

TOXIDROMES AND DRUG OVERDOSE MANAGEMENT

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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



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

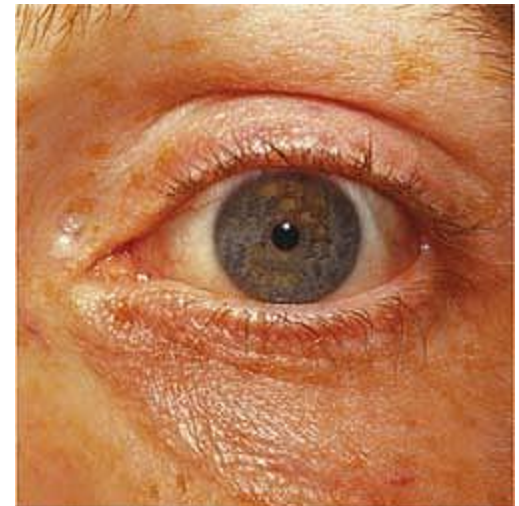
- S/Sx:

- 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), phencyclidine (PCP), ketamine
- S/Sx:
 - ▣ Hallucinations, anxiety, dysphoria, hyperthermia, mydriasis
- Possible interventions:
 - ▣ Supportive care
 - ▣ Control agitation
 - ▣ Seizure management

Hypoglycemic

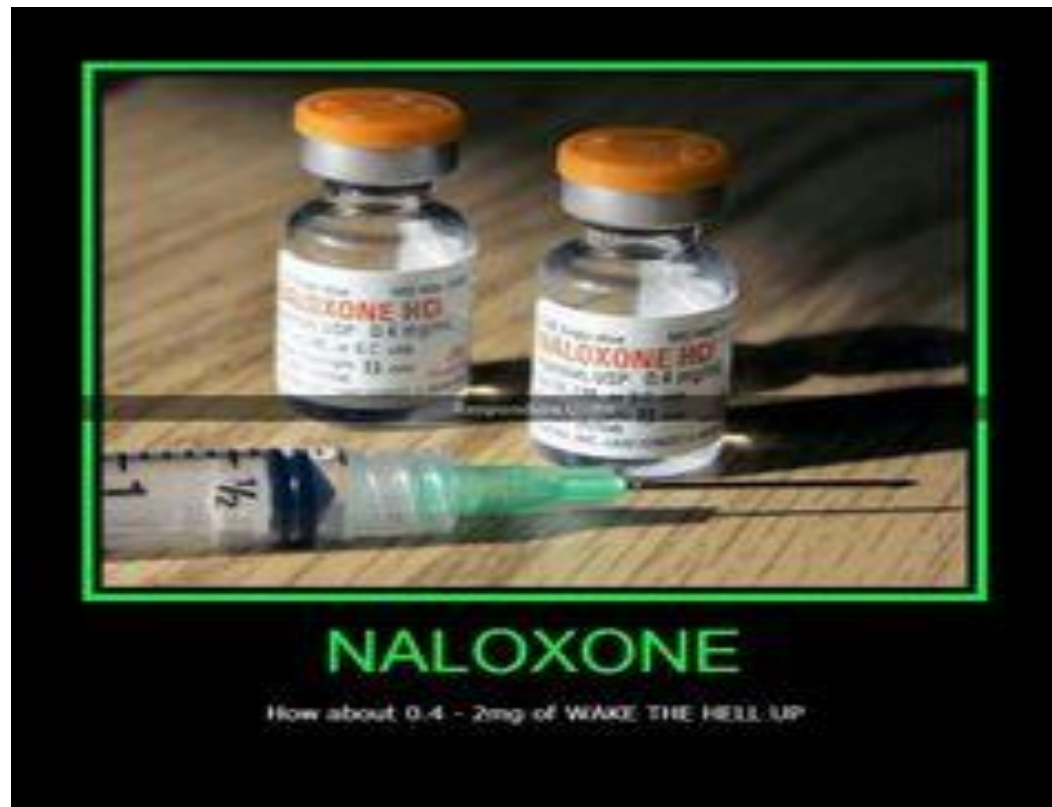
- Insulin (Lantus, Levemir, Novolog, Novolin)
- Sulfonylureas (glipizide, glyburide)
- S/Sx:
 - ▣ Altered mental status, sweating, tachycardia, hypertension, seizures, strange behavior, slurred speech
- Possible interventions:
 - ▣ Glucagon
 - ▣ D50
 - ▣ Octreotide

