TOXIDROMES AND DRUG OVERDOSE MANAGEMENT

Will Coolidge PharmD, BCCCP
Critical Care/Emergency Medicine Pharmacy Specialist
Ryan Waybright PharmD, BCCCP
Critical Care/Emergency Medicine Pharmacy Specialist
Objectives

- Recognize characteristics of common toxidromes
- Identify commonly abused prescription and non-prescription drugs
- Describe initial management of overdose patients
- Review appropriate use of reversal agents including flumazenil and naloxone
Outline

- Patient first impression and management
- Toxidromes
- Drugs
  - Prescription and non-prescription
- Excited delirium
- Toxic alcohols
- Body Packers
Poisoning

- What is poisoning?
- Routes of ingestion
- Accidental and intentional
- Altered medication kinetics
Overview of Management

- Toxicologic Physical Exam
- Resuscitation
  - C-A-B
  - Stabilization
  - GI decontamination
  - Enhanced elimination
- Supportive cares
- Antidotes
Toxicologic Physical Exam

- Mental and physical
- Agitation, confusion, obtunded pupil size, blood pressure, heart rate, sweating or dry skin, hydration status, temperature
- Vital signs
  - Trend
- Use as clues to a puzzle
Patient History

- Family members, friends, witnesses
- Pill bottles, needles, alcohol, patches, IV drug bottles, drug paraphernalia
  - Check all clothing
- Any odors?
- Suicide note
- Critically evaluate surroundings
Substance Ingestion

- What drug/drugs or substances?
- How much drug?
- What time?
- Any co-ingestions?
- Home medication list?
Supportive Care

- BLS/ACLS
- Airway
- Establish IV access
- Vital signs, mental status, pupil size, blood glucose
- EKG, pulse oximetry, cardiac monitoring
- Supportive care
- Antidotes if possible
Toxidromes

- Describe clinical syndromes caused by toxins
- Common toxidromes:
  - Stimulant
  - Sedative-hypnotic
  - Opioid
  - Anticholinergic
  - Cholinergic
  - Hallucinogen
  - Hypoglycemic
Stimulant

- Sympathomimetics
- Cocaine, amphetamines

S/Sx:
- Tachycardia, HTN, sweating, tremor, seizures, restlessness, hallucinations, excessive speech, heart attack

Possible interventions:
- Cooling
- Benzodiazepines
- Hydration

Goldfranks Toxicologic Emergency. 2011
Levine. CHEST. 2011
Sedative-Hypnotic

- Benzodiazepines
  - Lorazepam, diazepam, alpraxolam, clonazepam

- S/SX:
  - Sedation, confusion, delirium, ataxia, coma, apnea, bradycardia

- Possible Interventions:
  - Intubation with vent support
  - Flumazenil
Opioid

- Narcotics
  - Morphine, fentanyl, hydrocodone, oxycodone, hydromorphone, heroin

- S/Sx:
  - Miosis, bradycardia, respiratory depression

- Possible Interventions:
  - Intubation with vent support
  - Naloxone (Narcan)
Anticholinergic

- Diphenhydramine, loratadine, cetirizine, amitriptyline
- **S/Sx:**
  - Fever, flushed skin, dry mucous membranes, urinary retention, tachycardia, agitation, hallucinations, mydriasis, blurred vision
- **Possible interventions:**
  - Sedation with benzodiazepines
  - Cooling
  - IV fluids
  - Supportive management
  - Physostigmine?
Cholinergic

- Organophosphate insecticides, carbamate insecticides, bioterrorism
- S/Sx: SLUDGE
  - Salivation, lacrimation, urination, diarrhea, miosis, runny nose, bradycardia, bronchconstriction, GI distress, emesis
- Possible interventions:
  - Patient decontamination
  - Intubation and vent support
  - Atropine, pralidoxime
Hallucinogens

- Lyseric acid diethylamide (LSD), phencyclididine (PCP), ketamine

- **S/Sx:**
  - Hallucinations, anxiety, dysphoria, hyperthermia, mydriasis

- **Possible interventions:**
  - Supportive care
  - Control agitation
  - Seizure management
Hypoglycemic

