Tox Tale Trio: Prescription, Occupational, and Household Toxic Exposures

Objectives
• Identify common signs symptoms associated with prescription drugs, occupational hazards, and household agents
• Describe antidotes used to treat specific toxidromes including calcium channel blockers, cyanide poisoning
• Recommend a treatment regimen for a patient with household chemical exposure, including drain cleaner and laundry detergent pods
• Develop treatment recommendations and monitoring for patients presenting with cyanide and pesticide poisoning
• Create treatment plans for prescription drug overdoses including digoxin, calcium channel and beta blockers

What is the concern?
• Toxic ingestions cause significant morbidity and mortality in the United States
• The American Association of Poison Centers' National Poison Data System 2012 Annual Report:
  • > 2.6 million substance exposures
  • > 950,000 are related to pharmaceuticals
  • 761 pharmaceutical related deaths

Beware of the Deadly Medicine Cabinet: Management of Prescription and Over-the-Counter Medication Overdoses
Megan Musselman, Pharm.D., MS, BCPS
Clinical Pharmacist Specialist
North Kansas City Hospital
Kansas City, MO

Patient Case #1
DO is a 23-year-old male that presented to the ED with a complaint of right-sided abdominal pain. Otherwise, the patient has no other complaints (except for the hospital food). Patient admitted to taking about “three handfuls” of acetaminophen a couple of days ago.
PMH: polysubstance abuse including tobacco, alcohol, and marijuana
Patient Case #1 (cont.)

- **Vitals:**
  - HR: 79 beats/min
  - BP: 148/84 mmHg
  - RR: 14 breaths/min
  - Temp: 97.2°F
- **Labs upon admission:**
  - Acetaminophen: 191 mcg/mL
  - Scr: 0.9 mg/dL
  - INR: 1.7
  - ALT/AST: 678/1543 units/L

Would this patient be classified as an acute or chronic intoxication?
- Acute
- Chronic

Acetaminophen

- Over-the-counter analgesic, antipyretic medication
- Component of many combination preparations (over-the-counter and prescription)
- #1 medication overdose in the United States

Mechanism of Toxicity

- Acetaminophen is rapidly absorbed
- Peak levels within 30-120 minutes
- Delayed in sustained release preparations
- **Toxic Dose:**
  - **Acute:**
    - Children: 200mg/kg
    - Adults: 6-7grams
  - **Chronic:**
    - Children: 150mg/kg/d for 2 days or 100mg/kg/d for 3 days or more
    - Adults: 150mg/kg/d (or 6g/d) for 2 days or more

Clinical Presentation

- **Four Stages of Toxicity**
  - **Stage I (< 24 hours):**
    - Little to no symptoms
    - Anorexia, nausea, or vomiting
  - **Stage II (24-48 hours):**
    - ALT/AST increase, hepatic necrosis
    - Abdominal pain, RUQ tenderness, vomiting, oliguria
    - Encephalopathy, metabolic acidosis and increasing PT/INR
    - Acute renal failure may occur
  - **Stage III (72-96 hours):**
    - Transaminases peak at 72 hours; PT rises, multi-system organ failure or recovery
  - **Stage IV (4d-2 weeks):**
    - Resolution of hepatotoxicity
Diagnosis

- Patient history
- Serum acetaminophen level
  - 4-hour and/or 8-hour post-ingestion level
- Rumack-Matthew Nomogram
  - Not applicable in chronic ingestion or late presentation

Rumack-Matthew Nomogram

Antidote: N-acetylcysteine

- Glutathione substitute
- Increases glutathione synthesis
- Early indication
  - Potential for hepatotoxicity after acetaminophen or other hepatotoxin ingestion (e.g., amatoxin)
- Late indication
  - Acetaminophen related hepatic failure

Antidote: N-acetylcysteine

- Oral administration (72 hours):
  - Loading dose: 140 mg/kg
  - Maintenance: 70 mg/kg q4h x 17 doses
- IV administration (21 hours):
  - Loading dose: 150 mg/kg (max: 15 g) infused over 60 minutes
  - 2nd dose: 50 mg/kg (max: 5 g) infused over 4 hours
  - 3rd dose: 100 mg/kg (max: 10 g) infused over 16 hours
  - Evidence indicates administration of IV NAC is beneficial in patient’s presenting 10-36 hours since ingestion

Patient Case #1 (cont.)

- Patient was started on IV NAC
  - Loading dose: 11,000mg (150 mg/kg) infused over 60 minutes
  - 2nd dose: 4,000mg (50 mg/kg) infused over 4 hours
  - 3rd dose: 7,500mg (100 mg/kg) infused over 16 hours
- Repeat Labs (20 hours after NAC initiation):
  - Acetaminophen: 89 mcg/mL
  - Scr: 0.9 mg/dL
  - INR: 2.1
  - ALT/AST: 3089/4410 units/L
Would you continue the N-acetylcysteine?

- Yes
- No

Prolonged/Shortened Administration

- Obtain Serum AST/ALT and acetaminophen levels ~18 hours after starting NAC
- Continue treatment:
  - Serum AST/ALT is elevated OR if the serum acetaminophen is detectable:
    - Continue NAC at 100mg/kg IV ("third bag") or 70 mg/kg PO every four hours
    - Obtain a serum acetaminophen and AST/ALT every 12 hours
    - If the ALT is elevated, also measure the international normalized ratio (INR)


Prolonged/Shortened Administration (cont.)

- Discontinue treatment:
  - Serum acetaminophen undetectable, AST/ALT is "clearly decreasing" or in the normal range, **AND** the INR <2.0.
  - No uniform definition of "clearly decreasing."
  - One conservative definition is a decrease of more than 50% from the peak measurement or 3 consecutive decreasing values, all below 1000 IU/L.