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

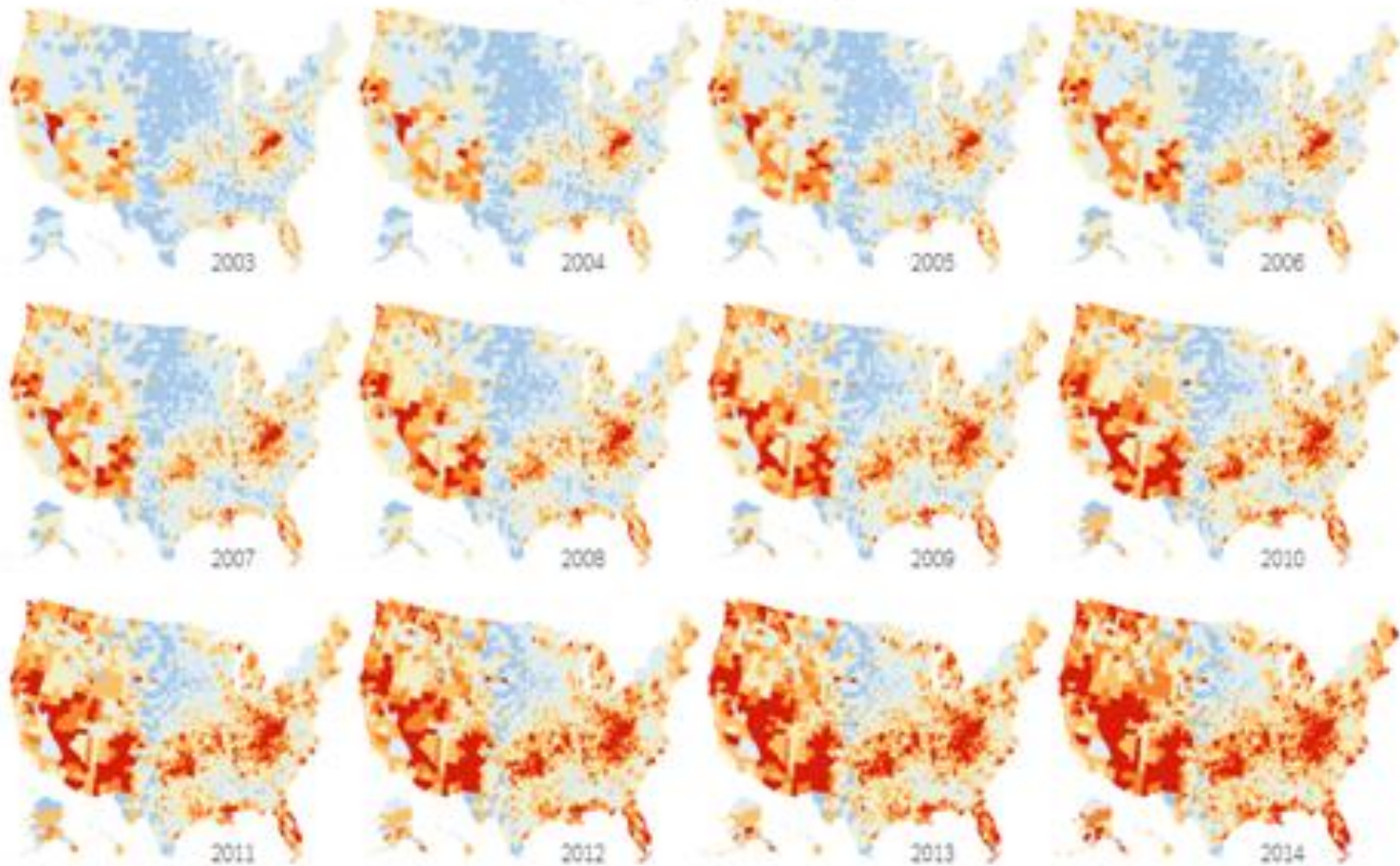
- 2011: 420,040 ED visits related to opioid misuse
- 2012: Drug overdose (OD) leading cause of death in 25-64 year olds
- 2013: 16,235 OD deaths due to opioids
- 2013: 34 overdose deaths in SD