- Insulin (Lantus, Levemir, Novolog, Novolin)
- Sulfonylureas (glipizide, glyburide)

S/Sx:
- Altered mental status, sweating, tachycardia, hypertension, seizures, strange behavior, slurred speech

Possible interventions:
- Glucagon
- D50
- Octreotide

Tintinalli’s Emergency Med. 2011
Goldfranks Toxicologic Emergency. 2011
Levine. CHEST. 2011
Specific overdoses

- Opioids
- Heroin
- Cocaine
- Benzodiazepines
- Methamphetamine
- Ecstasy
- K2/Spice
- Bath Salts
- Toxic alcohol
- Diphenhydramine
Opioid Overdose Deaths

- Overdose deaths due to opioids are PREVENTABLE!!!!
Opioid Overdose Statistics

- 2011: 420,040 ED visits related to opioid misuse
- 2012: Drug overdose (OD) leading cause of death in 25-64 year olds
- 2013: 16,235 OD deaths due to opioids
- 2013: 34 overdose deaths in SD
Opioids

- Prescription drug overdose epidemic
  - 2014 was a record year for opioid deaths
  - More than 6/10 deaths due to opioids
  - Rate of opioid overdose deaths has quadrupled since 1999
    - 78 Americans die every day from opioids
  - At least half of all opioid overdose deaths involve a prescription opioid
OD deaths Ripple Across American
RX Opioid Abuse and OD Risk Factors

- Obtaining overlapping prescriptions from multiple providers and pharmacies
- High daily dosages of prescription pain medications
- Mental illness or history of alcohol, or other substance abuse
- Living in rural area and having low income
Opioids

- Morphine, fentanyl, hydrocodone, oxycodone, hydromorphone
- Antidote: Naloxone (Narcan)
- Routes of Administration:
  - Oral, IV, IM, SubQ, transdermal
- Duration of action depends on formulation and route of administration

Tintinalli’s Emergency Med. 2011
Goldfranks Toxicologic Emergency. 2011
Levine. CHEST. 2011
Heroin

- Heroin use increasing in adults aged 18-25 years old
- 3 out of 4 new users report abusing prescription opioids prior to using heroin
- Increased availability, lower price, increased purity
- Often mixed with fentanyl
- More than 10,500 deaths in 2014
Heroin

- Risk factors for heroin addiction
  - Addiction to other prescription pain medications
  - Cocaine addiction
  - No insurance or enrolled in Medicaid
  - Non-hispanic whites
  - Males
  - Addiction to marijuana and alcohol
  - Living in large metropolitan area
  - 18-25 years old
Heroin

- Common names: Dope, Junk, Smack, H
- Semi-synthetic opiate derived from morphine
- IV, IM, snorted, smoked, oral
- Effects: euphoria, relaxation, sedation, analgesia, N/V, constipation, dizziness
- Onset:
  - IV: 3-5 seconds
  - Smoking: 5-15 seconds
  - IM injection: 5-10 minutes
  - Insufflated: 2-10 minutes
  - Oral: 60-90 minutes
- Duration: 2-4 hours
Naloxone aka Narcan

- Antidote for opioid overdose
- MOA: Opioid antagonist
- Route of administration:
  - IV (preferred), IM, SubQ, inhalation, endotracheal tube
- Dose:
  - Initial: 0.4 to 2 mg, repeat as needed
  - Continuous infusion
- Duration of action: 30-120 min
- Onset of Action:
  - IV: 2 min
  - IM: 5 min
Naloxone Adverse Effects

- Acute opioid withdrawal
- Agitation
- Vomiting
- Hypertension, hypotension
- Tachycardia
- Ventricular fibrillation, tachycardia
- Seizure
- Coma
- Pulmonary edema
Evzio (Naloxone)

- Approved in April 2014
- Single dose: 0.4 mg IM or SubQ
- Onset of action: 15 min
- Duration of action: 1.28 hr
- For use by family members, caregivers
Intranasal Naloxone

- Dose: 1 mg/nostril (total dose: 2 mg)
- Need syringe and atomizer
- Benefit:
  - No needles, less risk of exposure to blood borne pathogens
  - No need for IV

