# METHAMPHETAMINE

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# Beaman's Quick Classification of Substances

#### Uppers

- Methamphetamine
- Amphetamine
- Cocaine
- Synthetic Cathinones

#### Downers

- Alcohol
- Benzodiazepines
- Barbiturates
- Marijuana

#### Hallucinogens

- LSD
- Ecstasy
- PCP



### **Chemical Structure**

- Methamphetamine's structural similarity to the neurotransmitter, dopamine, explains its activity as a central nervous system stimulant.
- With increased methamphetamine use, dopamine production sites within the brain are destroyed—the user then becomes more heavily reliant on the drug to obtain pleasure.



Methamphetamine







- Amphetamine-type stimulants date back thousands of years
- Methamphetamine first synthesized in Japan in 1918
- Utilized to combat soldier's fatigue in WWII



### **Mechanism of Action**



[1] MA competitively inhibits reuptake of DA by DAT; [2] MA causes phosphorylation of DAT resulting in internalization; [3] MA inhibits DA synaptosomal uptake by VMAT-2; [4] Intracellular uptake of MA causes reverse transport of DA via DAT into synapse; [5] MA diffuses into synaptosomes impairing storage of DA



### Metabolism

Method of Use	Onset Characteristics
Smoking	Reaches brain in 6-8 seconds
Intravenous	Instantaneous/Very intense effects/Peaks in 4-7 minutes
Snorting	Slowest onset/Less peak effect/Longer half life

- Metabolized by the liver
  - CYP2D6/3A4
- Eliminated through urine

https://archives.drugabuse.gov/new s-events/nida-notes/1996/12/factsabout-methamphetamine



# **Intoxication Symptoms**

- Euphoria
- Increased energy and alertness

Decreased need for sleep

Decreased appetite



# **Intoxication Signs**

- Increased HR and blood pressure
- Pupillary dilation
- Hyperthermia
- Psychomotor excitation
- Analgesia



# **Intoxication Signs**

- Tactile hallucinations
  - Skin picking or cocaine bugs
  - Formication
- Paranoia
  - "Tweak Peak"
- Agitation
- Violence



### Withdrawal

- Withdrawal is not life threatening
- Treatment is supportive
- Depression, anhedonia
  - Suicidality in severe cases
- Fatigue, increased need for sleep
- Vivid dreams
- Sleep disturbance
- Increased appetite



# **Medical Emergencies**

- Rhabdomyolysis
  - Hyperthermia, seizures, decreased oral intake
  - Usually the result of acute intoxication
- Severe intoxication: grand mal seizures, stroke, cardiac arrhythmia, hyperpyrexia, death



### **Medical Consequences**

- Infection
- Hep C/HIV
- Skin abscesses
  - IV use and skin picking
  - Digging
  - Skin popping



First Year Geographic Focus Ending the HIV Epidemic: A Plan for America



#### Long Term Effects - Methamphetamine

- Meth mouth
  - Reduces salivary excretion
  - Psychomotor agitation leads to bruxism
  - Wearing down of enamel





# **Psychiatric Consequences**

- Psychiatric
  - Psychosis
    - \*Large contributor to inpatient psych hospitalization

Poor inhibitory control

Impaired attention

Impaired risk-reward decision making



# Manufacturing of Methamphetamine



#### **Multiple Routes using Same Precursor**



## **Comparison of Methods**

METHOD	REACTION TIME/PERCENT YIELD
P2P	6-8 hours; 60-85%
<b>Birch Reduction</b>	1-2 hours; 80-95%
Red Phosphorus	4-8 hours; 60-85%



### The P2P Method



- Reaction Characteristics:
  - Combination of P2P, methylamine, mercuric chloride, ethanol, and aluminum foil
  - Exothermic reaction
  - 12-18 hours
  - Mixture will separate, forming an oil layer (methamphetamine base) on top



# Flow of Precursor Chemicals from China



Source: U.S.-China Economic and Security Review Commission, 2016.



