Overdose & Poisoning

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With special thanks and gratitude to Dr. Art Wheeler
Overview

• ~6% of MICU admissions are overdoses
• Mortality is low (~1%) if they arrive alive
• Kids take one thing
• Adults usually take multiple drugs
• Deaths are from hypoxia and arrhythmias
• Few toxins have specific treatments
• Supportive care and judicious consideration of other processes are paramount
• WBC: 26.5  PCV: 40  Plt-Ct: 60
• Fibrinogen: <61
• Na: 148  K: 4.9  Cl: 117  CO2: 10
• BUN: 40  Creat: 2.97
• U-Myog: Positive
• Sedated and mechanically ventilated
• Vasopressors
• FFP for DIC
• Antimicrobials
• Passive cooling
• Dialysis
Careful neuromuscular examination
Consider lp and CT
What was taken?
How much
Timing
Look up the drugs involved
Poison control center/Toxicology consult
1-800-222-1222
## Examination Toxidromes

<table>
<thead>
<tr>
<th>Signs Symptoms</th>
<th>Anti-cholinergic</th>
<th>Cholinergic</th>
<th>Sympathomimetic</th>
<th>Narcotic Sedative</th>
<th>Serotonin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mental status</td>
<td>Delirium</td>
<td>Delirium</td>
<td>Delirium</td>
<td>Coma</td>
<td>Delirium</td>
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<tr>
<td>Skin</td>
<td>Dry/flushed</td>
<td>Sweating</td>
<td>Sweating</td>
<td>Normal</td>
<td>Flushed sweating</td>
</tr>
<tr>
<td>Temp</td>
<td>Elevated</td>
<td>Normal</td>
<td>Elevated</td>
<td>Normal /low</td>
<td>Elevated</td>
</tr>
<tr>
<td>Pulse</td>
<td>Rapid</td>
<td>Slow</td>
<td>Rapid</td>
<td>Slow</td>
<td>Rapid</td>
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<tr>
<td>Respiration</td>
<td>Normal</td>
<td>Bronchorrhea Wheezing</td>
<td>Rapid</td>
<td>Slow</td>
<td>Normal /rapid</td>
</tr>
<tr>
<td>BP</td>
<td>Normal/up</td>
<td>Normal/low</td>
<td>Up</td>
<td>Normal/low</td>
<td>Normal</td>
</tr>
<tr>
<td>Eyes</td>
<td>Dilated</td>
<td>Miosis/tears</td>
<td>Dilated</td>
<td>Miosis</td>
<td>Dilated</td>
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<tr>
<td>Peristalsis</td>
<td>Decreased</td>
<td>Diarrhea Vomiting</td>
<td>Increased</td>
<td>Decreased</td>
<td>Diarrhea</td>
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<tr>
<td>Others</td>
<td>Seizure, Myoclonus</td>
<td>Weakness Salivation Incontinence</td>
<td>Seizures</td>
<td>Flaccid Hyporreflexia</td>
<td>Trismus Tremor Myoclonus</td>
</tr>
</tbody>
</table>
# Toxidromes

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<tr>
<td>Atropine</td>
<td>Organophosphates</td>
<td>Amphetamines</td>
<td>Opioids</td>
<td>Fluoxetine</td>
</tr>
<tr>
<td>Tricyclics</td>
<td>Carbamates</td>
<td>Cocaine</td>
<td>Barbiturates</td>
<td>Paroxetine</td>
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<tr>
<td>Antihistamines</td>
<td>Physostigmine</td>
<td>Ecstasy</td>
<td>Benzodiazepines</td>
<td>Sertraline</td>
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<tr>
<td>Baclofen</td>
<td>Pilocarpine</td>
<td>Ephedrine</td>
<td>Ethanol</td>
<td>Trazadone</td>
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<tr>
<td>Benzotropine</td>
<td>Nerve gas (sarin)</td>
<td>Phencyclidine</td>
<td>Gamma-hydroxybutyrate</td>
<td>Clomipramine</td>
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<tr>
<td>Propantheline</td>
<td></td>
<td>Phenylpropanolamine</td>
<td>1,4, butane diol</td>
<td>Meperidine</td>
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<tr>
<td>Scopolamine</td>
<td></td>
<td>Phenylephrine</td>
<td>Anticonvulsants</td>
<td>MAO inhibitors</td>
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</tbody>
</table>
Toxins worth measuring