Robinson A. Am J Health-Syst. Pharm. 2014
http://intranasal.net/OpiateOverdose/#Treatment_protocol
Cocaine

- MOA: Enhances dopamine, norepinephrine and serotonin activity in the CNS by blocking re-uptake

- Adverse effects:
  - Tachycardia, HTN, tachypnea, hyperthermia
  - Myocardial ischemia, myocardial infarction, hypertension, tachycardia, vasospasm, vasoconstriction, QRS and QTc prolongation
  - Bronchospasm
  - Seizures, coma, headache, ICH
Cocaine Ingestion Management

- Cocaine use is a relative contraindication to use of succinylcholine use during RSI
- Fluids
- Cooling if patient is hyperthermic
- Agitation: Midazolam or diazepam
- Tachycardia or hypertension:
  - Beta-blockers and alpha-beta blocker contraindicated
  - Nitroprusside, nitroglycerin, nicardipine
  - Diltiazem or lidocaine
Benzodiazepines

- Antidote: Flumazenil (Romazecon)
- Routes of Administration:
  - Oral, IV, IM
- Onset on Action:
  - Dependent on route
- Duration of Action:
  - 4 hours to >24 hours based on specific drug and amount ingested
Flumazenil

- Antidote for benzodiazepines
- MOA:
  - Competitive inhibitor of benzodiazepines at GABA receptor
- Dose:
  - Initial: 0.2 mg
  - Repeat dose: 0.2 mg at 1 min intervals, max of 4 doses
- Onset of action: 1-2 min
- Duration of action: 20-50 min

Flumazenil. Micromedex. 2014
Flumazenil Pearls

- Limited use in mixed/unknown overdoses

- Indications for use:
  - **Must be pure benzo OD in non-tolerant patient**
  - CNS depression
  - Normal VS, ECG, otherwise normal neuro exam

- Contraindications:
  - Hx of seizures or current tx of seizures
  - Multi-drug overdose
  - Long-term use of benzodiazepines
Methamphetamine

- **MOA:**
  - CNS stimulation

- **Route of administration:**
  - IV, oral, inhalation, snorting

- **Onset and duration dependent route and dosage form**

- **S/sx:**
  - Euphoria, talkativeness, agitation, seizures, hyperthermia, sweating, tachycardia poor sleep, HTN,
Methamphetamine

- **Treatment:**
  - Benzodiazepines for agitation and seizures
  - Phentolamine, nitroprusside for HTN
  - Propranolol, esmolol for tachycardia
    - Avoid metoprolol
    - External cooling for hyperthermia

- **Deaths:**
  - Ventricular arrhythmias, seizures, head bleeds, and hyperthermia
Ecstasy

- **Names:** Ecstasy, Molly, Adam, Beans, E, X
- **Pill form:** white, tasteless powder
- **MOA:**
  - Stimulant
- **DOA:** 4-6 hours
- **S/Sx:**
  - Mydriasis, ataxia, dry mouth, seizures, hyperthermia, arrhythmias, increased energy
- **Treatment:**
  - Benzodiazepines, cooling, IV fluids
K2 and Spice

- Herbal/synthetic combinations
  - Similar effect to marijuana
  - Bind to cannabinoid receptor
- Smoked or make as tea
- S/Sx:
  - Effects similar to marijuana
  - Paranoia, anxiety, HTN, hallucinations, N/V, sedation, confusion, seizures, psychosis
- Tx:
  - Benzodiazepines
  - Supportive
Bath Salts

- Provide a high similar to methamphetamine
- Synthetic cathinones
  - Bath salts mixture of cathinones
  - Structurally similar to methamphetamine and Ecstasy
- “Not for human consumption”
  - Available on internet
- IV, IM, rectal, oral
- Dose: ?
- Onset: 30-45 min
- Duration: 2-7 hours

Tintinalli’s Emergency Med. 2011
Goldfranks Toxicologic Emergency. 2011
Erowid.com
Thornton M. Pediatr Emer Care. 2014
Bath Salts