Patient Case #2

- RC is a 56 year-old female who presents to the ED secondary to an intentional ingestion of metoprolol tartrate 25mg and verapamil SR 120mg. Patient’s family member states that RC has been depressed since her mother passed away 2 weeks prior. Patient last filled her prescriptions two days ago and both bottles are empty.
- Vitals: 64/42 mmHg, HR 45 beats/minute, O₂sat 96%

Calcium Channel Blockers/Beta-Blockers

- Both agents are commonly used for the treatment of hypertension, arrhythmias, angina pectoris, etc.
- Both agents can provide toxic effects with therapeutic dosages

Mechanism of Toxicity

\[ \beta = \text{Beta, receptor}; \ G_s = \text{G protein}; \ AC = \text{adenylate cyclase}; \ ATP = \text{adenosine triphosphate}; \ cAMP = \text{cyclic adenosine monophosphate}; \ 5' \ AMP = \text{5' adenosine monophosphate-activated protein kinase}; \ PKA = \text{protein kinase A}; \ PDE = \text{phosphodiesterase}; \ Ca^{2+} = \text{calcium ion} \]

Clinical Presentation

- **Primary feature of toxicity is hypotension and bradycardia**
- **Calcium channel blocker (CCB):**
  - N/V, AMS, hyperglycemia
- **Beta blocker (BB):**
  - CNS toxicity, bronchospasm, hypoglycemia, hyperkalemia

Diagnosis

- Based on history of ingestion
- Vitals signs
  - Presence of bradycardia and hypotension
- Laboratory tests
  - Electrolytes, glucose, BUN, creatinine, arterial blood gases or oximetry, and cardiac monitoring
  - Presence of hyperglycemia is indicative of CCB
- Differential diagnosis:
  - Digitalis
  - Antihypertensive drugs
  - Other sympatholytic drugs

Treatment

- Emergency and supportive measures
  - Open airway and assist ventilation
- Decontamination
  - Activated charcoal
  - Whole bowel irrigation for sustained release preparations
- Enhanced elimination
  - Hemodialysis or multiple dose charcoal
  - Limited

Treatment (cont.)

- Calcium
  - Reverses the depression of cardiac contractility
    - Calcium chloride 10% 1gm IV q10min PRN
    - Calcium gluconate 10% 2-3gm IV q10min PRN
  - Epinephrine
    - Both alpha-adrenergic and beta-adrenergic effects
    - IVP or continuous infusion
  - Transcutaneous pacing

Antidote: Glucagon

- Positive inotropic and chronotropic effects
- **Dose:**
  - 2.5 mg (50 mg/kg) slow IVP then 1-5 mg/hr (Max: 10 mg/hr)
- **Adverse effects:**
  - N/V, hypoglycemia, phenol toxicity
**Antidote: High Dose Insulin Therapy**
- Positive inotropic effects
- Enhances carbohydrate utilization and energy production by myocardial cells
- Effective in animal models and successful in multiple human case reports
- Dose:
  - 1 unit/kg bolus
  - 1-10 units/kg/hour infusion
  - Titrate q30mins to achieve or maintain hemodynamic stability
  - Monitor glucose and potassium (K⁺)

**Antidote: Lipid Emulsion Therapy**
- "Lipid Sink" - shift of lipophilic drugs from tissues into the vascular compartment for elimination
- **Indications:**
  - Anesthetics
  - Lipophilic agents (e.g., verapamil, bupropion, lamotrigine, propranolol)
- **Dose:**
  - 1.5 mL/kg of 20% ILE over 1 min; can be repeated twice every 5 mins
  - 0.25-0.5 mL/kg/min over 60 min
  - Only increase to 0.5 mL/kg/min if hypotension persists
- **http://lipidrescue.org/**

**Patient Case #3**
- An 89-year-old female with paroxysmal atrial fibrillation, chronic kidney disease, hypertension, diastolic heart failure, and hypothyroidism, presented to the ED from a NH with confusion
- She had recently been hospitalized 1 month prior for failure to thrive, manifested by increasing weakness and anorexia. These symptoms were attributed to worsening arthritis and hypothyroidism. During hospitalization, she was initiated on furosemide, and she was discharged to a SNF for physical therapy.
- One week prior to presentation she followed up with her primary with complaints of GI upset. Upon presentation to the ED, she denied recent falls, lightheadedness, syncope, CP, or SOB.

**Is this patient experiencing acute digoxin toxicity?**
- Yes
- No

**Patient Case #3 (cont.)**
- **Medications:**
  - Digoxin 0.25 mg oral daily
  - Furosemide, lisinopril, levothyroxine and omega-3 fish oil
- **Physical exam/Vitals:**
  - HR: 30 beats/min
  - BP: 110/60 mmHg
  - Grade II systolic ejection murmur
  - Bilateral lower extremity ulcers
  - Weight: 70kg
- **Laboratory values:**
  - Scr=2.0, BUN= 108 mg/dL, with estimated GFR 23
  - Digoxin level of 4.2 ng/mL (0.5-1.3)
  - Normal potassium and magnesium levels
  - U/A (+)

**Digoxin**
- Cardiac glycosides are found in several plants
  - Digitalis, oleander, foxglove, etc.
- Chinese herbal medication and herbal aphrodisiacs
- Used in heart failure and as an antiarrhythmic agent