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

U.S. | How the Epidemic of Drug Overdose Deaths Ripples Across America



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

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

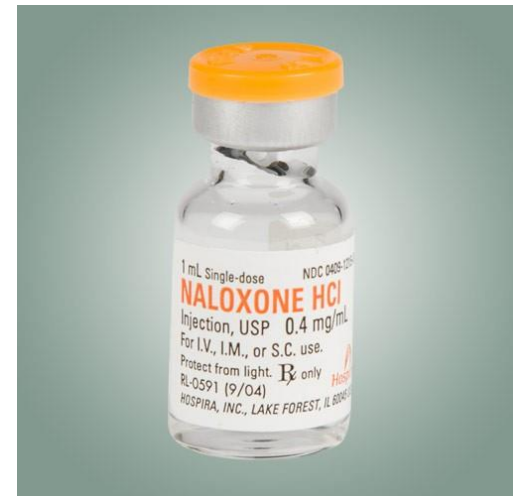
- Risk factors for heroin addiction
 - Addiction to other prescription pain medications
 - Cocaine addiction
 - No insurance or enrolled in Medicaid
 - Non-hispanic whites
 - Males
 - Addiction to marijuana and alcohol
 - Living in large metropolitan area
 - 18-25 years old

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

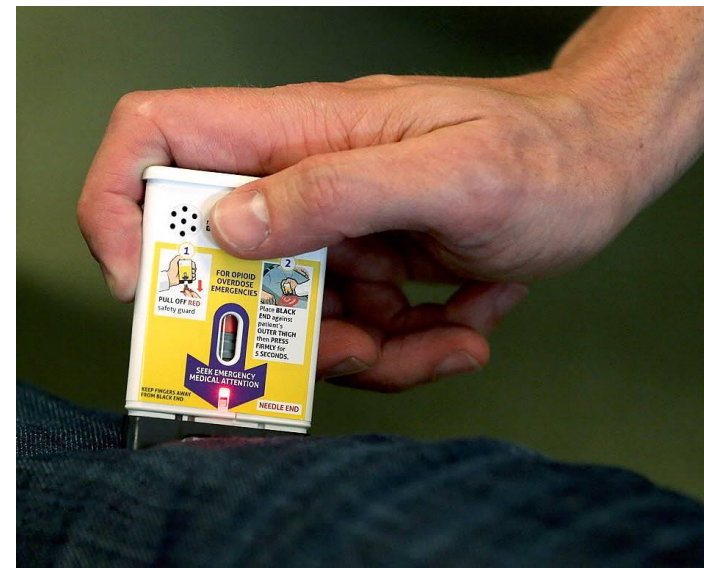


Naloxone Adverse Effects

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

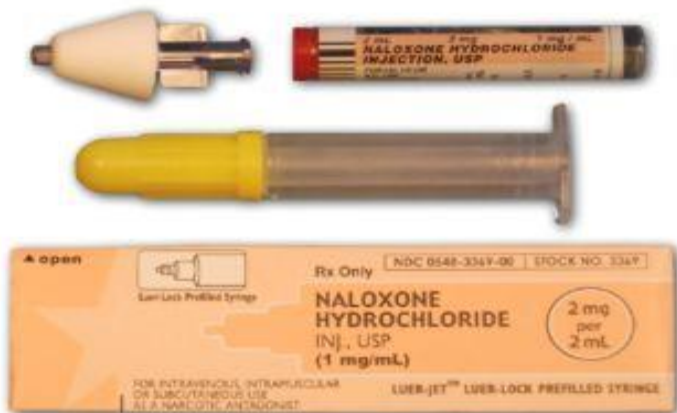
Evzio (Naloxone)