- **S/sx:**
  - Euphoria, increased energy, increased sexual interest, increased alertness, aggression, psychosis, HTN, tachycardia, hyperthermia, chest pain, palpitations, headache, tremors, insomnia, paranoia

- **Tx:**
  - No antidote
  - Agitation and seizures: Benzodiazepines
  - Hypertension: IV blood pressure medications
  - Hyperthermia: Cooling

Tintinalli’s Emergency Med. 2011
Goldfranks Toxicologic Emergency. 2011
Erowid.com
Thornton M. Pediatr Emer Care. 2014
Excited Delirium

- Methamphetamine, cocaine, bath salts
- Psychiatric disease

S/Sx:
- delirium, hallucinations, speech disturbances, disorientation, hyperthermia, insensitivity to pain, bizarre and/or violent behavior, CARDIAC ARREST

Differential diagnosis:
- Hypoglycemia, postictal state, psychiatric illness, head injury

Hyperthermia unique!!
Excited Delirium Treatment

- Agitation, Hyperthermia, Acidosis

- Agitation:
  - Least amount of restraint possible
  - Ketamine
    - 1-2 mg/kg IV or 2-4 mg IM
  - Benzodiazepines
    - Midazolam 1-5 mg IM or IV
    - Lorazepam: 1-4 mg IM or IV
  - Antipsychotics

Excited Delirium . JEMS.2011
Takeuchi A. West J Emerg Med. 2011
Excited Delirium Treatment

- **Hyperthermia:**
  - Check temperature - core preferred
  - Remove clothing, place in cool environment
  - Active external cooling
    - Misting water
    - Airflow across skin
    - Ice packs to neck, groin, axillae
    - Cold saline

- **Acidosis**
  - Fluids
  - Sodium bicarbonate
Toxic Alcohols

- 2011 US Poison Center Statistics
  - 1950 (M) & 7014 (EG) reported ingestions
  - 3 (M) & 7 (EG) reported deaths

- Methanol/Ethylene Glycol
  - Found in many products
    - Anti-Freeze
    - De-Icing Solutions
    - Solvents/Cleaners
  - Often ingested as an ethanol substitute or intentional self-harm
Toxic Alcohols

- Presentation
  - Early
    - Mild CNS depression (similar to EtOH intoxication)
    - Mild abdominal pain
  - Late (Delayed with EtOH co-ingestion)
    - Hypotension, hypopnea, seizures, coma
    - Pulmonary edema
    - Visual blurring/blindness (Methanol)
    - Flank pain, hematuria, oliguria (Ethylene Glycol)
Toxic Alcohols

- **Mechanism of Toxicity**
  - Parent alcohols — relatively non-toxic
  - Pharmacokinetics
    - Rapidly absorbed after oral ingestion
    - Metabolized by alcohol dehydrogenase and aldehyde dehydrogenase
  - Highly fatal at relatively low doses
    - ~1g/kg
Toxic Alcohol

- **Toxicity**
  - Methanol $\rightarrow$ Formate
    - Orbital disc edema, Blindness
  - Ethylene Glycol $\rightarrow$ Oxalate/Glycolate
    - Oxalate crystal formation, Anuric kidney injury
  - Both cause profound AG Metabolic Acidosis
    - Increases cell penetration
Toxic Alcohols

- Work up:
  - Telemetry
  - Airway/Oxygen
  - IV start and fluids
  - Physical exam (mental status, UO, vision)
  - EKG
  - Labs
    - CBC, CMP, lactic acid, ABG, Anion gap, serum osmolality
    - Volatile alcohol panel: Methanol, ethylene glycol
    - Acetaminophen, salicylate, ethanol
Toxic Alcohols

- **Work Up**
  - Serum Methanol, Ethylene Glycol
  - Serum Osmolality
    - Increased due to parent compounds
    - Decreases as metabolism occurs
    - Does not distinguish b/t toxic alcohols
  - Anion Gap
    - Increases due to metabolites

![Graph](image1.png)

*FIGURE 2. The Mountain.*

![Graph](image2.png)

