Chemical Terrorism Overview

Ziad Kazzi, MD, FAAEM
Assistant Professor of Emergency Medicine and Medical Toxicology
Center for Emerging Infections and Emergency Preparedness
University of Alabama at Birmingham

Objectives

- Describe the clinical presentation and management of patients poisoned with nerve agents
- Describe the clinical presentation and management of cyanide poisoning
- Discuss the various presentations and management strategies of victims exposed to sulfur mustard, Lewisite and pulmonary agents

Module 1

Nerve Agents: Part A

Introduction

“Nerve agents” are aptly named, since they affect the nervous system.
Structural name for these agents is organic phosphorous compounds (OPCs)

Introduction (continued)

- In fact, the OPCs also include several hundred “nonmilitary” compounds.
  – Malathion
  – Parathion
  – Others
- Used commonly as insecticides, where military OPCs are used in warfare or terrorism

Background

- Developed in pre-World War II Germany by Gerhardt Schrader, who discovered tabun in 1934.
- Germany later developed sarin and soman. These are the G agents.
- Never used by the Germans. The British (R. Gosh) synthesized VX (the acronym allegedly stands for venomous) after WWII.
Background (continued)

  - Iranian soldiers had atropine auto-injectors.

- Sarin gas was released in the Tokyo subway system by the Aum Shinrikyo Cult, creating more than 5,000 victims and causing 12 deaths.
- The same cult had released sarin in an apartment complex in Matsumoto in 1994, killing seven and injuring more than 600 people.
- In Tokyo, sarin was concealed in lunch boxes and bags. The terrorists punctured the bags with umbrellas and ran out of the subway tunnel.

Background (continued)

- The United States has around 30,000 tons of VX and sarin.
- The government is planning the destruction of this stock and has already destroyed small batches.
- There is an ongoing discussion about the best way to dispose of the end products.

Military Designations

- Tabun = GA
- Sarin = GB
- Soman = GD
- Cyclosarin = GF
- VX

Physical Properties

- Liquids with varying volatility and persistence
- VX is the least volatile but the most persistent; “oily.” Soman is odorless.
- Tabun, sarin, and soman have significant volatility. Sarin is the most volatile.
- Absorbed via skin, mucus membranes, lungs, and gastrointestinal system.

Toxicity

- Dermal toxicity: One drop of VX, 1–10 ml of the G agents may be fatal.
- Onset of symptoms may be delayed several hours from exposure to the liquid form, especially VX (up to 18 hours).
- Rapid development of symptoms after exposure is more likely.
Mechanism of Action

- Nerve agents bind and inhibit acetylcholine esterases.
- Acetylcholine esterase breaks down acetylcholine (ACh).
- ACh mediates neurotransmission at
  - Nicotinic receptors
    - nicotinic muscular junctions,
    - autonomic nicotinic synaptic junctions (sympathetic and parasympathetic), and
  - Muscarinic receptors:
    - end-organ synapses (GI tract, glands, bladder, pupils).

Mechanism of Action (continued)

- Enzyme inhibition is reversible within a certain period of time that is agent dependent.
- This time period in which structural changes to the enzyme occur is called "aging."
- Soman ages within minutes, whereas sarin takes hours.
- After aging occurs, the enzyme is inactivated. Enzyme regeneration usually takes several weeks.
- Excess ACh at all these synapses accounts for the clinical presentation.

Clinical Presentation

Muscarinic:
- SLUDGE—
  - Salivation
  - Lacrimation
  - Urination
  - Diaphoresis
  - GI distress (diarrhea, vomiting)
  - Emesis
  - Miosis

BBBs—
- Bradycardia
- Bronchorrhea
- Bronchospasm

Clinical Presentation (continued)

- Compared with adults, children exposed to nerve agents are thought to be less likely to have miosis and more likely to have increased secretions.
- Children are also thought to have more seizures, hypotonia, and weakness than adults.
Detection at the scene

- Military test paper
- Other equipment

Diagnostic Workup

- No lab workup is useful for acute nerve agent poisoning.
- RBC and plasma cholinesterase (butylcholinesterase) levels may be checked. These results are usually not immediately available.

Module 2

Nerve Agents: Part B

Prehospital Care and Decontamination

- First responders: Respirators, goggles, protective clothing
- Self-contained breathing apparatus (SCBA) is recommended in response to any nerve agent vapor or liquid.
- Butyl rubber gloves (most agents are lipophilic)
- 20% of healthcare workers in Tokyo had mild symptoms after taking care of patients. These symptoms included nausea, eye pain, and headache.