- Acetaminophen
- Aspirin
- Ethylene glycol
- Methanol
- Digitalis
- Lithium
- Theophylline
- Carbon monoxide
- Methemoglobin
- Phenobarbital
- Iron
Drugs with antidotes

- Acetaminophen - n acetyl cysteine
- Ethylene glycol - ETOH
- Methanol - ETOH
- Digitalis - Digibind
- INH - pyridoxime
Steps for (nearly) everyone

• **ABC’s**, check & fix glucose
• Stop exposure
  – Always remove contaminated clothing
  – Sometimes empty stomach (<60 min presentation)
  – Rarely use forced catharsis (extended release meds)
  – Almost never charcoal (Multidose for ASA, carbamazepine, theophylline, phenobarbital, dapsone, quinine)
• **ECG** (tachy, brady, blocks, QRS, QT)
• Electrolytes, creatinine, osmolarity
• **Arterial** blood gas, +/- co-oximetry
• Urinalysis for crystals
• Calculate anion and osmolar gaps
Anion Gap

- Anion gap = \( \text{Na}-[\text{Cl}+\text{HCO}_3^-] \) normal = 10
- S.L.U.M.P.E.D (M.U.D. P.I.L.E.S.)
  - Salicylates
  - Lactate
  - Uremia
  - Methanol
  - Paraldehyde
  - Ethanol / Ethylene glycol
  - Diabetic Ketoacidosis

- AG decreases with falling albumin
Osmolar Gap

• Calculate osmolarity =
  – $2 \times \text{Na} + \frac{\text{BUN}}{2.8} + \frac{\text{glucose}}{18} + \frac{\text{ethanol}}{4.6}$
  – Normal 275-295
  – If measured > calculated, search for other osmotic agents
    • Ethanol
    • Ethylene glycol
    • Methanol
    • Isopropyl alcohol
    • Mannitol
    • IV contrast
    • Glycerol
“Drug Screens”

- **No standard**
- **Most drugs that can be treated are not measured.**

**False positives**
- **Amphetamines:** ranitidine, chlorpromazine, bupropion, selegiline
- **Barbiturates:** ibuprofen, naproxen
- **Benzodiazepines:** oxaprozin
- **Marijuana:** pantoprazole, ibuprofen, naproxen
- **Opiates:** levofloxacain, oflocin, rifampin
- **PCP:** dextromethorphan, venlafaxine
- **Tricyclic:** cyclobenzaprine

**Not routinely measured**
- Fentanyl
- Salicylates
- Methanol
- Ethylene glycol
- Acetaminophen
- Digitalis
- Lithium
- Theophylline
Dialysis

- Ethylene glycol
- Methanol
- Potassium
- Aspirin
- Lithium
- Theophylline
- Iron
- Barbiturates
Acetaminophen

- Worlds most common poisoning
- Normal metabolism is to non-toxic sulfates and glucoronides.
- Toxic n-acetyl-p-benzoquinoneimine metabolite results when usual metabolic pathways overwhelmed
- Typical lethal dose 140 mg/kg (10 gm)
- Toxic dose lower in patients with P450 hepatic enzyme induction
  - Alcohol, barbiturates, BCP’s
Deciding who to treat

- Rumack-Matthew nomogram
- Applies to ingestions that are:
  - Single
  - Acute
  - In previously healthy persons
- Have a low threshold to start treatment
Acetaminophen treatment

