Patient Case Presentation: Acute Febrile Illness in Polysubstance Abuse

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Objectives

- Case Presentation
- Overview of methamphetamine abuse
- Methamphetamine associated complications
- Treatment recommendations
- Implications of methamphetamine addiction
- Resources

Subjective

Hospital Day 1

Patient: 42 YO Female, AB

CC: fever (all over body aches, cough x 4 days)

HPI: 42 YO female AB with known **polysubstance abuse** with amphetamines presents with diffuse fever, body aches, lethargy and weakness. **Injected herself with meth X 5 days ago. Symptoms started after her injection**.

Subjective

PMH:

Cardiac arrhythmia
Cardiomyopathy
Heart disease (diagnosed 2016)

At home medications:

- Cephalexin 500 mg cap, 1 cap qid X 7 days
- Lasix 40 mg, 1 tab po bid
- Coreg 25 mg, 1 tab bid with food
- Lisinopril 10 mg tab, 1 tab po qd
- Zofran 4 mg ODT, 1 tab q4h prn nausea

Subjective

Family History:

- Mother – psoriasis (deceased)
- Father – hypertension

Social History:

Past smoker ¼ ppd X 10 years (quit 1/29/18)

(-) Alcohol

Drug use: marijuana, other, stimulants, meth IV use

Subjective

Review of Systems: Negative for all systems, except for HPI

Allergies: Benadryl (type unknown)

Objective

ED Triage Vitals, Day 1

Height: 1.6 m (5’3”) Weight: 63.5 kg (140 lb)

BP: 135/83

Pulse: 132

Temp: 101.6°F (38.7°C)

RR: 23

SpO2: 100% (room air)

Objective

Physical exam:

Constitutional: + chills and fevers

HEENT: normocephalic, atraumatic, oropharynx clear

Eyes: EOM full, PERRL

Neck: supple , no JVD, trachea normal, no mass

Cardiovascular: RRR, no murmur, no rub

Objective

Physical exam:

Pulmonary: normal effort, no wheezes, no rhonci, no rales

Abdominal: normal appearance, no distension, no mass, no guarding

GU: no CVAT

Musculokeletal: normal range of motion

Neurologic: no sensory deficit

Lymphatic: no cervical adenopathy

Objective, Day 1

Physical exam:

Skin: warm, dry, intact, no rash

Psychiatric: normal mood, affect, normal behavior, normal speech and thought, normal judgment

Labs, Day 1

CBC	WBC 10.9, RBC 3.79, Hgb 10.8, Hct 34.0, **unremarkable**
Chemistry	Na+ 134, K+3.6, Cl 101, CO2 25, Ca 8.1, **unremarkable**
LFTs	AST 90, ALT 36
Renal	SCr 0.92, CrCl 72.9 mL/min
UA (urine analysis)	1+ urine protein, - leukocyte esterase, - nitrites, - ketones, - bilirubin
Urine chemistry	- Urine pregnancy, + amphetamines
Lactate	2.1 (0.4-2.0)
Procalcitonin	0.24 (<0.10)
CRP (C-reactive protein)	104. 9 (0.9-9.0)

Objective, ED, Day 1

XR Chest:

Comparison: 1/22/19

- Negative for pneumonia

Blood Cultures (1/27/19):

- Negative on Day 1, 2 different samples

Influenza A and B AG, rapid (nasopharyngeal):

- Negative (2 days prior, 1/25/19)

Assessment

1**) Acute febrile illness in IV drug user**

- Fever, chills and body aches
- Patient admitted to injecting herself with meth 5 days ago

2) **IV drug abuse with methamphetamine**

- + urine drug screen for amphetamines
- Known history of polysubstance abuse

3) **Cardiomyopathy with no current signs of decompensation**

- Continue carvedilol 25 mg po bid
- Continue Lasix

Plan

1) **Start NaCl 0.9% IV bolus 1000 mL** (30mL/kg/dose)
   - Start if lactic acid is 2.0-3.9 (pt's level: 2.1)

2) **Obtain Echo** because of concern for endocarditis in IV drug use

3) **Start on Tamiflu 75 mg po cap bid**
   - Based on patient's presentation of fevers, chills
   - Give despite (-) nasal swab d/t false (-) results

4) **Start Ceftriaxone 1 g Q24h empirically for SIRS due to sepsis concern, bacteremia risk with IV drug use (guideline dose)**
   - HR >90, RR >20, Temp > 38°

Medications on Hospital Day 1

- Ceftriaxone 1 g Q24h in 50 mL IVPB
  - 1st dose: 1542
- Carvedilol 25 mg po bid @1833
- NaCl 0.9% IV bolus for lactic acid >2.0
- Tamiflu 75 mg po @2138

Hospital Day 2

Echo: Normal

- Normal left ventricular size systolic function
- EF 60%
- No obvious vegetations
- No significant valvular disease

Temp: 36.1°C **(afebrile)**

Result ruled out Subacute Bacterial Endocarditis

- Continue Tamiflu
- Continue Carvedilol
- Continue Ceftriaxone
- Continue Lisinopril

Medications Hospital Day 2

- Ceftriaxone 1g Q24h in 50 mL IVPB @1432
- Tamiflu 75 mg cap po bid
  - 1st dose: 0932
  - 2nd dose: 2055
- Carvedilol Tab 25 mg bid with food
  - 1st dose: 0853
  - 2nd dose: 1731
- Lisinopril 10 mg tab @0853

Hospital Day 3

Labs: CRP down to 49

Temp: 36.8°C (afebrile)

Medications given:

- Carvedilol 25 mg tab @0917

Day by Day Changes

	Day 1 (1/27/19)	Day 2 (1/28/19)	Day 3 (3/1/19)
Labs and Results	Lactate 2.1 **CRP 104.9** Temp 101. 6°F (**38.7°C**)	Echo – EF 60% normal Temp 97°F (36.1°C)	**CRP 49.5** Temp 98.2°F (**36.8°C**)
Medications	• IV NaCl 0.9% bolus • Ceftriaxone 1 g Q24h • Tamiflu 75 mg po once @2138 • Carvedilol 25 mg once @ 1833	• Ceftriaxone 1 g Q24 h • Tamiflu 75 po bid • Carvedilol 25 mg po bid	Lisinopril 10 mg once Carvedilol 25 mg once

Discharge Plan

- Acute febrile illness
  - Unclear if it was due to methamphetamine or due to viral illness
  - CRP defervesced to 49 from 104.
- Cardiomyopathy
  - Previous cardiomyopathy may have been amphetamine related and resolved due to beta blocker
  - F/u with PCP. EF is normal now. May be able to stop medications
- Methamphetamine use
  - Social worker provided her resources

Discharge Medications

- **No new medications on discharge**
- Continue home medications:
  - Cephalexin 500 mg cap qid X 7 days
  - Furosemide 40 mg bid
  - Ondasetron 4 mg ODT prn nausea
  - Lisinopril 10 mg qd
  - Carvedilol 25 mg bid

May be able to stop medications now that EF is normal. Follow up with PCP in 1-2 weeks

OVERVIEW OF METHAMPEHTAMINE ABUSE

What is Methamphetamine?

- HIGHLY addictive illicit drug and **CNS (central nervous system) stimulant**
- **Street names:** “crystal”, “ice”, “chalk”, “crank”, “glass”, “rock candy” or “speed”
- **Routes: oral, smoking, snorting, injecting**
- 2 most common forms:
  - **Crystalline Powder:** white to light brown
  - **Crystal, rock-like form:** white color, known as “crystal meth”

Common Forms of Street Methamphetamine

Left: Crystal Meth

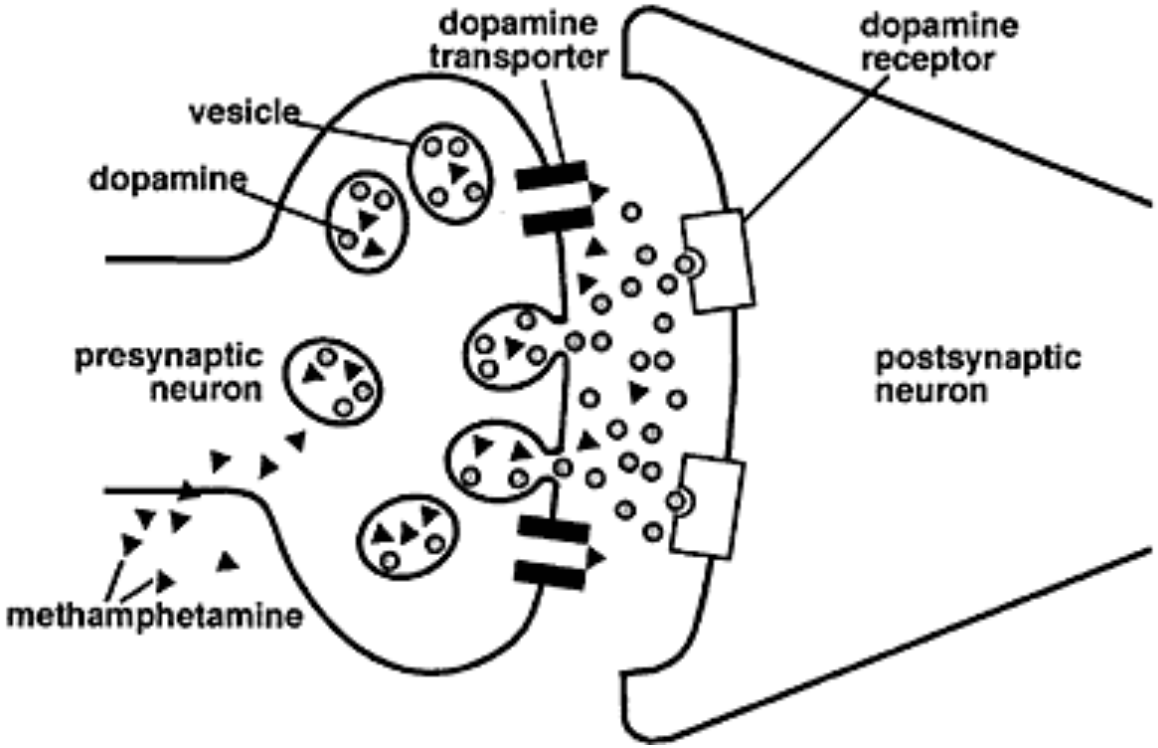
Right: Powder Meth

Methamphetamine is a psychostimulant

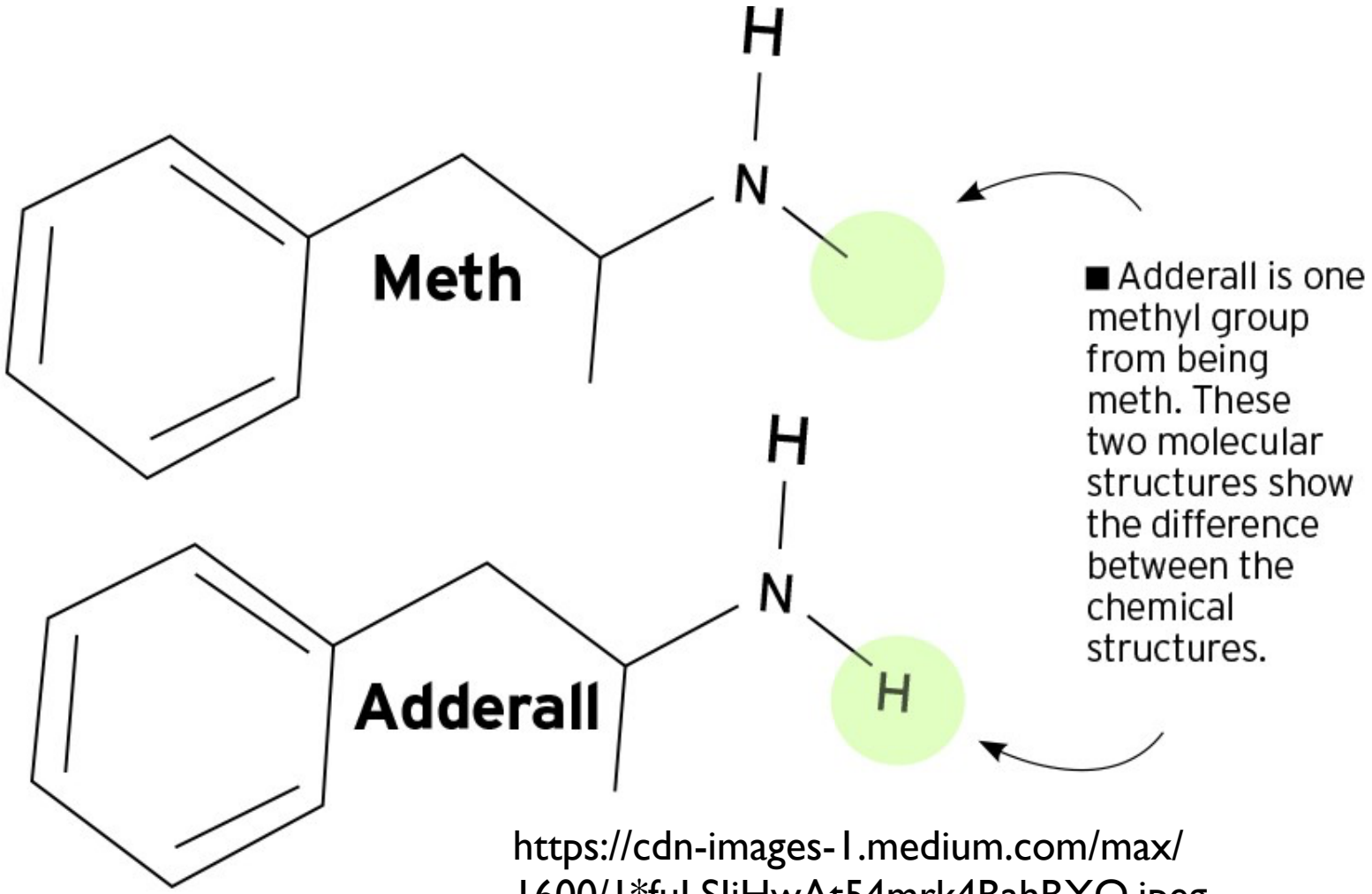
- Methamphetamine increases dopamine release from storage vesicles, leading to high levels of dopamine in the brain
  - Reverses the function of Dopamine transporter (DAT)
  - Forces monoamines (dopamine, serotonin, noradrenaline) out of the vesicles and into the synaptic space which causes an extreme rush or euphoric effect

Mechanism of Action

Excessive dopamine release: involved in the feeling of intense pleasure and reward which is sought after with drugs of abuse



Structural differences between Methamphetamine and Adderall



https://cdn-images-1.medium.com/max/1600/1*fuLSIjHwAt54mrk4BahBXQ.jpeg

Compared to Adderall, Methamphetamine is…

- More potent
- Has longer-lasting effects
- More damaging to the CNS (central nervous system)

https://www.missouristate.edu/assets/mchhs/METHAMPHETAMINE_FACTS.pdf

Methamphetamine Quick Facts

Half-life	**~10 hours (5-16 hr range)**
Low-moderate doses	5-30 mg
High-doses	≥ 50 mg
Metabolism	Liver, via CYP2D6 enzyme Metabolite: amphetamine
Effects at low to moderate doses	Arousal, positive mood, cardiac stimulation, improved attention and coordination
Effects at higher doses	Psychosis
Effects of repeated doses	Neurotoxicity (psychiatric symptoms, cognitive impairment, Parkinson's disease risk)
Urine detection time (10 or 35 mg intravenous dose)	36-48 hours (single dose)

Addiction, 104, 1085-1099; Methamphetamine Toxicity

Comparison of Powder and Glass forms of Methamphetamine

Street Meth Dosage forms	Route of administration	Typical Color	Interesting facts
Powder	Snorted, or injected (dissolves in water or alcohol)	White to off-white, but can be yellow or pink or other colors	Can resemble cocaine or chalk dust depending on how coarse it is
Rock, glass (solid)	Smoked or injected	Translucent or bluish-white	**More potent:** Triggers longer-lasting high and physical effects than the powder

Less common street form: oral pills
Don't produce a very good high!

Typical Ingredients used to make Methamphetamine:

- Drano
- Ephedrine/PSE
- Lye
- Brake fluid
- Rubbing alcohol
- Lighter fluid
- Camp stove fluid
- Lithium from batteries
- Drain cleaner
- Paint thinner
- Freon (refrigerant)