© 2014 American Society of Health-System Pharmacists
Mechanism of Toxicity
- Inhibits the function of the sodium-potassium-ATPase pump
- Direct effects and potentiation of vagal tone results in slowing of the sinus rate and decreased sinus and atrioventricular node conduction velocity
- Increased atrial and ventricular automaticity occurs
  - Accumulation of intracellular calcium
  - Enhanced diastolic depolarization
  - Development of afterdepolarizations
  - Increased in the presence of hypokalemia and hypomagnesemia
- Toxic Dose:
  - Acute:
    - > 10 mg (adult) or > 4 mg (child) or a serum level of >10 ng/ml (6-8 hours post-ingestion)

Clinical Presentation
- Acute:
  - Vomiting, hyperkalemia, and cardiac arrhythmias (brady- or tachyarrhythmia)
- Chronic:
  - Nausea, anorexia, abdominal pain, visual disturbances, weakness, cardiac arrhythmias (brady- or tachyarrhythmia), mental status changes
  - Diuretic use can cause hypokalemia and hypomagnesia worsening tachyarrhythmia

Diagnosis
- History of recent overdose
- Characteristic arrhythmias in patients on chronic therapy
- Hyperkalemia may suggest acute ingestion
  - K > 5.5mEq/L is associated with severe poisoning
  - Not useful in chronic toxicity
- Serum digoxin level
  - Time since ingestion is important (peak vs. trough)
- Electrolytes, BUN, creatinine, serum magnesium and ECG monitoring

Treatment
- Emergency and supportive measures
  - Maintain an open airway and assist ventilation
  - Monitor the patient closely for 12 to 24 hours
  - Treat hyperkalemia
    - Calcium
      - Calcium gluconate 10% 2-3gm
      - Calcium chloride 10% 1gm
    - “Stone heart”
      - Dextrose and insulin
      - Sodium polystyrene sulfonate
  - Treat any underlying electrolyte disorders that may contribute to cardiac toxicity

Treatment (cont.)
- Treat bradycardia or heart block
  - Atropine 0.5mg IVP
  - Temporary transvenous cardiac pacemaker may be needed (rare circumstances)
- Decontamination
  - Activated charcoal
- Enhanced elimination
  - Not effectively removed by hemodialysis
  - Repeat-dose activated charcoal

Antidote: Digoxin-specific Antibodies
- Effective in both digoxin and digitoxin toxicity
- Affinity of digoxin-specific antibodies to digoxin is > than the affinity of digoxin for Na⁺/K⁺-ATPase
- Fab fragment-digoxin complex accumulates in the blood and is excreted by the kidney
- Net effect is less binding of digoxin to its receptors in the body reversing its effects
- Indication:
  - Severe ventricular arrhythmias, bradycardia, second or third degree heart block not responsive to atropine, and/or hyperkalemia (>5.5 mEq/L)
Antidote: Digoxin-specific Antibodies (cont.)

- **Dose:**
  - Amount ingested unknown
  - **Acute:**
    - Adult and children: 10-20 vials IV over 30 minutes
    - Administer 10 vials followed by 10 additional vials to avoid febrile reaction
    - Monitor volume overload
  - **Chronic:**
    - Adult: 3-6 vials
    - Children: 1-2 vials

Antidote: Digoxin-specific Antibodies (cont.)

- Amount ingested known (mg):
  - Dose (vials) = digoxin body load (mg) / 0.5 mg digoxin bound/vial
- **Steady state serum concentration (concl) known:**
  - Dose (vials) = serum dig conc (ng/ml) x weight (kg) / 100
- **Additional Considerations:**
  - Serum measurements are not clinically useful post administration
  - Assays measure both bound and unbound digoxin
  - Decision to retreat should be based on clinical observations

How many vials should we administer to our patient?

- 1 vial
- 3 vials
- 5 vials
- 10 vials

Patient Case #3 Revisited

- **Medications:**
  - Digoxin 0.25 mg oral daily
  - Furosemide, lisinopril, levothyroxine and omega-3 fish oil
- **Physical exam/Vitals:**
  - HR: 30 beats/min
  - BP: 110/60 mmHg
  - Grade II systolic ejection murmur
  - Bilateral lower extremity ulcers
  - Weight: 70kg
- **Laboratory values:**
  - Scr=2.0, BUN=108 mg/dL, with estimated GFR 23
  - Digoxin level of 4.2 ng/mL (0.5-1.1)
  - Normal potassium and magnesium levels
  - U/A (+)

Patient Case #3 Revisited

- An 89-year-old female with paroxysmal atrial fibrillation, chronic kidney disease, hypertension, diastolic heart failure, and hypothyroidism, presented to the ED from a NH with confusion

  - She had recently been hospitalized 1 month prior for failure to thrive, manifested by increasing weakness and anorexia. These symptoms were attributed to worsening arthritis and hypothyroidism. During hospitalization, she was initiated on furosemide, and she was discharged to a SNF for physical therapy.

  - One week prior to presentation she followed up with her primary with complaints of GI upset. Upon presentation to the ED, she denied recent falls, lightheadedness, syncope, CP, or SOB.

How many vials should we administer to our patient?

- 1 vial
- 3 vials
- 5 vials
- 7 vials

Dose (vials) = serum dig conc (ng/ml) x weight (kg) / 100
Are we giving too much?

- Clinical benefit of digoxin-specific antibodies in non-life threatening toxicity is questioned
- **Acute ingestions:**
  - 1-2 vials at a time and observe for clinical response
  - If no response after 60 minutes, administer another vial
- **Chronic ingestions:**
  - 1 vial at a time and observe for clinical response.
  - If no response after 60 minutes, administer another vial

How you ever seen a patient present with a suspected opioid overdose?

- Yes
- No

Patient Case #4

- A 30-year old male, who is a known opioid addict, presents to the ED after an intentional overdose of methadone. The patient is obtunded and unable to respond when questioned. The amount ingested is unknown.