Different types of PPE

Pick the appropriate PPE?

A

B

C

D
Prehospital Care and Decontamination (continued)

• Inhalation exposure: removal from exposure
• Dermal: wash with soap and water or mild (0.5%) sodium hypochlorite (bleach) solution if availability of water is limited
• Ingestion: no charcoal as these patients are at risk for vomiting and aspiration

Antidotes: Atropine

• Muscarinic receptor antagonist.
• Only treats muscarinic symptoms.
• Given IV, IM, or by ET tube.
• Dose is 2 mg every 5–10 minutes. End point is resolution of bronchorrhea.
• For children, give 0.5–1.0 mg IM/IV every 5–20 minutes. For children < 6 months old, the dose is 0.05 mg/kg, with the minimum dose being 0.1 mg. Same end point.

Antidotes: Oximes

• Reverses the binding of the nerve agent to the enzyme, especially if given prior to aging.
• Pralidoxime: Slow IV bolus. Dose is 25–50 mg/kg in children or 2 g in adults. Is given IM via the MARK I kit.
• May repeat dose in 1 h. Effect may decrease after 3 h of exposure to sarin because of aging.

Antidotes: Oximes (continued)

• Side effect: elevated BP and occasional EKG abnormalities
• Other oximes (such as obidoxime and P2S) are used in other countries and have variable efficacy.
• There is ongoing research to develop better agents.

Antidotes: Benzodiazepines

• Used to treat the seizures
• Diazepam IM/IV appears to be better than other benzodiazepines.
• Diazepam dose is 5 mg IV/IM. May be repeated every 5–15 minutes.

Antidotes: Pyridostigmine

• Subjects pretreated with pyridostigmine will be less vulnerable to nerve agents.
• The U.S Army used pyridostigmine during the Gulf War.
• Pyridostigmine is a carbamate that binds reversibly to AChE. It does not cross the CNS.
• Pretreated individuals will have a store of AChE that is bound to pyridostigmine and is protected from the nerve agent.
Antidotes: Pyridostigmine (continued)

- Bound pyridostigmine-AChE spontaneously breaks after several hours, releasing normal AChE.
- Administration of 2-PAM stimulates release of AChE that was protected from the nerve agent by pyridostigmine.

Antidotes: MARK I Kit

- Contains pralidoxime (600 mg) and atropine (2 mg) self injectors

Long-term effects

- Organophosphate-induced delayed neuropathy (OPIDN) was described in one victim of the Matsumoto and one victim of the Tokyo attacks


Long-term effects

Residual symptoms after 1 year (n = 303)

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eye symptoms</td>
<td>56 (18.5%)</td>
</tr>
<tr>
<td>Fear of the subway</td>
<td>39 (12.9%)</td>
</tr>
<tr>
<td>Easy fatiguability</td>
<td>36 (11.9%)</td>
</tr>
<tr>
<td>Fear concerning escape from the attack</td>
<td>35 (11.6%)</td>
</tr>
<tr>
<td>Flashbacks</td>
<td>53 (17.6%)</td>
</tr>
<tr>
<td>Headache</td>
<td>26 (8.6%)</td>
</tr>
<tr>
<td>Depressive feelings</td>
<td>24 (7.9%)</td>
</tr>
<tr>
<td>Lack of concentration</td>
<td>23 (7.6%)</td>
</tr>
</tbody>
</table>

Okumura T, Hisaoka T. Environmental Toxicology and Pharmacology 19 (2005) 447–450

Module 3

Cyanide
Sources and means of exposure

- Exposures are mostly intentional (suicidal lab technicians who have access to CN)
- They may also be occupational, homicidal (Chicago Tylenol tampering in 1982, Decongestant in 1991), Jonestown massacre (900 people died)

Sources and means of exposure

- Via ingestion of cyanogens:
  - Cassava
  - Prunus fruits (Cherry, apricot, peaches and bitter almonds)
  - Laetrile (contains amygdalin)

Sources and means of exposure

- Acetonitrile (false-nail glue remover) or Propionitrile
- Iatrogenic with Nitroprusside

Pharmacokinetics

- Absorbed via GI, Skin or lung depending on its form.
- Very toxic: 200 mg for PO.
- Mostly excreted by the kidney as thiocyanate.