### **Regulation of Precursor Chemicals**

- In 2005, the United States Congress passed the Combat Methamphetamine Epidemic Act (CMEA) in an effort to reduce the availability of precursor chemicals specifically, pseudoephedrine
- The CMEA requires pharmacies to keep record of purchases of products containing pseudoephedrine and limits the number of those products that can be purchased
- Pseudoephedrine is common in decongestants such as Sudafed
- Mexico introduced similar regulations regarding precursor chemicals shortly after the enactment of the CMEA specifically against ephedrine and pseudoephedrine





Ephedrine

Pseudoephedrine



### **Production of Methamphetamine**

- According to the DEA's National Drug Threat Assessment of 2020, for Mexican drug cartels, the current primary method for synthesizing methamphetamine is via a reductive amination, using the precursor phenyl-2-propanone (P2P)
- This method is reminiscent of one used by motorcycle gangs in the U.S. from the 1960s to the 1980s which involved combining:
  - P2P
  - Methylamine
  - Mercuric Chloride
  - Ethanol
  - Aluminum Foil



Phenyl-2-Propanone (P2P)



#### **Birch Reduction Method**

(other names include Anhydrous Ammonia, Nazi, Lithium, and "Annie" or "Amy" method)

#### **Required Materials**

- Pseudoephedrine (no need to extract)
- Dry lithium (commonly stripped from lithium batteries)
- Anhydrous Ammonia (sources of ammonia include compressed gas cylinders, liquid ammonium fertilizer, refrigerant gas, and DIY)

o Common fertilizer nitrogen source

- Water
- Organic Solvent





### Shake & Bake Method

- Quick (40-60 minutes) and dangerous method; fires are common
- Common vessel is 1- or 2-liter soda bottles

#### **Reaction Steps**

- Mix pseudoephedrine (not extracted), organic solvent (e.g. Coleman fuel), ammonium nitrate (from cold packs), lithium (from batteries), capful of water, lye (from Drano) in small increments over time
- 2. "Burp" bottle periodically to relieve pressure and maintain gas production
- 3. Assemble HCI gas generator (methamphetamine HCI will precipitate out from solvent)





### **Red Phosphorous Method**

• Unless ephedrine or pseudoephedrine is already in powder form, it must be extracted from cold medication





# **Red Phosphorous Method**

#### **Red Phosphorous**

 Most common source is match striker plates (33-65% red phosphorous).

 Less common source is road flare striker plate caps (30-40% red phosphorous).







#### Oklahoma

- Domestic production has decreased over the past few years
- Most methamphetamine comes from Mexico via the P2P method of manufacturing
  - Controlled by Mexican DTO's
  - Fewer "seized labs" but that's because more of it is being produced in Mexico. Purity has increased
  - 950 KG seized in 2016
- Price: \$40-\$100 per gram



#### Methamphetamine Geospatial Hotspot, United States



Jalal, H., Buchanich, J. M., Roberts, M. S., Balmert, L. C., Zhang, K., & Burke, D. S. (2018) Changing dynamics of the drug overdose epidemic in the United States from 1979 through 2016. Science 361 (6408), eaau1184. 10.1126/science.aau1184



# 2018

#### More Oklahomans died of methamphetamine overdose than prescription opioid overdose.

## 2010 – Meth Arrests by County





# 2019 Meth Arrests by County





#### 2010-2019 Tulsa County Meth Arrests





#### **Methamphetamine Deaths**

	Number of Deaths		
Drug	2008	2017	Total
Prescription	509	342	5312
Prescription opioid	457	277	4653
Anti-anxiety	153	95	1616
Alcohol	98	119	1152
Methamphetamine	37	307	1613
Illicit opioids	11	69	295



#### Unintentional Methamphetamine Overdose Death Rates by Age Group\* and Gender, Oklahoma, 2013-2017



Source: OSDH, Injury Prevention Service, Fatal Unintentional Poisoning Surveillance System (Abstracted from Medical Examiner reports)

#### Methamphetamine Deaths from 2007 - 2017 in Oklahoma





#### Most Common Substances by Year of Death, Oklahoma, 2015-2017

#### Average number of Meth Cases per 100K across from 2010-2019



#### Treatment

- No FDA approved medications
- Residential programs or inpatient
- CBT
  - Even 1-2 sessions has shown benefit
- Contingency Management
  - Demonstrated to have a significant reduction used alone or with CBT
- Motivational interviewing
- 12 step groups
  - Narcotics Anonymous
- Psychosocial therapies are not sustained following cession
- Less effective for severe disorder
  - Long duration
  - Frequent use



#### Treatment

- Inpatient residential
  - Superior to detox or no treatment alone

• Effect not maintained to year 3 or follow-up





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#### **Questions?**

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