- **Physical exams/vitals:**
  - GCS 3
  - HR 48 beats/min
  - RR 4 breaths/min, O₂ sat 91% on RA
  - Pinpoint pupils

Opioids

- Opiates are derived from the juice of the poppy, *Papaver somniferum*
- Opioids refer to opiates and any derivatives or synthetic opiate analogs
- Wide variety of prescription medications contain opioids
  - Oftentimes found in combination with other agents
- Opioid overdose is considered an epidemic
  - ~15,000 people die/year of overdoses involving opioids
  - 1 in 20 people use prescription opioids for nonmedical reasons in the US

Mechanism of Toxicity

- Over stimulation of specific opiate receptors in the CNS
  - Mu, kappa and delta
- Results in sedation and respiratory depression
- Can cause acute non-cardiogenic pulmonary edema
- **Toxic dose:**
  - Varies depending on offending agent, route and rate of administration, and tolerance to the effect of the agent

Clinical Presentation

- Mild to moderate intoxication
  - Lethargy, miosis, hypotension, bradycardia, and diminished/absent bowel sounds
- Severe intoxication
  - Coma, respiratory depression, apnea, non-cardiogenic pulmonary edema, and sudden death
- Seizures
  - Uncommon
  - Codeine, dextromethorphan, meperidine, methadone and tramadol
- Cardiotoxicity
  - Prolonged QT interval and torsades de pointes
  - Methadone

© 2014 American Society of Health-System Pharmacists
**Diagnosis**

- Usually based on clinical presentation
- Miosis and respiratory and CNS depression
- Serum drug levels have little significance
- Poor correlations with clinical effects
- Resolution of symptoms post-naloxone administration
- Electrolytes, glucose, arterial blood gases or oximetry, chest radiography and STAT serum acetaminophen or salicylate levels

**Treatment**

- Emergency and supportive measures
- Maintain and open airway and assist ventilation
- Decontamination
- Activated charcoal
- Enhanced elimination
- No role

**Antidote: Naloxone**

- Specific opioid antagonist
- Dose:
  - Intranasal: 2mg (1mg per nostril) q5min, if respiratory depression continues
  - IV/IM: 0.2-0.4mg q2-3 minutes, if no response
  - Endotracheal: 0.8-1mg (2-2.5x the initial IV dose)
  - Auto-injector: 0.4mg IM/SC q2-3mins, if no response
  - Continuous infusion: calculate dose/hr based on effective intermittent dose and duration
    - Reserved for long acting opioids, sustained release products and symptomatic body packers
  - Monitor for opioid withdrawal syndrome
  - Anxiety, piloerection, heightened sensation of pain, abdominal cramps, diarrhea and insomnia

**Patient Case #5**

- A 27-year old male, weighing 86kg was brought to ED via ambulance with decreased conscious state, approximately 1 hour after intentionally ingesting 100 x 1mg of alprazolam tablets with one alcoholic drink (approximately 30mls of scotch with coke) following a disagreement with his partner.
- He had no prior history of suicidality or drug misuse and had been prescribed alprazolam for management of anxiety attacks in the setting of PTSD following a MVC the previous year.
- Following the ingestion, he notified his partner almost immediately and she contacted emergency services. He denied ingestion of any other substances and no other medication was found at the scene by paramedics.

**Patient Case #5 (cont.)**

- En route to the ED, he became drowsier and at the time of assessment, was opening eyes only to painful stimuli, localizing to pain and groaning (GCS 9)
- **Vitals:**
  - HR: 70 beats/min
  - BP: 110/65 mmHg
  - ECG was normal
- **PMH:**
  - Closed head injury
  - Seizures
  - PTSD

**Would you administer flumazenil to this patient?**

- Yes
- No
Benzodiazepines

- Death from overdose is rare unless combined with other CNS-depressant agents
- Ethanol, opioids, and barbiturates
- Newer potent, short-acting agents have been considered as more deadly
- Triazolam, alprazolam and midazolam

Mechanism of Toxicity

- Enhance the action of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA)
- Inhibits other neuronal systems
  - Poorly defined
- Leads to generalized depression of spinal reflexes and reticular activating system
  - Coma and respiratory arrest
- Toxic Dose:
  - Toxic-therapeutic ratio is very high

Clinical Presentation

- Onset:
  - 30-120 minutes depending on offending agent
- Signs/symptoms:
  - Lethargy, slurred speech, ataxia, coma, and respiratory depression/arrest
  - Hyporeflexia, small pupils, and hypothermia are possible

Diagnosis

- Based on history from patient or bystanders
- Urine and serum drug levels are rarely of value in the ED
  - Benzodiazepines are extensively metabolized, and the parent compounds are not detected in urine
  - Most immunoassays are only sensitive to agents that metabolize to oxazepam
  - Diazepam, chlordiazepoxide and temazepam
- Differential diagnosis:
  - Other sedative-hypnotic agents
  - Antidepressants
  - Antipsychotics
  - Narcotics

Treatment

- Emergency and supportive measures
  - Maintain airway and assist ventilation
  - Treat coma, hypotension, and hypothermia if they occur
    - Oxygen, IV fluids/positioning, and warm blankets
- Decontamination
  - Activated charcoal if ingestion within 30-60 minutes of presentation
- Enhanced elimination
  - No role

Antidote: Flumazenil

- Specific benzodiazepine receptor antagonist
- Limited role/not routine care
  - Seizures in patients who have co-ingested pro-convulsant agents or history of seizures
  - Acute withdrawal (autonomic instability and seizures) in patients chronically on benzodiazepines
  - Re-sedation after drug wears off ~ 1-2 hours after administration
    - Repeated dosing or continuous infusion may be necessary
- Dose:
  - 0.1-0.2mg IV repeated PRN up to a max of 3mg
Would you administer flumazenil to this patient?

