Module Four: Cyanide & Fumigants

Robert Hoffman MD, FACMT
American College of Medical Toxicology
Ottawa, Ontario  February 5, 2014

Chemical Agents of Opportunity
Faculty Disclosure

• Faculty: Robert Hoffman MD
  – Relationships with commercial interests: none
  – Speakers Bureau/Honoraria: none
  – Consulting Fees: none
  – Other: none
Learning Objectives

• Indicate the sources and uses of cyanide and fumigants
• Describe therapies used to treat cyanide poisoning
• List the four most common fumigant gases
• Describe the clinical effects of exposure to these gases
• Explain how to treat victims exposed to these gases
Cyanide & Fumigants

• Cyanide
  – Salts (solids)
  – Gas

• Fumigant gases
  – Vikane (sulfuryl fluoride)
  – Methyl bromide
  – Phosphine
Cyanide

• Notoriety well deserved
• Historical relevance
  – Mass poisoning
• Pharmaceutical terrorism
• Weapon of Mass Destruction
Cyanide (CN): Properties

- Small molecule (26 Dalton)
- Boiling Point 27.7°C
- Colorless
- Bitter Almonds? Myth
- Water soluble

Sodium Cyanide
Cyanide: Two Common Forms

Hydrogen Cyanide
Gas
Toxic when Inhaled

Solid Cyanide Salts
(sodium cyanide, potassium cyanide, calcium cyanide)
Toxic when Ingested
Generating HCN Gas from Salts

Solid Cyanide Salt (X-CN) + Acid (H-X) → Hydrogen Cyanide Gas (HCN)
Cyanide

• Sources of cyanide (solid)
  – Industrial applications (electroplating, hardening steel, mining, fumigation,…)
  – Sodium, potassium and calcium cyanide are all readily purchased on the internet

• Other sources
  – Cyanogen chloride
  – Acetonitrile, acrylonitrile
  – Natural occurring cyanogens (laetrile)
Cyanide: Mechanism of Action

- Readily enters cells
- Inhibits mitochondrial respiration
Cyanide

Other Cytochrome Oxidase Inhibitors:

- Hydrogen sulfide
  - “sewer gas”
- Sodium azide
  - Component of airbags
- Carbon monoxide
  - minor mechanism
Cyanide: Toxic Quantities

- **Cyanide salts**
  - Lethal dose: 200-300 mg (3 mg/kg)
- **Hydrogen Cyanide (HCN) gas**
  - Lethal dose: 50-100 mg
    - 10 ppm for 2-hours = headache
    - 100-200 ppm = death in 1-hour
    - 200-300 ppm = death in several minutes
Cyanide: Clinical Manifestations

• “Gasp poison”
• Central Nervous System
  – Headache, confusion, agitation, syncope, convulsions, coma, death
• Cardiovascular
  – Tachycardia, hypertension
  – Bradycardia, hypotension
  – Cardiac arrest
• GI
  – Nausea, vomiting, abdominal pain
Knock-Down Gases

Some possible suspects:

- Hydrogen cyanide
- Hydrogen sulfide
- Carbon monoxide
- Oxygen-deficient air
Cyanide: Onset of Symptoms

Time to Onset of Symptoms

• Cyanide salt and cyanide gas (HCN)
  – Minutes
  – Inhalation of gas >> ingestion >> dermal
  – Survival > 10 minutes, most likely will survive
    • All or Nothing

• Aliphatic cyanogens & Natural cyanogens
  – Hours – must be metabolized
Cyanide: Diagnostic Testing

- **ABG**
  - Anion gap metabolic acidosis
- **VBG**
  - “Arteriolization” of venous blood gas
- **Lactate**
  - Elevated
- **Blood cyanide levels**
  - Whole blood or serum
  - 2-3 day turn around time
Cyanide: Real World Scenarios

• Battlefield
• Mass Murder
• Mass Suicide
• Homicide
• Pharmaceutical Terrorism
• Environmental Terrorism
• Economic Terrorism
Cyanide: Battlefield

