Introduction to medical toxicology: common toxidromes

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What is medical toxicology?

• A medical subspecialty focusing on the diagnosis, management and prevention of poisoning and other adverse health effects due to medications, occupational and environmental toxins, and biological agents

• Overdoses of therapeutic medications and drugs of abuse
• Exposure to industrial / environmental hazards
• Naturally occurring poisons / envenomations

• Emergency departments
• Inpatient consult services
• Poison control center administration / backup
• Industry (esp. pharmaceuticals)
• Government agencies (e.g. FDA, EPA)
• Private clinics

• ACGME accredited 2 year fellowship
• Accepts graduates of emergency medicine, internal medicine, pediatrics, and occupational medicine residencies
• Board exam offered every other year
• Joined the NRMP in 2013
A 20 y/o male is brought to the ED by paramedics after assaulting the owner of a gas station. He appears markedly agitated and diaphoretic despite receiving 10 mg of midazolam prior to arrival.

BP: 200/110, pulse 170, RR 24, temp 104° F

### Sympathomimetic syndrome

- Amphetamines
- Cocaine
- ‘Bath salts’
- MDMA
- Methylphenidate
- Ephedrine
- Pseudoephedrine
- Dopamine
- Epinephrine
- Norepinephrine
**Pathophysiology**
- Activation of autonomic sympathetic nervous system
- Increased myocardial inotropy/chronotropy
- Vasoconstriction
- Glycogenolysis / gluconeogenesis
- Increased CNS psychomotor activity

**Clinical presentation**
- Hypertension
- Tachycardia
- Hyperthermia
- Altered mental status
- Agitation
- Seizures
- Diaphoresis
- Mydriasis

“Spinning Wild” by Neveragain: 500 mg of Eight Ballz

“Within 30 seconds, felt a rushing, felt as if I had insufflated the largest dose of cocaine in my entire life. I walked around, experiencing one of the greatest euhorias of my life. Easily cutting out oxycodone. I progressively felt as if I had poisoned myself...soon progressed to extreme nausea, leading to me dry heaving in the middle of the street. I calmed down enough for the euphoria to shine brightly again. I was singing in the streets, talked to a friend on the phone about how amazing I felt, and visited an old girlfriend.”

“As time went on, the euphoria dissipated and left me feeling empty and depressed. Eyes unable to close for more than 3 seconds top. So I laid in my bed, hating my life, unable to sleep until approximately T+10.5 hours. A horrific price to pay for astounding euphoria and joy. Would need alprazolam or diazepam to attempt again in an effort to sleep if I were to try again. I do not believe it is a good idea.”
Amphetamines

1. Amphetamine molecule
2. Crystal form of amphetamine
3. Hydroxyamphetamine molecule
4. Crystal form of hydroxyamphetamine
Amphetamines

Cocaine vs amphetamines

- Amphetamines last longer (up to 24 hours)
- Amphetamines less likely to cause seizures, dysrhythmias, and myocardial infarction
- CNS manifestations often predominate
- Aggression, psychosis, severe agitation

Methamphetamine

- Multiple epidemics
- Direct neurotoxicity to dopaminergic neurons
- Easily synthesized using ephedrine or pseudoephedrine
- ‘Meth mouth’
MDMA

- Euphoria, heightened sexuality, inner peace
- Serotonin
- High doses can still produce severe sympathomimetic toxicity!
- Hyponatremia
- ‘Molly’

Molly

- ‘Pure’ form of MDMA
- Faster peak, more subtle ‘come down’ period
- Perceived as being safer than other forms of MDMA

Khan DE, et al. 3 cases of primary intracranial hemorrhage associated with “Molly”, a purified form of 3,4-methylenedioxyamphetamine (MDMA).

J Neurol Sci 2012;323:257-60
Bath salts

- Actually: Synthetic cathinones like MDPV, mephedrone
- Popular in Europe ~2008-2010
- Peak popularity in United States probably in 2011
- Federally scheduled in fall 2011

Treatment

- Control agitation
- Benzodiazepines
- Manage hyperthermia
- Active cooling, rehydration
A 27 y/f is brought to the ED by paramedics after being found unresponsive in a parked car. On arrival, the patient was noted to have shallow respirations at a rate of 6/min with constricted pupils. She rapidly regained consciousness after administration of an antidote.

Opioid toxidrome

Agents

Pathophysiology

- $\mu$ receptor-mediated reduction in sympathetic autonomic tone
- Respiratory depression, bradycardia, miosis, gastrointestinal dysmotility, supraspinal analgesia
- Hypoventilation: reduced sensitivity of medullary chemoreceptors to hypercapnia & hypoxia

Miosis? Not always

- Often not seen with:
  - Meperidine
  - Propoxyphene
  - Speedball
Noncardiogenic pulmonary edema

Treatment

- **Naloxone**
- Competitive antagonist of the μ receptor
- Titrate to adequate ventilation

Krokodil Q&A

- Q: Is Krokodil a real thing?
- A: Yes, Krokodil is a real thing
Krokodil

- Q: Will my skin fall off if I use Krokodil?
- A: Maybe. But don’t we have something else in this country- in this city- that can do that?

Krokodil

- Q: Will Krokodil be a big problem in the US?
- A: I highly doubt it. We have waaaay better drugs!!

A 14 y/o male is brought to the ED by paramedics after his friends called 911. He was severely combative, with dry, flushed skin and dilated pupils.

BP 150/80, pulse 140, RR 22, temp 103° F

Anticholinergic Syndrome

Agents

- Antihistamines
- Antispasmodics
- Cycloplegics
- H2 blockers
- Neuroleptics
- TCAs
- Cyclobenzaprine
- Ipratropium
- Belladonna alkaloids
- Antiparkinson drugs
Datura users speak...

- Truly The Devil’s Weed
- Unintelligent Experiment
- Nightmares In Flux
- A Window To Insanity
- Eating Bugs While My Friends Convulsed
- I No Longer Live In The Real World

Screaming Voices

- “...quite excited to find a large bush of deadly nightshade at a local park...”
- “...grabbed a twig to examine the purple berries...squeezed the contents into my eye”

Pathophysiology

- Competitive antagonism of acetylcholine at muscarinic receptors
Peripheral signs
- Dry skin / mouth
- Flushing
- Hyperthermia
- Urinary retention
- Diminished bowel sounds
- Myoclonus
- Tachycardia
- Hypertension
- Dysrhythmias

Central signs
- Agitation
- AMS
- Ataxia
- Coma
- Delirium
- Dysarthria
- Extrapyramidal signs
- Hallucinations
- Lethargy
- Psychosis

Management
- Most cases not life-threatening
- Major toxicity usually due to agents that have other properties (e.g. TCAs)
- Delayed gastric emptying / absorption
- Benzodiazepines, cooling
- Anticholinesterase therapy?

Physostigmine
- Reversible cholinesterase
- Calabar bean
- Peripheral
- Safe?

Asystole Complicating Physostigmine Treatment of Tricyclic Antidepressant Overdose
- 32 y/o male presents 1 hour s/p ingestion of 2,300 mg amitriptyline
- Intubated
- Status epilepticus
- EKG

Asystole Complicating Physostigmine Treatment of Tricyclic Antidepressant Overdose
- 25 y/m presents 1 hour s/p ingestion of 5,000 mg imipramine, 150 mg propranolol
- '2 major motor seizures'
- Physostigmine after each seizure
- ECG
Physostigmine
• Appropriate for patients with peripheral or central cholinergic toxicity without evidence of cardiac disturbance (e.g. QRS / QTc prolongation)
• Asthma / pulmonary disease?
• Atropine at bedside
• Short lived, may require repeat dosing
• Not recommended in TCA overdose

A 40 y/o male immigrant from Sri Lanka is brought to the ED after ingesting “something from his garage”. He complains of SOB and incontinence. Exam shows bradycardia, diffuse pulmonary wheezing, diaphoresis, and miosis.

Cholinergic Syndrome

What can we learn from Hollywood?
• “What do you know about VX poison gas?”
• “Liquid, used as pesticide, discovered by accident in 1952.”
“Stops the brain sending nerve messages down the spinal column within 30 seconds. Small twitch in your back. That’s the poison. Muscles freeze, can’t move. Spasm so hard you break your own back and spit your guts out. That’s after your skin melts off.”

What can we learn from Hollywood?

Clinical manifestations

- Depressed mental status
- Miosis
- Fasciculations
- SLUDGE / DUMBBELS

Management

- Diarrhea
- Urination
- Miosis
- Bronchorrhea
- Bronchospasm
- Emesis
- Lacrimation
- Salivation
Decontamination

- Rapid cutaneous absorption
- Remove all clothing
- Wash skin with soap and water
- Gastric lavage?
- Activated charcoal?
- Health professionals: caution

Supportive care

- Airway management
- Oxygen, intubation if necessary
- Comatose, copious secretions, or significant muscular weakness
- Avoid succinylcholine
- Hypotension
- IV fluids, vasopressors if necessary
- Seizures
- Benzodiazepines

Antidotal therapy

- “This is atropine. If you come into contact with the gas, you have twenty seconds to inject it into your heart.”

Atropine

- Competitive antagonist of acetylcholine at muscarinic receptors
- Reverses excessive secretions, vomiting, miosis, diarrhea, urinary incontinence
- Adults: 1-5 mg boluses
- Pediatrics: 0.05 mg/kg
- Repeat doses every 2-3 minutes

What can we learn from Hollywood?

- “This is atropine. If you come into contact with the gas, you have twenty seconds to inject it into your heart.”

Atropine

- Treat until ‘atropinization’ occurs
- Dry skin and mucous membranes, decreased secretions, decreased bowel sounds, mydriasis (not always)
- Drying of pulmonary secretions most important!
- Tachycardia not a contraindication
- Large doses may be necessary!
• 41 patients
• Minimum daily atropine dose: 168 mg
• Maximum daily dose: 1,124 mg

“This is atropine. If you come into contact with the gas, inject 84 of these directly into your heart.”

Remember

• Atropine is not effective at nicotinic receptors
• Will not reverse skeletal muscle weakness!

Pralidoxime

• Regeneration of phosphorylated AchE
• Direct inactivation of free organic phosphorus molecules
• Reversal of muscarinic and nicotinic effects
• Concept of ‘aging time’
Pralidoxime

- Pralidoxime cannot regenerate affected AchE once it has been ‘aged’
- Most useful when started early
- Aging times vary significantly among different pesticides
- 1-2 g IV over 10-15 minutes