Cyanide Poisoning

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Learning objectives

• Describe the clinical syndrome, treatment, and epidemiology of cyanide

• Identify the key public health agency response in a cyanide chemical terrorism event
Overview / Background

• Cyanide:
  – recognized since antiquity
  – present in bitter almonds, cassava, and other foods
  – used extensively in industry for fumigation, electroplating, and mining activities
Overview / Background

• Several forms exist; all may have an odor of bitter almonds, but this is not always detectable
  – Gas: colorless, dissipates rapidly
    • hydrogen cyanide [HCN] and cyanogen chloride [CNCl, also known as CK]
  – Liquid: ranges from blue to colorless, stable
    • hydrocyanic acid; an aqueous solution of HCN
  – Solid: white granular powder, stable
    • sodium, potassium, or calcium
Overview / Background

• Tylenol tampering in 1982
  – 7 deaths
  – subsequent events involved other over the counter medications and prepared foods

• Easily available
  – cheap
  – plentiful supplies in industry
  – large scale contamination (eg. municipal water supplies) unlikely due to enormous quantity required to achieve toxic levels in a large body of water.
  – single or multiple local events are more likely
Overview / Background

• Current threat is both domestic and international
  – 2003 search of a Texas property revealed cyanide salts that were possibly intended for use in domestic militia activities (1)
  – international terrorist groups have also been found to possess stores of cyanide (2, 3)

Sources
(1) ATF www.atf.gov/press/fy04press/field/051104dal_chemweapons.htm
(3) CBWInfo www.cbwinfo.com/Chemical/Blood/AC.shtml
Epidemiology

• Acute v. Chronic poisoning
  – Varying clinical presentation
  – This presentation will focus on acute intoxication, consistent with a terrorist event or industrial accident
Epidemiology - Routes of exposure

• Gas: Inhalation
  – hydrogen cyanide
  – cyanogen chloride
• Liquid: Inhalation (aerosol), ingestion, skin contact
  – hydrocyanic acid
• Solid: Inhalation, ingestion, skin contact
  – cyanide salts
Clinical manifestations

- Mechanism:
  - inhibits mitochondrial cytochrome oxidase
  - an “asphyxiating” agent
- Primarily targets CNS and cardiac tissue, but multiple systems involved
- Presentation depends on dose and route of exposure
Clinical manifestations

• Common final pathway for cyanide intoxication is cellular hypoxia. Exposure to any form of cyanide:
  – Metabolic acidosis: nonspecific symptoms
  – CNS: dizziness, nausea, vomiting, drowsiness, tetany, trismus, hallucinations
  – CV: arrhythmia, hypotension. Tachycardia and hypertension may occur transiently in early stages
  – Respiratory: dyspnea, initial hyperventilation followed by hypoventilation and pulmonary edema. Cyanosis not apparent, since blood is adequately oxygenated
Clinical manifestations

- Time to onset of symptoms, as well as additional signs of exposure, depends on dose and route of exposure:
  - Inhalation
    - Rapid onset: seconds to minutes
    - Additional signs: Metallic taste; burning sensation in GI / respiratory tract
  - Ingestion
    - Delayed onset: 15 to 30 minutes
    - Additional signs: Sore throat; burning sensation in GI / respiratory tract; diarrhea
  - Skin contact
    - Delayed onset: 15 to 30 minutes
    - Additional signs: Erythema, pain at site of contact
Diagnosis

*Diagnosis is primarily made by index of suspicion and clinical judgement*

- **Case history**
  - suspicion of exposure
- **Clinical presentation**
  - metabolic acidosis, multisystem involvement
  - odor of bitter almonds
- **Laboratory diagnosis**
  - blood cyanide levels can be drawn, but empiric treatment is almost always required before lab results are available
  - high anion gap metabolic acidosis
  - arterial and venous pO2 may be elevated
Treatment

• Treatment protocol differs between United States and other industrialized nations
• Within the United States, new consensus is developing regarding best practices
• Treatment regimen depends on severity of symptoms, route of exposure (to some extent), and what is available
Treatment: overview