- WMD
  - Researched as a weapon in WW I
  - Used in concentration camps in WW II and in caves (Adjimushkaiskye)
    - Zyklon B
Cyanide: Mass Murder

Nazi Death Camps

- Millions of Jews, gypsies, and others died in CN gas chambers
- Gas chambers disguised as communal showers
- Some suffering more than 20 min before death
Execution by Cyanide Gas Chamber

- CN salts dropped into sulfuric acid $\rightarrow$ HCN
- Few states now use it
- 1930 to 1980 (11 states):
  - 945 men
  - 7 women
- 1960 Caryl Chessman told reporters he would nod his head if it hurt. He nodded his head for several minutes before he died.
Cyanide: Other Sources

The most common source of cyanide exposure is incomplete combustion of:

- Wood
- Plastic
- Rubber
- Polyurethane
- Wool
- Silk
Cyanide: Incomplete Combustion

Happy Land Social Club Fire Bronx 1990: 87 deaths
Cyanide: Incomplete Combustion

The Station Nightclub Fire Providence 2003: 100 deaths
Cyanide: Homicide

Teen charged with poisoning friend

Friday, January 10, 2003 Posted: 1:59 PM EST (1859 GMT)

ELLIOTT CITY, Maryland (AP) -- A teenager was charged Thursday with first-degree murder for allegedly killing a romantic rival by spiking his soda with cyanide.

Police said Ryan Furlough, 18, laced his friend's drink with the poison as they played video games in Furlough's basement in Ellicot City in suburban Baltimore.

Benjamin Vassiliev, 17, went into respiratory arrest last Friday after drinking the soda and died Wednesday.
Cyanide: Homicide

Timeline:
- 17 yr old male drinks KCN spiked soda
- Feels unwell and goes to the bathroom
- Emerges from the bathroom and collapses
- EMS intubate for apnea. Vital signs present.
- Cardiac arrest in hospital. ACLS and recovery.
- Transfer to tertiary care center.
- Dx made. Steps 2 & 3 of antidote kit administered.
- No neurologic recovery.
Cyanide: Suicide

- 55 yr old male ingests KCN tablets at sentencing hearing.
- Subject tells lawyer who tells judge
- In minutes: lethargy > collapse > shock
- No antidote kit at scene
- Subject received antidote kit at hospital (~15 min post-ingestion)
- No neurological recovery.
Cyanide: Suicide

• The following video is taken from courtroom footage of a sentencing hearing in Phoenix in 2012

• It demonstrates the delay to onset, initial symptoms and rapidity of progression of a suicidal ingestion of cyanide
Cyanide: Mass Murder

The Jonestown Massacre
- Jonestown, Guyana (1978)
- CN-laced Kool-Aid
- 913 Deaths
Cyanide: Drug Tampering

• Pharmaceutical Terrorism
  – 1982 – Acetaminophen
  – 1991 – Pseudoephedrine
Cyanide: Copycat Events

- Cyanide has been implicated or suspected in a number of medication and food supply tampering or terrorist events.
- These will be discussed in more detail in the “Water/Food/Medication as a Vehicle for Terrorism Module” (Module 5).
- This next video clip provides an example of the potential impact of a single tampering event.
Cyanide: Terrorism

Appearance at incidents:
- NY WTC (1993)
  - Ingredients for HCN in the truck
- Tokyo Subway (1995)
  - Sarin
  - Ingredients for HCN in bathroom
Cyanide: Environmental Terrorism?