Pharmacokinetics

- Thiocyanate is formed by donation of a sulfur group to the cyanide. The enzyme is catalyzed by Rhodanese that relies on appropriate sulfur stores. When these are depleted, the enzyme is slowed down.

Pathophysiology

- The binding to Cytochrome a3 will interrupt the electron transport chain and therefore uncouple oxidative phosphorylation. ATP is no longer produced despite adequate supply of oxygen.
- Anaerobic metabolism prevails and Lactic acid is formed.
Acute clinical findings
• CNS: HA, anxiety, convulsions and coma
• CV: end point is cardiovascular shock
• GI: ingestion of salts will cause N/V/D and hemorrhage.
• Bitter almond: only 60% of population can detect it.
• Cherry red skin

Chronic clinical findings
• Survivors may develop parkinsonism over weeks to months.
• May be seen on CT or MRI as changes in the basal ganglia.

Diagnosis
• Whole blood Cyanide levels difficult to get.
• Lactic acid
• O2 extraction will be impaired
• Urinary thiocyanate levels

Cyanide treatment
• Supportive care including Oxygen
• Administer the cyanide antidote kit (Lilly Kit)
  ➢ Amyl nitrite or sodium nitrite Converts hemoglobin to methemoglobin. Promotes dissociation of CN from the cytochrome. Forms non toxic cyanomethemoglobin.
  ➢ Sodium thiosulfate promotes the conversion of cyanohemoglobin to thiocyanate and hemoglobin through enzymes such as rhodanase
• Hydroxycobalamin (Vitamin B12) Exchanges hydroxyl group with CN to form cyanocobalamin. Concentrated form of drug not available in the United States yet

Module 4
Sulfur Mustard

**Background**
- Vesicant alkylating agent
- Originally used in World War I
- Other names: Yellow cross, Hun Stoff and Mustard
- Used also by Japan and Italy (1930’s), Egypt (1960’s) and Iraq (1980’s)

**Physical Properties**
- Oily liquid
- Persistent more than volatile yet deaths are usually secondary to vapor exposure

**Mechanism of Toxicity**
- Alkylating agent that
  - Binds sulfhydryl and amino groups
  - Cell necrosis occurs
- Weak cholinergic properties

**Clinical Presentation**
- Eye exposure
  - Latency of hours
  - Pain, miosis, photophobia, lacrimation, blurred vision, blepharospasm, and corneal damage
  - Permanent blindness is rare

An eye injury of lesser severity in an Iranian casualty (shown 7 d after exposure) caused by exposure to mustard. The characteristic findings were edema of the lid and conjunctival injection.
Clinical Presentation

• Dermal exposure
  – Latency of 4-12 hours
  – Burns with blisters of different sizes
  – Go through clothes
  – More damage over moist and warm areas such as the axillae
  – Possible long term effects:
    • Punctate hyperpigmentation

Skin blisters secondary to dermal
Exposure to sulfur mustard

Large and extensive bullae on the
hands and the feet of Iranian casualties
as they appeared 5 days after exposure to mustard

The back of an Iranian casualty seen
16 hours after exposure to mustard

Erythema of the chest of an Iranian casualty
as it appeared 5 days after his exposure to mustard

Clinical Presentation

• Respiratory exposure
  – Chemical tracheobronchitis
  – Respiratory failure

By 32 days after exposure, this Iranian casualty has punctate hyperpigmentation in a healing deep mustard burn
Clinical Presentation
• Highly incapacitating
• Mortality rather low (<5%) several days later from bacterial pneumonia and respiratory failure as well as bone marrow suppression

Management
• Decontamination
• Supportive care
• Blister unroofing
• Topical antibiotics

Background
• Alternative to Mustard:
  – More volatile
  – Less persistent
• Causes immediate pain upon contact
• Similar clinical findings as mustard
• BAL is the antidote (IM or topical) in addition to supportive therapy

Lewisite

Pulmonary Agents

Phosgene and Chlorine
• Cause pulmonary edema and respiratory failure
• Chlorine causes a pungent odor
• Phosgene produces a freshly mown hay smell
• Toxicity may be delayed several hours
Chlorine exposure

Phosgime exposure

Helpful Resources

- [http://www.bt.cdc.gov/agent](http://www.bt.cdc.gov/agent)
- Your regional poison center
- Medical Management of Chemical Casualties Handbook