1) Activated charcoal
2) Supplemental oxygen
3) Supportive care / ACLS
4) Sodium nitrite
5) Amyl nitrite
6) Sodium thiosulfate
7) Hydroxocobalamin
Treatment

1) Activated charcoal
   - For alert, asymptomatic patients following ingestion

2) Supplemental oxygen
   - 100% for suspected exposure

3) Supportive care / ACLS
Treatment

4) Sodium nitrite
-Mechanism: forms methemoglobin, competes with cytochrome oxidase for free cyanide; combines with cyanide to form cyanmethemoglobin
-Dose: Adults: 300mg IV over 5 minutes; slower if hypotension develops
Children: 0.12 to 0.33 mg/kg IV infused as above
-Adverse reactions: Hypotension associated with rapid infusion, tachycardia, syncope, cyanosis due to methemoglobin formation, headache, dizziness, nausea, vomiting. Frequency of events is not clearly defined

5) Amyl nitrite
-An inhaled drug, similar to sodium nitrite but with little systemic distribution: second line agent used when sodium nitrite is not available
Treatment

6) Sodium thiosulfate

-Mechanism: sulfur donor promotes rhodanase activity: detoxifies cyanide as it is released from cyanmethemoglobin. Directly detoxifies cyanide by conversion to thiocyanate; too slow to be useful as a first-line intervention

-Dose: Adults: 12.5g IV over 10-20 minutes following administration of sodium nitrite

Children: 412.5mg per kg IV over 10-20 minutes

-Adverse reactions: Hypotension, CNS depression and coma due to thiocyanate intoxication, psychosis, confusion, weakness, tinnitus, contact dermatitis. Frequency of events is not clearly defined
Treatment

7) Hydroxocobalamin

- **Mechanism:** direct binding agent, chelates cyanide
- **Dose:** 4 to 5 g IV
- **Adverse reactions:** minimal toxicity

**Additional information:**
- not the drug of choice in the United States, in part due to its high cost; more common in Europe
- other chelating agents, such as dicobalt edetate, are not generally used in the United States due to toxicity
- not yet approved by FDA

Treatment

• Typical cyanide treatment kit in the United States is stocked with:
  – Amyl nitrite ampules
  – Sodium nitrite solution
  – Sodium thiosulfate solution

• Speed is critical for survival
Clinical outcomes

• Without treatment:
  – Lethal exposure levels will result in rapid death

• With supportive treatment and specific antidotes:
  – Lethal exposure levels can be survived with immediate medical management
Decontamination

• Gas:
  – exposure does not require decontamination or contact precaution

• Liquid or solid:
  – treatment team is at risk for contact exposure or inhalation of gas produced by significant quantities of remaining cyanide compounds
  – skin decontamination can be achieved using a rinse with dilute detergent
  – contaminated clothing should be removed, preferentially by the patient if alert and asymptomatic, and placed in sealed bags
Differential Diagnosis

• Causes of anion gap metabolic acidosis:
  – “CATMUDPILES”
    • CO, CN
    • Alcoholic ketoacidosis
    • Toluene
    • Methanol
    • Uremia
    • DKA
    • Paraldehyde
    • Iron, INH
    • Lactic acidosis
    • Ethylene glycol
    • Salicylates
Public health response

• Reporting
  – Critical for enabling surveillance: used to establish baselines that are used for comparison when analyzing a potential terrorist event
  – Reporting is the first step in coping with a covert chemical event
  – County or state Department of Health
Summary

• Cyanide intoxication diagnosis and treatment has current bearing on clinical practice
  – terrorism
  – industrial accident
• The hallmark of cyanide is asphyxiation and metabolic acidosis without cyanosis
• Effective treatment is available
• Both baseline and outbreak reporting are critical
Resources

• Anne Arundel County physician link

• Essential Reading

• Additional Reading
Resources

• Web Resources
  – Centers for Disease Control and Prevention, Emergency Preparedness and Response  www.bt.cdc.gov/agent/cyanide
  – CBWInfo Factsheets on Chemical and Biological Warfare Agents, Hydrogen Cyanide http://www.cbwinfo.com/Chemical/Blood/AC.shtml