- Stop exposure (empty stomach, stop orders)
- Replete glutathione using n-acetylcysteine
  - IV 150 mg/kg over 1 hr, then 50 mg/kg over 4 hr, then 100 mg/kg over 16 hr
    - Consider extending duration if patient remains sick
  - Oral 140 mg/kg load, then 17 doses of 70 mg/kg given q4hr
Salicylates

- Rare, highly lethal, fixable
- Rapidly absorbed (except bezoar)
- Acute toxic dose >150 mg/kg (10-30 gm)
- Delirium, fever, tinnitus, seizures
- Anion gap, mixed metabolic acidosis & respiratory alkalosis
- Toxicity unusual with < 30 mg/dL in acute ingestion but possible at lower levels with chronic use.
Salicylates

- Drug distribution highly dependent on pH
- Sedation or intubation can be fatal
- Treatment
  - Buffer acidosis
    - Hard to do
    - Treat hypokalemia
  - Dialysis if:
    - initial >120 mg/dL
    - 6 hr >100 mg/dL
Ethylene Glycol & Methanol

- The parent alcohols cause intoxication
- The metabolites (via alcohol dehydrogenase) cause toxicity
  - Methanol $\rightarrow$ formic acid & formaldehyde
  - Ethylene glycol $\rightarrow$ oxalic, glycolic & glyoxylic acids
- If early, organ failure may be absent; if late parent alcohol (osmoles) often absent.
Methanol

- "Wood alcohol"
- Sweet, moonshine contaminant
- Common in paint stripper, windshield washer fluid, antifreezes, tractor tire ballast
- More neurotoxic (eyes) than ethylene glycol
  - "Blind drunk"
- Causes metabolic acidosis
Ethylene glycol

• Common component of antifreeze
• Toxic dose ~100 mL
• More likely to cause hypertension and tachycardia than methanol.
• Early: intoxication
• Later:
  – Nephrotoxic: “coffin lids”
  – Metabolic acidosis
# Clinical Features of Alcohols

<table>
<thead>
<tr>
<th></th>
<th>Ethanol</th>
<th>Methanol</th>
<th>Ethylene glycol</th>
<th>Isopropanol</th>
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</thead>
<tbody>
<tr>
<td><strong>Osmolar gap</strong></td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td><strong>Ketones</strong></td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td><strong>Acidosis</strong></td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td><strong>Visual changes</strong></td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Calcium oxalate</strong></td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td><strong>Rx</strong></td>
<td>Nothing</td>
<td>Ethanol + dialysis</td>
<td>Ethanol + dialysis</td>
<td>Rarely dialysis</td>
</tr>
</tbody>
</table>
Treatment of “alcohols”

- Ethylene glycol
  - Glycoaldehyde
  - Glycolate
  - Glyoxylate
  - Oxalate
  - Dialysis

- Ethanol
  - Alcohol dehydrogenase
  - Acetaldehyde
  - Acetate

- Methanol
  - Formaldehyde
  - Formic acid
  - Dialysis
Alcohol dehydrogenase manipulation

- Ethanol serum target = > 100 mg/dL,
  - Load 800 mg/kg, maintenance 130 mg/kg/h
  - 100 mL of 10% ethanol/hr
  - (3-4 shots then 1-2 per hour)
- 4-MP
  - Load 15 mg/kg
  - Maintenance 10 mg/kg q12 h
- Both compounds are removed by dialysis therefore doses must be increased
Organophosphates / Carbamates

- Cholinergic toxicity
  - STUMBLED: salivation, tremor, urination, miosis, bradycardia, lacrimation, emesis, diarrhea
- Memorable smell: “insecticide”
- Lab confirmation: plasma pseudocholinesterase, erythrocyte acetylcholinesterase
- Treatment:
  - Protect yourself—decontamination
  - Airway protection
  - Atropine 2-4 mg
  - Pralidoxime (2-PAM) 1-2 gm, may repeat once (no effect on carbamates)
Digitalis