- ❑ 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



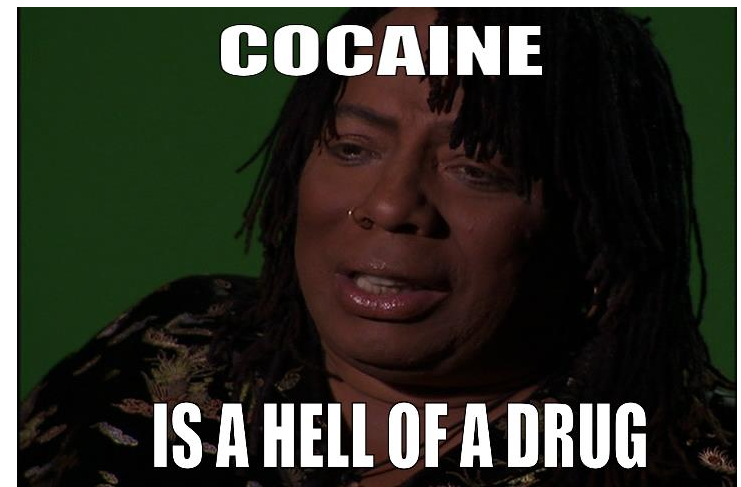
Intranasal Naloxone

- 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



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 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

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

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 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
 - ~1 g/kg

Toxic Alcohols

- Toxicity
 - Methanol → Formate
 - Orbital disc edema, Blindness
 - Ethylene Glycol → 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

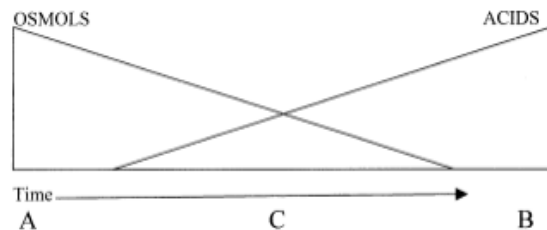


FIGURE 2. The Mountain.

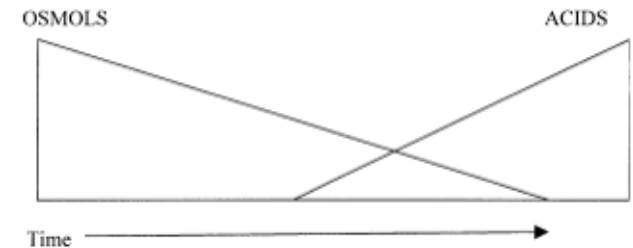


FIGURE 3. The Mountain in the presence of ethanol levels ≥ 100 mg/dL.

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)

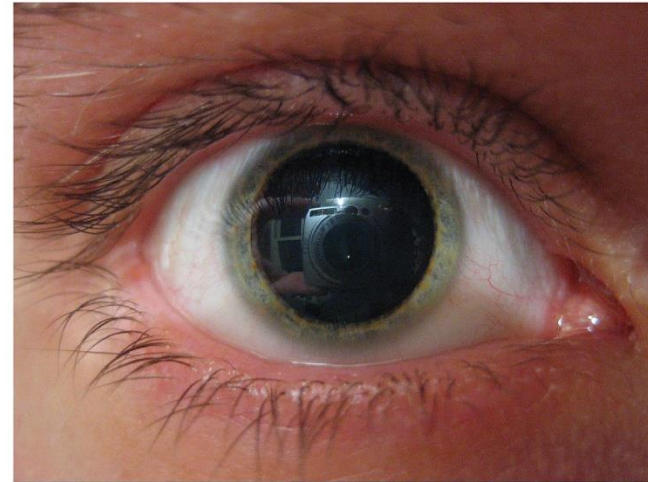
□ Presentation

▣ 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 (≥ 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



Figura 2: contenido del estómago.

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 toxidromes 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



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