- Yes
- No

Key Takeaways

1. N-acetylcysteine should be tailored to patient-specific parameters resulting in either prolonged or shortened courses.
2. Administration of digoxin-specific antibodies should be based on clinical presentation and complete neutralization is oftentimes not necessary.
3. Naloxone can be administered multiple routes in an emergent situation when an IV line cannot be obtained (i.e. intranasal, endotracheal, intramuscular).
4. Flumazenil has a limited role in an overdose situation unless the patient is a child or is known to be previously benzodiazepine-naive.

What type of insecticide is malathion?

- Carbamate
- Pyrethrins and pyrethroids
- Organophosphate
- Organic chlorines

Harms to Humans and Domestic Animals

**WARNING.** Harmful if swallowed, inhaled or absorbed through skin. Use with adequate ventilation. Avoid breathing spray mist. Avoid contact with skin, eyes or clothing. Causes eye irritation.

**NOTE TO PHYSICIAN:** This product contains a cholinesterase inhibitor.
Understanding Pesticide Labeling

- **Signal Word**
- **Toxicity Category I: DANGER**
- **Toxicity Category II: WARNING**
- **Toxicity Category III: CAUTION**
- **Toxicity Category IV: None Required**
- **First aid statement**

Pesticide Chemical Search

http://iaspub.epa.gov/apex/pesticides/f?p=CHEMICALS

Office of Pesticide Programs

Chemical Name: [Blank]
CAD Number/PC Code: [Blank]

Commercial OP Products

- **High Risk**
  - Paraoxon
  - Oxoniox
  - Paraoxon
  - Ethion

- **Moderate Risk**
  - Chlorpropham
  - Methamidophos
  - Phosphamidon

- **Low Risk**
  - Dicrotophos
  - Dithianon
  - Diuron

Clinical Manifestations

- **Muscarinic effects**
  - Runny nose
  - Watery eyes
  - Abdominal cramps

- **CNS effects**
  - Confusion
  - Agitation
  - Coma

- **Nicotinic effects**
  - Skin rash
  - Skin irritation
  - Skin swelling

Laboratory Assessment

<table>
<thead>
<tr>
<th>RBC Acetylcholinesterase</th>
<th>Pseudocholinesterase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accuracy</td>
<td>Greater</td>
</tr>
<tr>
<td>Pseudocholinesterase</td>
<td>Less</td>
</tr>
</tbody>
</table>

- **Toxicity Category I: DANGER**
- **Toxicity Category II: WARNING**
- **Toxicity Category III: CAUTION**
- **Toxicity Category IV: None Required**

- **Muscarinic effects**
  - Runny nose
  - Watery eyes
  - Abdominal cramps

- **CNS effects**
  - Confusion
  - Agitation
  - Coma

- **Nicotinic effects**
  - Skin rash
  - Skin irritation
  - Skin swelling

- **Laboratory Assessment**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Later</th>
<th>Early</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute infections</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Anticholinergic</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Antihypertension</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Antiparkinsonian</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Antipsychotic</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

Lactate: 6.8 mmol/L
RBC acetylcholinesterase: 8.6 units/g/dL
Pseudocholinesterase: not detectable

57 y.o. male "unresponsive with possible seizure activity"

HPI: cleaned up malathion spill previous day
General Principles in the Management

<table>
<thead>
<tr>
<th>Decontamination</th>
<th>Airway Protection</th>
<th>Treatments</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Skin</td>
<td>• Airway</td>
<td>• Atropine</td>
</tr>
<tr>
<td>• Eyes</td>
<td>• Breathing</td>
<td>• Pralidoxime</td>
</tr>
<tr>
<td>• GI</td>
<td>• Circulation</td>
<td>• Seizure management</td>
</tr>
</tbody>
</table>

Atropine Pearls

- Adults: 1 to 3 mg, may doubled every 3-5 min
- Children: 0.02 mg/kg, minimum of 0.1 mg
- Atropinization
  - Clear lungs
  - Reversal of muscarinic toxic syndrome
  - HR / BP (?)

**Reversal of miosis should not be an endpoint**

AtroPen® autoinjectors

- Adults and Children > 90 lbs 2 mg
- Children 40 lbs – 90 lbs 1 mg
- Children 15 lbs – 40 lbs 0.5 mg
- Infants < 15 lbs (0.05-0.1 mg/kg) 0.25 mg

Pralidoxime IV Infusion Dosing

- Adults: 1-2 gm over 30 min, may repeat after 1 hour if symptoms persist
- Children: 20-50 mg/kg (max 2 gm), may repeat after 1 hour if symptoms persist
- 2-PAM until atropine not needed for 12-24 hours
- Intermittent vs. continuous infusion
Pralidoxime (2-PAM) – IM Dosing

<table>
<thead>
<tr>
<th></th>
<th>Mild/Moderate</th>
<th>Severe symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult</td>
<td>600 mg</td>
<td>1800 mg</td>
</tr>
<tr>
<td>Adolescent (&gt;10 years)</td>
<td>15 mg/kg</td>
<td>25 mg/kg</td>
</tr>
<tr>
<td>Child (2-10 years)</td>
<td>15 mg/kg</td>
<td>25 mg/kg</td>
</tr>
<tr>
<td>Infants (0-2 years)</td>
<td>0.05 mg/kg</td>
<td>0.1 mg/kg</td>
</tr>
</tbody>
</table>

Based on patient’s presentation, what is the most likely culprit?