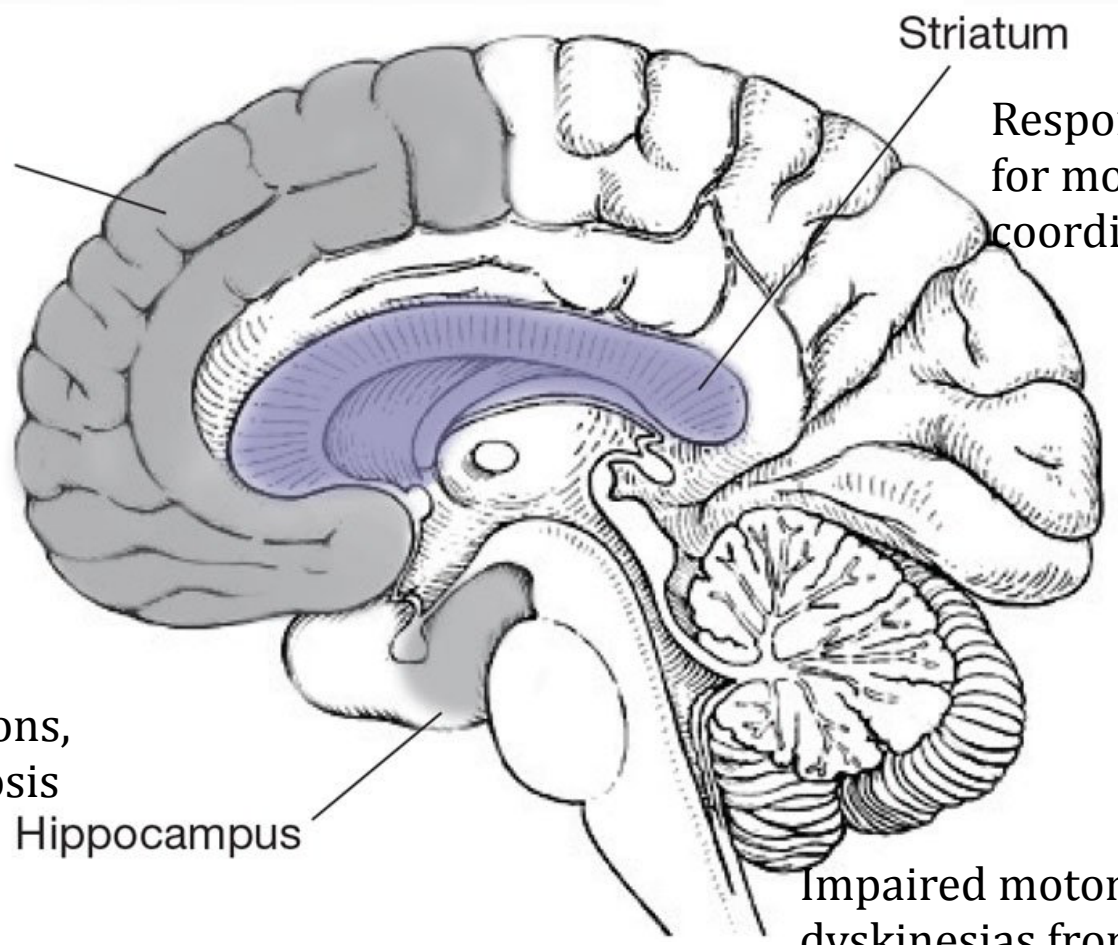
DO NOT TRY AT HOME!!!

Aforeverrecovery.com

A Little History Lesson…

- A Japanese chemist first synthesized methamphetamine from another stimulant in 1893
- Early use included treatment for narcolepsy, asthma, and weight loss
- Meth was used during World War II by US, German, and Japanese soldiers to help increase performance status and ward off fatigue during long campaigns

Parts of the Brain Affected by Methamphetamine



Responsible for movement coordination

Impairments in memory, cognition, executive function, information processing and language

Impaired emotions, violence, psychosis

Impaired motor skills, dyskinesias from deficit in striatum

Addiction, 104, 1085-1099

Physiologic Effects of Methamphetamine

Acute effects:

- **Deep pleasure and intense euphoria**
- Increased alertness
- Increased energy
- Increased heart rate
- Increased blood pressure
- Increased body temperature
- Decreased appetite

Prakash et al. Methamphetamine: Effects on the Gut, Brain, and Immune System

Physiologic Effects of Methamphetamine

Long-term effects:

- Severe tooth decay
- Infection
- Weight loss
- Malnutrition
- Kidney damage
- Liver damage
- Altered brain function

"Meth mouth"

Prakash et al. Methamphetamine: Effects on the Gut, Brain, and Immune System

Risky Behavior

- Increased aggression, domestic violence
- Increased need and urgency for sex (meth is considered an aphrodisiac)
- Increased STDs – disregard for unprotected sex and risky sexual behaviors

Withdrawal

Can be very unpleasant and uncomfortable, but it is very unlikely to lead to death

Stages	Typical presentation	Duration
Stage I: "Crash" phase	• **Sharp decline in energy** and cognitive function • **Hallucinations** • **Paranoia** • anxiety	3-10 days
Stage II: Intense cravings	• **Strong desire for intense high** experienced initially • **Depression** • Insomnia	10 days
Stage III: Recovery Phase	• Cravings begin to fade and become less potent	Up to 30 weeks