- Na-K pump poison
- Vision (yellow) changes, heart block, heart failure
- Diagnosis measure digitalis level
- Treatment
  - Correct hyperkalemia
  - Administer Digibind® / DigiFab® (10 vials usual dose)
    - Each vial of DigiFab® binds 0.5 mg of digitalis (1 vial/2 pills)
    - Drug levels unreliable after dosing
- Need functioning kidneys to clear antibody-drug complex
Cyclic antidepressants

• Toxicity is largely anticholinergic
  – Arrhythmias
  – Seizures
• Avid tissue binding means:
  – Levels correlate poorly with toxicity.
  – Dialysis ineffective
• ECG key: rate and QRS duration (> 0.12 sec)
  – No tachycardia = no toxicity
  – Common practice is to observe for 12 h after QRS normalizes
• Treatment: Usually observation
  – NaHCO$_3$: 1-2 mEq/kg, repeat until QRS < 0.12 or pH 7.45-7.55
  – Lidocaine or phenytoin second line antiarrhythmics
  – Fluid and norepinephrine for hypotension
  – Lorazepam, phenytoin, phenobarbital for seizures
• 56 yo married male
• Hx ETOH, oxycodone abuse, Paxil use
• Confused, sweaty, vomiting, diarrhea
• Unresponsive at OH, intubated (rocuronium)
• T 107.7
• LP and head CT negative
The likely diagnosis is:

a) Organophosphate poisoning
b) Lithium toxicity
c) Salicylate toxicity
d) Heat Stroke
e) Serotonin Syndrome
Serotonin toxicity

• Symptoms
  – Fever
  – Hyperreflexia, myoclonus, rigidity
  – Confusion
  – Seizures
  – Mydriasis

• Treatment supportive
  – External cooling
  – ? Cyproheptadine
  – Lorazepam for seizures, agitation
• Libby Zion
• 18yo admitted with delerium
• *Given* meperidine, haloperidol, restrained,
• Hyperthermia to 107
• Cardiac arrest
• She had been taking phenelzine (Nardil) and MAO inhibitor
• Change in house officer work hours
Beta Blockers

- Bradycardia and hypotension
- NS counteracts vasodilation induced hypotension and may have boost heart rate.
- Add vasopressors for hypotension
  - Vasopressin
  - Catecholamines
- Isoproterenol & atropine inconsistent effects
- Insulin should work
- Glucagon may work (no human trials)
- Calcium: might work
- Lipid infusion?
Calcium Blockers

- Bradycardia and hypotension
- Fluid counteracts vasodilation induced hypotension
- Calcium: inconsistent effects, 1 gm q 15 min x 4
  - Continuous infusion 0.2-0.4 mg/kg/hr CaCl\textsubscript{2}
- Glucagon: no human trials
- Lipid infusion?
Glucagon Treatment

• Activates g-proteins to generate cAMP
  – Inotropic
  – Chronotropic
• 3-10 mg bolus with 1-5 mg/hr infusion
• Tachyphylaxis in 4-24 hours
• Vomiting common
• Glucose: rises early, then falls as insulin levels rise
• Potassium: declines as insulin rises
• Very expensive
Euglycemic Insulin Treatment

• Increased inotropy and peripheral vascular resistance
• Increased myocardial metabolism
• If glucose < 200 1 amp D50W + 1 U regular insulin/kg
• 0.5-1.0 U/kg/hr titrate to effect
• D10W maintenance; check sugars q30-60 min
• Hypokalemia nearly routine
• 56 yo landscaper admitted with tremor, vomiting, and diarrhea for 6 hours
• Acutely ill, 98.6, 45, 12, 105/62, 98% RA
• Drooling, urine and stool stained pants, pupils 2 mm and reactive

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<tbody>
<tr>
<td>140</td>
<td>114</td>
<td>10 / 0.9</td>
</tr>
<tr>
<td>4.0</td>
<td>25</td>
<td>110</td>
</tr>
</tbody>
</table>
What is the dx?

- Serotonin syndrome
- Anaphylaxis
- Organophosphate poisoning
- Narcotic overdose
- Salicylate poisoning