- Cyanide spill into Tisza River, Romania (2000)
- 100,000 cubic meters of cyanide containing water released when a gold mine dam overflowed
- All river life killed for miles downriver
Cyanide: Economic Terrorism

- Hoax - 1989
- Chilean Grapes Imported into the US Alleged to Contain Cyanide

- 15-gallon drum of sodium cyanide was lost from a delivery truck
- Located after 1-week search in N. Dakota
  - Was being hauled for delivery to beekeepers
  - Used to fumigate and kill excess bees
  - Not legally registered for this use
- Became a multi-state investigation
Cyanide: Treatment

Prehospital Care

• Safely remove victims from source
• Restore or maintain airway patency
• Maximize oxygenation
  – 100% NRBM or BVM
• Cardiopulmonary support to maintain VS
  – IVF and/or dopamine, norepinephrine
• Decontamination
Cyanide Antidote Kit (CAK)

• 3-steps
  – Amyl nitrite
  – Sodium nitrite
  – Sodium thiosulfate
• Converts cyanide to thiocyanate
• One kit treats two people
Cyanide: CAK

CAK Dosing

• Amyl nitrite - inhale if no IV access yet
• Sodium nitrite (3% solution)
  – Adults → 300 mg (10 ml) IV over 15-20 min
  – Peds → Hgb based
• Sodium thiosulfate (50 ml 25% solution)
  – Adults → 12.5 g (50 ml) IV
  – Peds → 1.65 ml/kg IV
• May repeat if large cyanide exposure
Cyanide: CAK

- Effective
- Safe
- Side Effects
  - Nitrite
    - Hypotension
    - MetHb
  - Sodium Thiosulfate
    - vomiting
Cyanide: Cyanokit™

Cyanokit
• Hydroxocobalamin
• Converts cyanide to cyanocobalamin (vitamin B12)

Dosing
• 5g IV
• 10g IV in cardiac arrest
Cyanide: Treatment

Treatment: Cyanokit

- Effective
- Safe
- Adverse Effects
  - Red urine
  - Red skin
  - Interferes with cooximetry measurements because of its intense red color
Cyanide as a Weapon

An Ideal Terrorist Weapon

- Plentiful
- Readily available
- Special knowledge not required
- Capable of causing mass casualties
- Capable of causing social disruption
- Requires large quantities of resources to combat its effects
Any terrorist attack that involves explosions or fire will likely result in HCN release
Fumigant Gases

- Sulfuryl fluoride (Vikane 7)
- Methyl bromide
- Phosphine
Fumigants

Applications
- Insect or rodent control in grain storage
- Insect or rodent control in structures
- Eradication of soil pests in farming
Fumigant Gases

- Like HCN, could be introduced into a closed space through ventilation system or other conduits
Sulfuryl Fluoride

- Used in 85% of building fumigations
- Colorless
- Odorless
- Irritating
- 3.5 times heavier than air
- Exposure to fatal concentrations possible without warning odor
- No re-entry until air levels < 5 ppm
Sulfuryl Fluoride

• Clinical Manifestations
  – High concentrations
    • Seizures
    • Syncope / dysrhythmias
    • Respiratory arrest
  – Lower concentrations:
    • Vomiting
    • Diarrhea
    • Salivation
    • Lung injury
Sulfuryl Fluoride: Treatment

Management

• Removal from source of exposure
• Ventilation
• Oxygen
• Monitor for hypocalcemia
  – ECG (prolonged QTc)
  – Serum or ionized Ca2+
• Administer calcium as needed
Sulfuryl Fluoride

Elderly couple reenter fumigated home before Vikane had fallen to a safe levels:

• Husband:
  – Shortness of breath, seizures
  – Death 48 hrs after reentry

• Wife:
  – Weakness, nausea, vomiting
  – Death 72 hrs after reentry (lung damage)
Methyl Bromide

- Odorless, colorless gas
- Chloropicrin (lachrymator) added as warning agent
- MeBr heavier than air
- Broad spectrum of activity
  - Alkylating agent
- Penetrates rubber and neoprene
- Being phased out due to environmental concerns
Methyl Bromide: Clinical Signs

• Acute high-level exposure → rapid onset of sxns
  – CNS depression, delirium, seizures, pulmonary edema
  – Skin injury, burns, blistering reported with high-level dermal exposure
• Lower level exposure
  – Delayed onset toxicity well-documented
  – Mucosal irritation
  – Headache, dizziness, Nausea, vomiting
  – Progression (hours) to visual symptoms, ataxia, tremor, delirium, seizures
• Sxns reversible with mild intoxication
  – Permanent effects have been reported in severe cases
Methyl Bromide: Case Study

