Chemical-warfare Agents: An Overview

U.S. ARMY MEDICAL RESEARCH INSTITUTE OF CHEMICAL DEFENSE

CHEMICAL CASUALTY CARE DIVISION
Objectives

- **Course**
  - Overview and relevance
  - Agent characteristics and effects
  - Patient presentation and management

- **This lecture**
  - Conceptual framework
  - NATO codes
  - General concepts
Overview

Chemical Agent: Definition (FM 8-285)

- “A chemical substance…intended for use in military operations to kill, seriously injure, or incapacitate humans (or animals) through its toxicological effects.”

- Compare and contrast
  - Chemical agents (chemical-warfare agents)
  - Biological agents (biological-warfare agents)
  - Toxins
  - “Toxicants”
Chemical Agent: Definition (FM 8-285)

- “A chemical substance…intended for use in military operations to kill, seriously injure, or incapacitate humans (or animals) through its toxicological effects.”

- Excluded by FM 8-285
  - Riot-control agents (CS, CN, DM)
  - Chemical herbicides (e.g., Agent Orange)
  - Smoke and flame materials
Excluded Agents I: Riot-control Agents

- Irritant agents (lacrimators)
  - CS ("tear gas")
  - CN (Mace®)
  - CA
  - CR

- Vomiting agents
  - DM (Adamsite)
  - DA
  - DC
Overview

Riot-control Agents

- **Local irritants** with high safety ratio
- **Short onset** (seconds to minutes)
- **Short duration** (15-30 minutes)
- In low concentrations, cause intense **pain** and **lacrimation** (tearing) with (Adamsite only) or without **vomiting**
Overview

Excluded Agents II: Herbicides (Defoliants)

- **Agent Blue** (cacodylic acid)
- **Agent Orange** (1:1 mixture of 2.4.5-T and 2.4-D)
  - Contaminant: TCDD (Dioxin)
- **Agent White** (4:1 mixture of 2.4-D and picoram)
- Paraquat
Excluded Agents III: Smokes

- Petroleum oil smokes (fog oil=SGF)
- Diesel fuel
- HC
- RP (RED phosphorus) in butyl rubber
- WP (WHITE phosphorus)
- FS
- FM
Classification of “Official” Chemical Agents

- **TOXIC AGENTS** (producing injury or death)
  - *LUNG-DAMAGING AGENTS* (choking agents)
    - Chlorine (CL), phosgene (CG) [smokes] [vesicants]
  - “**BLOOD**” AGENTS (cyanogens): AC and CK
  - **BLISTER AGENTS** (vesicants)
    - Mustard (H), Lewisite (L), phosgene oxime (CX), [riot-control agents] [T-2 mycotoxin]
  - **NERVE AGENTS** (anticholinesterases)
    - GA, GB, GD, GF, VX
- **INCAPACITATING AGENTS** (producing temporary effects)
  - BZ, Agent 15, [riot-control agents]
Overview

“Official” Chemical Agents I: Toxic Agents

- **Lung-damaging agents** (choking agents)
  - Chlorine (CL), phosgene (CG) [smokes] [vesicants]

- **“Blood” agents** (cyanogens): AC and CK

- **Blister agents** (vesicants)
  - Mustard (H), Lewisite (L), phosgene oxime (CX), [riot-control agents] [T-2 mycotoxin]

- **Nerve agents** (anticholinesterases)
  - GA, GB, GD, GF, VX
Lung-damaging Agents

- Chlorine (CL)
- Chloropicrin (PS)
- Phosgene (CG)
- Diphosgene (DP)
- [Mustard (HD, H) