetamine exposed maternal-child pairs and 208 unexposed pairs (Derauf et al., 2007).

• At one month, 33% methamphetamine-exposed mothers did not have custody compared to 2% of unexposed.

• At age 3 years, heavy prenatal methamphetamine use (≥ 3 days per week) was associated with anxiety/depression and attention problems.

• At age 7.5 years, methamphetamine-exposed children had poorer cognitive function.

• UCLA Study of 4-5 year olds found impoverished vocabulary and poorer fluency with language.
Dental Effects

- Rampant caries and tooth fracture most common (Shaner, 2002; 2006)
- Periodontal disease
- Mechanisms:
  - Poor oral hygiene
  - Xerostomia (dry mouth)
    - Alpha 2 receptor stimulation inhibits saliva
    - Dehydration from appetite suppression and increased psychomotor activity
  - Soft drink consumption
  - Bruxism
  - Acidic content of MA (controversial)
  - Corrosive contaminants of MA (smoking)
Background

- Methamphetamine (MA) use has been linked anecdotally with dental disease.
- Teeth descriptions include, “blackened, stained, rotting, or crumbling teeth.”
- Explanations include reduced or absent saliva flow; the acidic nature of smoked MA.
- This study sought to objectively verify the presence of dental disease in MA users compared to non-users.
Methods

- Participating physicians provided comprehensive medical and dental assessments for MA users (n=301).
- Trained interviewers collected patients’ self-reports on oral health and substance use.
- Scores were compared to a matched comparison group of non-users from the Third National Health and Nutrition Examination Survey.
Results

• Prevalence of dental or oral disease was high in MA users (41.3%).
• MA users had significantly more missing teeth than matched controls (4.58 vs 1.96 missing, p<.001).
• MA users were significantly more likely to report oral health problems (p<.001).
• IV use of MA was significantly more likely to be associated with missing teeth than smoking MA.
Conclusions

• MA users express concern over the cosmetic aspects of their dental disease which could be a way to facilitate treatment entry.
• Most of the participants did not receive needed care for extended periods.
• Higher levels of dental conditions with IV use is counter to expectations that smoking with resultant local effects would be worse. Authors speculate that IV users are more severely addicted and thus less likely to attend to oral hygiene.
• Dentists can play a key role in early detection of MA use and can participate in collaborative care of MA users.
Dermatological Effects

- Pruritis from vasoconstriction
- Cutaneous ulcers and excoriations from skin picking (formication, “meth bugs”)
- Abscesses (“skin popping” confers greatest risk)
- Cellulitis
- Burn injuries
Acute Management Strategies
Methamphetamine Presentations to an Emergency Department: Management and Complications (Isoardi et al., 2019)

• 329 patients (378 presentations) in 2016
• ED in Brisbane, Australia
• Clinical effects:
  – Behavioral disturbance, 78%
  – Tachycardia, 56%
  – Hypertension, 42%
  – Hyperthermia, 5%
Clinical Management of Individuals who use Stimulants: 
**Acute Psychosis**

- Symptoms of acute psychosis: Auditory hallucinations, and visual (flashing lights, peripheral artifacts), olfactory, and tactile sensations. In addition, powerful paranoia and persecutory delusions are extremely common, along with ideas of reference, stereotypy and compulsive acts, blunt affect, poverty of speech, delirium, and violence.

- Stimulant-induced psychosis is generally transient and may require use of either a benzodiazepine or an antipsychotic, both of which should be discontinued when acute symptoms have resolved. Risperidone and olanzapine are less likely to cause extrapyramidal symptoms and their sedative properties may ameliorate psychomotor agitation. Monitor for hyperthermia and dehydration when antipsychotics are used in patients with acute stimulant intoxication.
Clinical Management of Individuals who use Stimulants

**Intoxication**

- Symptoms include: Euphoria, hyperexcitability, hypersexuality, increased locomotor activity, agitation, and psychotic symptoms, including paranoia and hallucinations. Objective findings of hypertension, tachycardia, and arrhythmias that present on EKGs of users reflect sympathetic overdrive.

- Acute agitation from MA intoxication is most often the condition that leads users to seek medical attention, and “talking down” the patient in a calm environment is the first course of action. Addressing possible cocaine/MA toxicity may involve emetics or lavage to remove MA pills. Benzodiazepines may be effective in acute management of agitation and distress and may reduce seizure potential in patients.
Introduction

- MA withdrawal is characterized by depression, fatigue, sleep disturbance, increased appetite, depression, and anxiety.
- Symptoms can persist 4 weeks.
- There is a significant impairment in daily functioning.
- Withdrawal can pose a barrier to harm reduction practices.
- Recent studies have identified increasing rates of MA injection.
- This study looks at the prevalence, frequency, and severity of MA withdrawal symptoms in a cohort of Persons Who Inject Drugs (PWID).
Results

• Drug use past 30 days
  – Median frequency: 173 times
  – Median number of injections: 112 times
• MA withdrawal in past 6 months
  – 53% of PWID reported withdrawal
  – 25% reported weekly symptoms
  – 20% reported very or extremely painful symptoms
Discussion

- Tranquilizer use which is associated with MA withdrawal may be reflective of self-medication of anxiety and sleeplessness in withdrawal.
- MA withdrawal symptoms are common among PWID and are associated with receptive syringe sharing.
- Receptive syringe sharing is associated with rushed injecting in public settings with increased risk of overdose and other adverse outcomes.
- Safe supply and syringe services programs targeting people who inject MA are indicated.
Clinical Management of Individuals who use Stimulants: Withdrawal

- Stimulant withdrawal symptoms consist of severe fatigue, cognitive impairment, feelings of depression and anxiety, anergia, confusion, and paranoia. For the majority of patients experiencing acute withdrawal/early-phase abstinence, most symptoms resolve within 2 to 10 days.

- Rest, exercise, and a healthy diet may be the best management approach for most people in withdrawal. Those with heightened agitation and sleep disturbance may respond to benzodiazepines, but acute depression and anhedonia associated with early abstinence generally resolve without intervention.
QUESTIONS?
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