- Adult female occupying a guest house rapidly developed headache, flu-like symptoms
- Within 24 hours, found in status epilepticus
- Initial labs remarkable for severe liver, kidney injury
- Expired 19 days post-exposure
- A building next door had undergone fumigation with methyl bromide. Seven 1-2 inch underground conduits connected the buildings.
- Methyl bromide had traveled from the adjacent building into the cottage.
Phosphine (PH$_3$)

- **Forms**
  - Gas (vapor density 1.17)
  - Aluminum and Zinc phosphide pellets
- Smells like garlic and rotten fish
- Many uses in agriculture & structural pest control
- Used in semiconductor industry
- Concentration effects
  - 400-600 ppm - severe toxicity in 30 min
  - 1000 ppm - immediate death
Generating Phosphine Gas

Solid Phosphide Pellets / Tablets + Water or Acid → Phosphine Gas
Phosphine: Treatment

Clinical

• Early/mild cases
  – Non-specific
  – GI effect, cough, chest tightness, eye irritation

• Late/serious exposure
  – Pulmonary edema, coma, seizures, death
  – Knock-down gas
    • Rapid progression and deterioration in fatal cases
Phosphine: Case Study

- 5-year-old girl suddenly develops difficulty breathing at home
- Has a cardiac arrest - Unable to resuscitate
- Family members were ill as well
  - Developed acutely after a period of heavy rainfall
  - Odor noted in basement
- Investigation: a cupful of aluminum phosphide pellets had been placed in a hole adjacent to the basement foundation
- Child’s father was a professional exterminator
Phosphine

Inhalation of phosphine from illicit Methamphetamine production labs:

• Willers-Russo (1998)
  – 3 victims found dead in motel room
  – First responders noted significant chemical odor
  – Phosphine gas levels far greater than 0.3 ppm (TLV)

• Burgess (2001)
  – Acute symptomatic inhalation exposure in first-responder (law enforcement)
    • 2.7 ppm for 20-30 minutes
  – Persistent, objective signs of obstructive pulmonary impairment weeks after initial exposure
Treating Fumigant Poisoning

- No antidotes available
- Remove victim from source
- Thorough decontamination
- Oxygenation
- Symptomatic and supportive care as indicated
## Fumigants: Summary

<table>
<thead>
<tr>
<th>Gas</th>
<th>Properties</th>
<th>Clinical manifestations</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vikane</td>
<td>Poorly detectable (occasionally mixed with chloropicrin)</td>
<td>Neurologic, Gastrointestinal</td>
<td>Remove from exposure, Flush skin/eyes, 100% O2, Supportive care</td>
</tr>
<tr>
<td>Methyl Bromide</td>
<td>Poorly detectable (occasionally mixed with chloropicrin)</td>
<td>Potentially delayed onset, Mucous membranes irritation, Neurologic, Seizures, Lung</td>
<td>Same</td>
</tr>
<tr>
<td>Phosphine</td>
<td>Fishy / garlic odor</td>
<td>Neurologic, Cardiac, Lung</td>
<td>Same</td>
</tr>
</tbody>
</table>
Audience Response

Which of the following is added to fumigants to make them more easily detectable?

1. Mercaptans
2. Hydrogen sulfide
3. Chloropicrin
4. Organophosphates
5. Yellow dye number 20
Which of the following is added to fumigants to make them more easily detectable?

1. Mercaptans
2. Hydrogen sulfide
3. Chloropicrin
4. Organophosphates
5. Yellow Dye number 20
Summary

• Forced air ventilation systems could be used by terrorists to disperse toxic gases or aerosols.
• Cyanide gas and fumigants are easily obtained and well-suited for airborne dispersal.
• Cyanide gas exposure should be treated with oxygenation, supportive care, and antidotal therapy.
• No antidote is available for the fumigants discussed in this module. Treatment should focus on decontamination and supportive therapy.
Questions?