Withdrawal

- **Anhedonia**, due to the decrease in the dopamine receptor levels in the brain, **leads to loss of the ability to feel pleasure**
- The **resultant depression can cause users to relapse to seek relief** from emotional distress
- Anhedonia and depression **can persist up to 2 years after a person** successfully **quits** the drug
- Strong craving for the drug will also persist during this time

"Crystal Meth Withdrawal and Detox". Therecoveryvillage.com

Treatments for Methamphetamine Withdrawal

Anti-depressants and other CNS drugs to help manage depression, anxiety, help ease cravings during withdrawal:

- Bupropion**
  - Has mild stimulating properties
  - Reduces cravings for mild to moderate users
- Paxil
  - Reduces cravings in abstinent crystal meth users
- Prozac
- Remeron
  - May help prevent relapse during withdrawal
- Modafanil
  - Mild stimulant
  - Reduces issues of disruptive sleep pattern

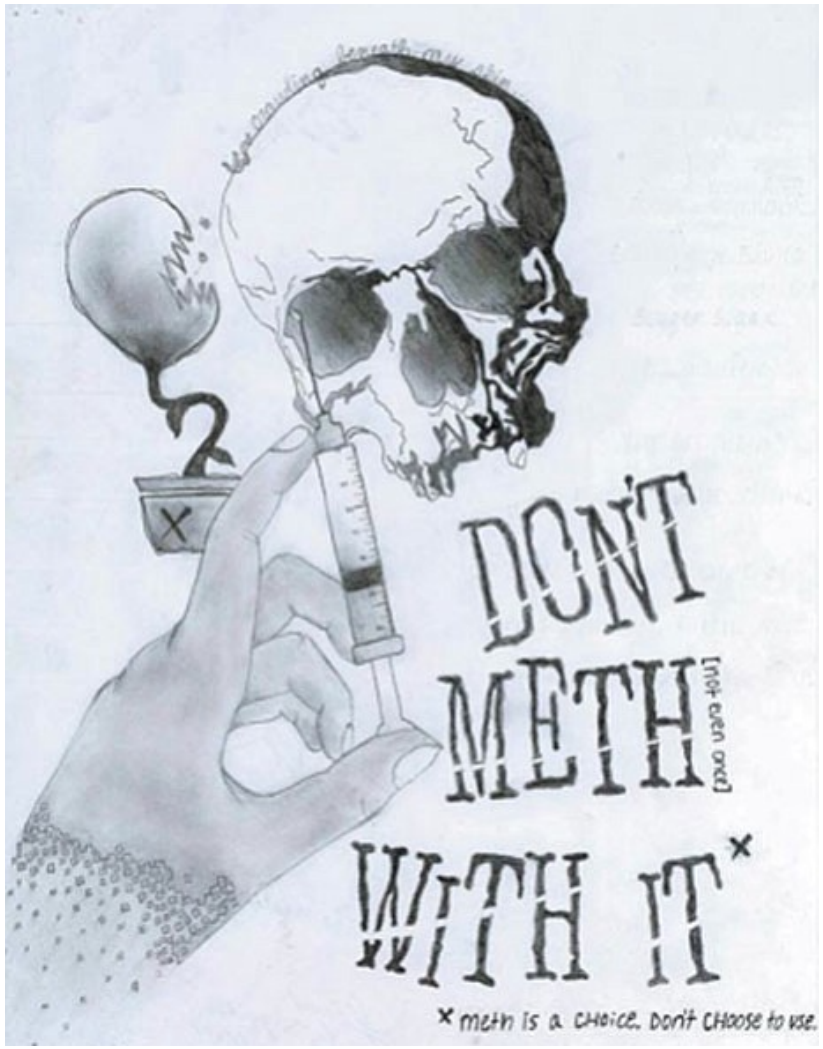
** Bupropion has a study to show efficacy for meth dependence, and may be a better option than an SSRI

"Crystal Meth Withdrawal." American Addiction Centers

Overdose

Signs of overdose:

- Arrhythmias
- Chest pain
- Hypertension or hypotension
- Agitation
- Hallucinations
- Psychosis
- Seizures



"The Signs of Meth Overdose". American Addiction Centers

Antidote for Overdose?