*FIGURE 3. The Mountain in the presence of ethanol levels ≥ 100 mg/dL.*
Toxic Alcohols

- Treatment
  - Maintain airway and respiratory function
  - No GI Decontamination
    - Activated charcoal does not adsorb alcohols
  - Sodium bicarbonate infusion for acidosis
    - General practice but no solid evidence
Toxic Alcohols

- **Treatment**
  - **Fomepizole**
    - Prevents alcohol metabolism to toxic components
    - Allows parent compounds to be excreted
  - **Dosing (IV)**
    - 15 mg/kg loading dose
    - 10 mg/kg Q 12 hours maintenance dose
    - Continue until toxic alcohol level < 20
  - **Ethanol IV**
    - Same mechanism of action as fomepizole
Toxic Alcohols

- Treatment
  - Hemodialysis
    - High Anion Gap metabolic acidosis
    - Evidence of end-organ damage
      - Visual changes, renal failure
    - Fomepizole dialysis dosing – Q4 hours
  - Cofactors
    - Methanol
      - Folic Acid 50 mg (IV) every 6 hours x 24h
    - Ethylene glycol
      - Pyridoxine and thiamine
Diphenhydramine (Benadryl)

- Easily accessible
  - Many products
    - Allergy medications
    - Cough & Cold formulations
    - Sleep aids
- Anticholinergic Toxidrome
Diphenhydramine (Benadryl)

- **Presentation**
  - Anticholinergic effects
    - Tachycardia
    - Mydriasis
    - Dry mouth
    - Agitation/Confusion/Hallucinations
  - Severe
    - Seizures
    - Coma
    - QRS widening, Torsades de Pointes
Diphenhydramine (Benadryl)

- Work up:
  - Telemetry
  - Airway/Oxygen
  - IV start and fluids
  - Physical exam
  - EKG
  - Labs
    - Acetaminophen, salicylate, ethanol
Diphenhydramine (Benadryl)

- **Treatment**
  - Maintain airway and respiratory function
  - Supportive Care
  - Benzodiazepines
    - Agitation/Seizures
  - Sodium Bicarbonate
    - QRS widening/Dysrhythmias
Diphenhydramine (Benadryl)

- **Treatment**
  - Antidotal – Physostigmine
    - Acetylcholinesterase inhibitor
    - Reversal of peripheral and central anticholinergic effects
    - 0.5-2 mg slow IVP ($\geq$ 5 minutes)
    - Can repeat dose (lasts 15-30 minutes) in 20-30 minutes
      - Generally not necessary/recommended
Diphenhydramine (Benadryl)

- **Treatment**
  - **Antidotal – Physostigmine**
    - **Contraindications**
      - Asthma, Diabetes, Cardiovascular disease, Mechanical obstruction of GI or GU tracts
      - Widened QRS on ECG
    - **Adverse effects**
      - Bradycardia
      - Diarrhea
      - Seizures
      - Bronchospasm
    - **Discontinue use if excess cholinergic symptoms develop**
Body Packers

- Body Packing
  - Swallow or insert drug filled packets into a body cavity
  - Typically in attempt to smuggle across borders

- Body Stuffers
  - Ingestion of drugs to avoid immediate apprehension by authorities
Body Packers

- Presentation
  - By authorities - clearance
  - Toxicity
  - Obstruction

- Work up
  - Physical exam/History
  - Abdominal Xray
  - Urine drug screen?
Body Packers

- Treatment
  - Asymptomatic
    - Close observation
    - Consider WBI (GoLytely)
    - +/- Promotility agents (metoclopramide, erythromycin)
  - Toxic
    - Tailored to agents ingested
    - Sympathomimetic agents – potentially require surgical decontamination
Conclusion

- Opioid abuse and overdose is an epidemic in the USA
- Naloxone saves lives and will see increased use as heroin abuse increases in all areas
- EDs see a wide variety of doses and using todidromes will help with treatment of unknown ingestion
- Call Poison Control
Poison Control

- 1-800-222-1222
- Call with any questions and concerns
- Immediate help and recommendations
Questions
References


- Erowid. [www.erowid.com](http://www.erowid.com)


References


References


References