- Carbon monoxide poisoning
- Cyanide poisoning
- Phosgene poisoning
- Methane gas poisoning

Clinical Manifestations

**Cyanide Toxicity**
- Nausea, vomiting
- Headache, agitation, confusion
- Bradycardia followed by hypertension with reflex tachycardia
- Lethargy, seizures, coma

**CO Poisoning**
- Nausea, vomiting
- Headache, confusion, ataxia
- Chest pain, cardiac dysrhythmias, MI
- Dyspnea, tachypnea
- Weakness, lethargy
- AMS, seizures, coma

Patient was given hydroxycobalamin for possible cyanide toxicity. Do you agree with the above treatment?

- Yes
- No
Suspecting Cyanide Poisoning

• Fire victim with coma or metabolic acidosis
• Suicide attempt with unexplained coma or metabolic acidosis
• Ingestion of artificial nail remover
• Patient on nitroprusside therapy with AMS, metabolic acidosis

General Principles in the Management

<table>
<thead>
<tr>
<th>Decontamination</th>
<th>Airway Protection</th>
<th>Treatments</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Skin</td>
<td>• Airway</td>
<td>• Hydroxocobalamin</td>
</tr>
<tr>
<td>• Eyes</td>
<td>• Breathing</td>
<td>• Amyl nitrite</td>
</tr>
<tr>
<td>• GI</td>
<td>• Circulation</td>
<td>• Sodium nitrite</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Sodium thiosulfate</td>
</tr>
</tbody>
</table>

Cyanide Toxicity Antidotes

- Cyanide Antidote Kit
- "5-Drug Antidotes" Amyl Nitrite, Sodium Nitrite, Sodium Thiosulfate
- CyanoKit Hydroxocobalamin
- Nathiodote Sodium Nitrite, Sodium Thiosulfate

Nitrites / Sodium Thiosulfate

- **Amyl nitrite**
  - Temporizing measure
  - Break one amyl nitrite ampule and inhaled for 15 secs and 15 secs off until IV access

- **Sodium nitrite**
  - 300 mg (10 ml of 3% solution)
  - Followed by sodium thiosulfate

- **Sodium thiosulfate**
  - Adult: 12.5 gm bolus or infused over 10-30 minutes (may repeat at ½ the initial dose)
  - Children: 0.5 gm/kg, up to the adult dose

Hydroxocobalamin Pearls

- Adults: 5 gm over 15 minutes
- Children: 70 mg/kg, up to adult dose
- Synergistic with sodium thiosulfate
- Adverse effects

BP 106/59 HR 68 RR 18 T 36.3°C SpO2 99% RA

No acute abnormalities of conjunctivae and eye lids

Normal range of motion: Right lower extremity has approximately 8 x 6 cm lesion with nearly full thickness burn with dark eschar on the dorsum of the foot

ERG: normal

20 y/o male "burn on his right foot"

HPI: spilled undiluted unknown chemical while working at a car wash
**Based on patient’s presentation, what is the most likely culprit?**

- Ammonium hydroxide
- Hydrofluoric acid
- Sodium hydroxide
- Sodium hypochlorite

**Hydrofluoric Acid**

- Dermal effects
  - Delayed pain
  - Ulcerations
  - Skin necrosis

**Calcium**

- Calcium gluconate topical gel 2.5%
- Preparation:
  - Calcium carbonate tablets 10 gm
  - Calcium gluconate powder 3.5 gm
  - Calcium gluconate 10% solution 25 ml
  - + 5 ounces of K-Y Jelly
- Intradermal, intraarterial, and IV calciums

**What type of toxins do you think is the culprit?**

- Warfarin abuse
- Brodifacoum rodenticide
- Bromethalin rodenticide
- Arsenic trioxide rodenticide

**Brodifacoum**

- “superwarfarins” or “long-acting anticoagulants”
- Use as active ingredient of rodenticides
- Other superwarfarins:
  - difenacoum, bromadiolone, coumaphos, chlorophacinone, diphacinone
- 100 x more potent than warfarin
**Brodifacoum**

- Greater affinity for vitamin K1-2,3-epoxide reductase
- Hepatic accumulation
- High lipid solubility
- Longer duration of action
- Elimination $t_{1/2}$ varies, 243 – 1,656 hours

**Clinical Features**

- Nonspecific symptoms
- Significant coagulopathy
- Spontaneous hemorrhage
  - Skin, nose, gums (common)
  - Hematuria
  - Vital organs (GI, CNS)

**Laboratory**

- PT/INR on admission
- A single INR at 48 hours should identify acute known exposures at risk for coagulopathy
- Vitamin K-dependent factors (II, VII, IX, and X)
- Brodifacoum levels not readily available

**Brodifacoum - Treatment**

- Similar to management of warfarin-induced bleeding
  - Cryoprecipitate
  - FFP
  - PRBC
  - PCC
  - Factor VII (?)
  - Intravenous
  - Subcutaneous
  - Oral
  - Vitamin K
Phytonadione

- Oral is preferred route for maintenance therapy
- Maintenance of normal INR depends on the t½ of anticoagulant involved
- Reserved IV route for life-threatening bleeding and serious bleeding at any elevation of INR
- Optimal dosage is unclear
- Repeat dosage two to four times daily

Key Takeaways

1. In suspected or known organophosphate poisoning, decontamination is key!!
2. Atropine should be given until atropinization occurs
3. 2-PAM should be given in conjunction with atropine in moderate to severe organophosphate poisoning
4. Hydroxocobalamin is considered the first line antidote for cyanide poisoning
5. Duration of Phytonadione (Vitamin K) treatment for brodifacoum is dependent on clinical symptoms and laboratory values