- No current antidote for reversal
- Treatment is supportive, based on symptoms or conditions involved
- Benzodiazepines for seizures or anxiety
- Haloperidol for psychosis
- Blood pressure medications to slow blood pressure
- IV fluids for dehydration, EKG changes or renal failure

"Meth Overdose Fact and Statistics." MentalHelp.net;
CNS drugs, 28(12), 1115-1126

Complications of long-term Methamphetamine Abuse

- Heart attacks
- Stroke
- Brain damage (damaged axons)
- Psychosis (hallucinations, delusions)
- Paranoia
- Violence
- Depression
- Heart disease, heart failure (Cardiomyopathy)

Prakash et al. Methamphetamine: Effects on the Gut, Brain, and Immune System

Association between Methamphetamine and Heart Disease

- Adrenergic stimulation leads to increase blood pressure (hypertension) and increased heart rate (tachycardia)
- Meth is linked to several cardiac pathologies:
  - Arrhythmias
  - Accelerated atherosclerosis
  - Sudden cardiac death
  - Acute coronary syndrome
  - Circulatory collapse
  - Cardiomyopathy

Clinical Cardiology, 36(12),737-42.

Mechanisms of Methamphetamine-associated Cardiomyopathy (MAC)

- **Catecholamine excess**: increased epinephrine, norepinephrine and dopamine levels from repeated meth administration
- Coronary vasospasm
- **Ischemia** (restriction of blood flow)
- Mitochondrial injury
- Changes in myocardial metabolism
- Increases in reactive oxygen species (ROS)
- Direct toxicity with methamphetamine

Clinical Cardiology, 36(12) 737-42.

Treatments for MAC

- Methamphetamine induces hyperadrenergic state (hypertension, increased cardiac stress)
- **Beta-blockers:** help reverse cardiac remodeling (caution in concomitant meth use)
  - Decrease cardiac output
  - Decrease cardiac stress
- **RAAS inhibitors** recommended for patients with reduced systolic LV function (ACC/AHA Guidelines 2005 for the treatment of HF in adults)

Clinical Cardiology, 36(12) 737-42.

Medical use of Methamphetamine

- Methamphetamine hydrochloride – marketed as Desoxyn is **FDA-approved schedule II substance** for treatment for ADHD, obesity
  - Dose: **5 mg oral tablet**
  - **Obesity:** Take **once daily** 30 minutes before each meal
  - **ADHD:** 5 mg tablet once or twice daily; **max: 20-25 mg daily**
- Rarely prescribed now due to its highly addictive potential and also adverse effects (sudden cardiac death, mania, psychotic disorder, etc)

Implications of Meth Addiction

- **Physical Problems**
  - HIV/blood-borne diseases
  - Heart disease
  - Kidney and liver damage
  - Meth mouth
  - Scarring from open sores “meth sores”
  - Aged skin
  - Hair loss

Implications of Meth Addiction

- **Mental Problems**
  - Short-term memory deficit
  - Long-term memory loss
  - Impaired ability to think
  - Chronic depression
  - Anxiety

- **Social and financial problems**
  - Violence (domestic violence)
  - Loss of career
  - Loss of relationships
  - Social withdrawal

Treatment for Meth Addiction

No FDA-approved medication for methamphetamine addiction; treatment is supportive

- **Detoxification** under medical supervision – medications may be given to ease discomfort
- **Inpatient or residential treatment** – receive intensive therapeutic services while living in a drug-free environment
- **Outpatient treatment** – structured substance abuse therapy 1-3 times/week; good option for those who have been able to maintain sobriety for some time

"Meth Overdose". https://drugabuse.com/methamphetamine/overdose/

Treatment for Meth Addiction

- Cognitive Behavioral therapy is the mainstay of meth addiction treatment programs

"Meth addicts must relearn certain behaviors. Because meth has trained them to associate all pleasure with the drug, they need to learn to modify their thinking and expectations." –PBS's frontline

Alta Mira Recovery Programs

Best Prevention for Methamphetamine Abuse?

Don't start!

References

1. Cruickshank, C., & Dyer, K. (2009). A Review of the Clinical Pharmacology of Methamphetamine*. Addiction,*104,1085-1099.

2. Dabel, Tyler. (2016). There is Hope for Treating Depression After Meth Addiction. Alta Mira Recovery Programs. Available from: https://www.altamirarecovery.com/blog/hope-treating-depression-meth-addiction/

3. Elkashef AM et al. (2007). Bupropion for the treatment of Methamphetamine Depedence. *Neuropsychopharmacology,* 33(5), 1162-70.