Duration of Vitamin K₁ Treatment

<table>
<thead>
<tr>
<th>Spahr, et al.</th>
<th>Amount of Brodifacoum Ingested</th>
<th>Vitamin K₁ Treatment</th>
<th>Duration of Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patient 1: unknown</td>
<td>PO 100 mg BID x SQ 10 mg BID</td>
<td>120 days</td>
</tr>
<tr>
<td></td>
<td>Patient 2: unknown</td>
<td>PO 70 mg BID</td>
<td>16 days</td>
</tr>
<tr>
<td>Lo, et al.</td>
<td>170 gm</td>
<td>PO 10 mg daily</td>
<td>35 days</td>
</tr>
<tr>
<td>Gunja, et al.</td>
<td>100 mg daily</td>
<td>180 days</td>
<td></td>
</tr>
<tr>
<td>Altay, et al.</td>
<td>100 mg daily</td>
<td>90 days</td>
<td></td>
</tr>
<tr>
<td>Underwood, et al.</td>
<td>Unknown up to 80 mg daily</td>
<td>up to 365 days* intermittent therapy</td>
<td></td>
</tr>
</tbody>
</table>

Drain Cleaner

- 50 year old woman en route via helicopter
- EMS reports bilateral self inflicted lacerations to neck, attempted hanging, and ingestion of “a bottle of Drano"
Would this pre-hospital report freak you out?

Yes
No

What do you want to know?

• How is the patient?

What do you want to know?

• How is the patient?
  • Airway patent, hemodynamically stable, $O_2$ sats normal, drooling, GCS 15, flat affect

What do you want to know?

• How is the patient?
  • Time of ingestion?
    • Patient found 30 minutes prior to EMS arrival
    • Last seen 2 hours prior to EMS activation

What do you want to know?

• How is the patient?
  • Time of ingestion?
  • Product ingested?
    • ACE brand liquid drain cleaner
  • Quantity of product ingested?
    • Empty 1 L bottle found on scene
What do you want to know?

• How is the patient?
• Time of ingestion?
• Product ingested?
• Quantity of product ingested?
• Co-ingestants?
  • None reported, APAP and ASA level sent

Drain Cleaner

• Many brands, many different compositions
• Typically a strong base (i.e. sodium hydroxide)
  • Strong bases cause liquefactive necrosis
    • Protein dissolution, collagen destruction, fat saponification, cell membrane emulsification
    • Penetration into tissues continues until OH⁻ concentration neutralized by tissues

Types of Exposure

• Oral ingestion
  • Highest morbidity and mortality
• Respiratory tract
  • Can occur following aspiration in oral exposure
• Ocular
• Skin

Signs and Symptoms

• Oral ingestion
  • Pain in mouth, throat, chest, and abdomen
  • Oropharyngeal edema can lead to drooling, stridor, airway compromise
  • Dysphagia, hematemesis can be signs of esophageal or gastric involvement
  • Systemic absorption can lead to end organ damage

Treatment of Alkaline Ingestions

• Start with supportive care
  • Airway edema can progress very quickly
  • Signs of airway edema should prompt prophylactic endotracheal intubation
    • Signs include stridor, change in voice, visual indication of swelling
    • Consider dexamethasone
  • Distributive shock possible, consider IV fluids and pressors as needed
Going Back to the Case…

Should gastric lavage be performed at this time?

Yes
No

Treatment of Alkaline Ingestions

• DO NOT attempt gastric decontamination
  • Insertion of orogastric or nasogastric tube could lead esophageal perforation
  • No role for activated charcoal
• DO NOT attempt to neutralize
  • Exothermic reaction and gas formation can exacerbate tissue damage
• Consider dilution with milk or water if solid alkaline substance ingested (eg Drano crystals)

Assessing the Damage

• CT and radiographs can be useful for identifying perforations
  • If PO contrast used, water soluble preferred
  • Avoid if patient at risk for aspiration
• Endoscopy within 12 hours
  • Grade I – edema without ulceration
  • Grade II – submucosal lesions, ulcerations
  • Grade II a – non-circumferential lesions
  • Grade II b – near to full circumferential
  • Grade III – deep ulceration, tissue necrosis

A Chance to Cut is a Chance to Heal

• Surgical intervention indicated if...
  • Evidence of perforation
    • Radiologic or endoscopic findings
    • Severe abdominal rigidity
  • Persistent hypotension
  • Grade II b or grade III injuries
    • Dependant on surgeon

What Can a Pharmacist Do?

• Assist with supportive care
• Recommend steroids for upper airway obstruction
• Recommend against steroids if no upper airway obstruction, but grade III injury
  • Increased risk of perforation
• Recommend antibiotics if perforation present
• Harm reduction
Back to the Case...
• Intubated for airway protection
• Remained hemodynamically stable
• Patient was taken to OR for endoscopy
  • Revealed grade II b lesions
• Laparotomy performed
  • No evidence of perforation
• Neck wounds explored, no damage
• Discharged to inpatient psychiatric facility 4 days after admission

It’s Not Over Yet
• Patient presents 6 months after index case for polysubstance overdose
  • Besides treating the acute ingestion, what long term complications are expected from the caustic ingestion?

Long-Term Complications
• Formation of aorto-esophageal or tracheo-esophageal fistulas
• Formation of esophageal strictures
• Impaired gastric and esophageal motility
• Increased risk of esophageal and gastric cancer

Toddler Death Pods
• 18 month old patient brought in by EMS after ingesting a laundry detergent pod
  • Per EMS, patient appears lethargic, multiple episodes of emesis

What do you want to know?
• How is the patient?
What do you want to know?
• How is the patient?
  • Lethargic, intermittently arousable, vomit on shirt
  • Course breath sounds bilaterally
  • HR 132, BP 98/57, RR 32, O₂ sat 94% on RA

What do you want to know?
• How is the patient?
  • Time of ingestion?
    • Approximately 45 minutes prior to arrival

What do you want to know?
• How is the patient?
• Time of ingestion?
• Product ingested?
  • Tide pod

What do you want to know?
• How is the patient?
• Time of ingestion?
• Product ingested?
• How much product was ingested?
  • Patient was found with 2 pods, one had been chewed

Epidemiology
• Laundry pods first brought to market in 2011
• In 2013, 10,387 exposures in children ≤ 5 yo

© 2014 American Society of Health-System Pharmacists
**Signs and Symptoms of Toxicity**
- Similarities to other detergent ingestions
  - Coughing and choking
  - Conjunctivitis
  - Nausea
- More common with laundry pods
  - Vomiting
  - Lethargy and drowsiness

**Laundry Pods**
- Highly concentrated detergent in a water soluble membrane
  - Membrane typically contains polyvinyl alcohol, ethylated alcohols
  - Combination of anionic and nonionic detergents and a cationic surfactants
- Many brands available on the market
- Mechanism of toxicity not well defined

**Laundry Pod Ingestion Treatment**
- Supportive care
  - Fluids and electrolytes
  - Antiemetics
  - Intubation may be necessary if nausea and vomiting present in the setting of decreased LOC to prevent aspiration

**Do Not Eat Warning?**

**Silica Gel Packets**
- Totally safe to eat, despite all of the warnings
- Caution: not very tasty, hard to swallow

**Back to the Case...**
- Given 20 mL/kg fluid bolus for hypotension
- Became increasingly lethargic
- Multiple episodes of vomiting
Which of the following outcomes are likely in a patient who is vomiting and is too drowsy to protect their airway?

- Aspiration of gastric contents
- Intubation

Back to the Case...

- Intubated for airway protection
- Admitted to PICU
- On vent for 36 hours
- Extubated and discharged several days later after resuming normal PO intake

Hydrocarbons

- 4 year old male was hanging out in the garage with his dad
- Dad looked up from under the hood of his car when he heard crying
- Saw the child near an open container of gasoline with stains on shirt, wet hands, face, and mouth

What do you want to ask?

- How is the patient?
  - How is the patient?
    - Upon arrival, patient is crying loudly, uncooperative with exam, smelled heavily of gasoline
What do you want to ask?
- How is the patient?
- Time of exposure?
  - Approximately 20 minutes prior to arrival

What do you want to ask?
- How is the patient?
- Time of exposure?
- Product involved?
  - Possibly gasoline

What do you want to ask?
- How is the patient?
- Time of exposure?
- Product involved?
- How much product was ingested?
  - Unknown

What do you want to ask?
- How is the patient?
- Time of exposure?
- Product involved?
- How much product was ingested?
- Other medical problems/medications?
  - None

Examples of Hydrocarbons
- Baby oil
- Mineral oil
- Petroleum jelly
- Cooking oil
- Paraffin wax
- Gasoline
- Kerosene
- Paint thinner
- Lighter fluid
- Turpentine

Types of Exposure
- Dermal
- Ocular
- Oral ingestion
- Inhalation
- Injection
Hydrocarbon Ingestion

- Nausea and vomiting are common
- Aspiration in main cause of injury
  - Direct toxicity to pulmonary tissue
  - Interstitial inflammation, alveolar edema and hemorrhage, bronchiolar necrosis, and vascular thrombosis
  - Disruption of the lipid surfactant layer

Factors Influencing Toxicity

- Viscosity
  - Resistance of a fluid to flow
  - Low viscosity increases aspiration risk
- Surface tension
  - Force generated between molecules
  - Low surface tension increases aspiration risk
- Volatility
  - Tendency for a liquid to become a gas
  - Volatile substances considered more toxic

Which of the following hydrocarbons has the lowest risk of aspiration following ingestion?

- Gasoline
- Paraffin wax
- Lighter fluid
- Diesel

Inhalation of Hydrocarbons

- Inhalation of volatile hydrocarbons can cause...
  - CNS effects
    - CNS depression
    - Ataxia, slurred speech, dementia
  - Cardiac dysrhythmias
  - Peripheral neuropathy

Injected Hydrocarbon Toxicity

- Subcutaneous injection
  - Tissue necrosis, abscess formation
- Intravenous injection
  - Severe pneumonitis
  - Damage to alveolar capillary bed
  - Follows similar clinical course to aspiration

Timeline for Pulmonary Toxicity

- Within 30 minutes - coughing or choking
  - Tachypnea, hypoxia, and respiratory distress within hours to days after
  - Radiographic evidence within 4 hours
  - Resolution typically occurs within 5-7 days
### Management of Exposure
- Decontamination
- Supportive care
- Antiemetics
- Intubation may be required to prevent aspiration of hydrocarbon
- Gastric decontamination
  - No role for activated charcoal
  - Gastric lavage?

### Back to Case...
- Patient remained rather uncooperative
- Chemosis in left eye
- No erythema noted
- When asked if he got any in his mouth, replied “It was yucky”
- Ocular decontamination with 2 liters NS
- Patient observed for 8 hours in ED, discharged home with new set of clothes

### In Conclusion...

### Prevention is the Best Medicine

### Key Takeaways
1. Do not drink drain cleaner (or attempt gastric decontamination in someone who has)
2. Be very concerned when a child is exposed to a laundry detergent pod
3. Feel free to eat silica packets despite the warnings
4. The viscosity of a hydrocarbon can help predict the toxicity of the agent