4. Glasner-Edwards S., & Mooney LJ. (2014). Methamphetamine Psychosis: Epidemiology and Management. *CNS drugs,* 28(12), 1115-1126. doi: 10.1007/s40263-014-0209-8.

5. History of Meth. [updated 2018 Aug 21; accessed 25 Mar 2018]. A&E Television Networks. Available from: https://www.history.com/topics/crime/history-of-meth

6. Kaf, W., Black, L., Najem, F. Methamphetamine: Its Effects on You, the Environment, and Young Children. [accessed 26 Mar 2019]. Available from: https://www.missouristate.edu/assets/mchhsMETHAMPHETAMINE_FACTS.pdf

7. Lee, Mary. (2009). *Basic Skills in Interpreting Laboratory Data*, 4th ed. Delhi: American Society of Health-System Pharmacists, Inc.

8. Prakash et al. Methamphetmaine: Effects on the Brain, Gut and Immune System. *Pharmacological Research,*120(2017),60-67.

References

9. Richards, JR. & Laurin, EG. Methamphetamine Toxicity. [updated 2019 Mar 2]. In: StatPearls [internet]. Treasure Island (FL) : StatPearls Publishing; 2019 Jan -. Available from: https://www.ncbi.nlm.nih.gov/books/NBK430895/

10. “Signs of Meth Overdose.” (2019). American Addiction Centers. Available from: https://americanaddictioncenters.org/meth-treatment/overdose

11. U.S. National Library of Medicine. Procalcitonin Test. [updated 2018 Nov 7; cited 2019 Mar 24]. Available from: https://medlineplus.gov/lab-tests/procalcitonin-test/

12. What does Meth Look Like? [updated 2018 May 18; cited 2019 Mar 25]. Orlando, FL: DrugRehab.com. Available from: https://www.drugrehab.com/addiction/drugs/crystal-meth/what-meth-looks-like/

13. Won, S. Hong, R. A., Shohet, R.V., Seto, T. B., & Parikh, N. I. (2013). Methamphetamine-associated Cardiomyopathy. *Clinical Cardiology,* 36(12),737-42.


Questions

Supplemental Slides

Definitions of medical acronyms used in the physical exam:

- **Normocephalic:** head and all major organs of the head are in normal condition
- **EOM:** extraocular muscles
- **PERRL** – pupils equal, round, reactive to light and accommodation
- **JVD:** jugular vein distension – happens when there is increased central venous pressure (pressure inside the vena cava)
- **RRR:** (referring to heart) regular rate and rhythm

Supplemental Slides

Definitions of medical terms:

- **Rub:** the scraping sound produced when the 2 inflamed membranes of the heart (pericardium) rub together
- **Rhonci:** low-pitched rattling breath sounds caused by bronchial secretions of the lungs; could indicate pneumonia or bronchitis
- **Rales:** the sounds you hear when the lung has filled with fluid
- **CVAT:** costovertebral angle tenderness – pain in the back area overlying the kidney, could indicate kidney infection (pyelonephritis)

Definition of CRP

CRP (C-reactive protein)

Reference range: 0-0.0-5 mg/dL

- Increases in response to tissue injury and infection
- Suggested role: binding with necrotic cell membranes at inflammation site
- Released in response to inflammatory markers present within atherosclerotic plaques
- There's a correlation between elevated levels and cardiovascular events in patients with coronary heart disease

Procalcitonin Blood Test

- Obtained if patient has signs of sepsis or other serious infections such as:
  - Fevers and chills
  - Sweating
  - Confusion
  - Extreme pain
  - Rapid heartbeat
  - Shortness of breath
- Levels are used to guide antibiotic therapy
- Non-specific test
  - This test is used in combo with other tests to help make a diagnosis

More Resources

- *Beautiful Boy*, by David Sheff, a memoir about a father's journey through his son's addiction
- National Institute on Drug Abuse: https://www.drugabuse.gov/publications/research-reports/methamphetamine/what-methamphetamine
- Rehabilitation Center in Michigan for drug addiction called A Forever Recovery: https://aforeverrecovery.com/drug-addiction/meth/
- A study on the use of bupropion for the treatment of methamphetamine dependence: Elkashef AM et al. (2007). Bupropion for the treatment of Methamphetamine Dependence. *Neuropsychopharmacology,* 33(5), 1162-70. Available from: https://www.nature.com/articles/1301481
- Thomas, S. (2019). "Crystal Meth Withdrawal." American Addiction Centers. Available from: https://americanaddictioncenters.org/meth-treatment/withdrawal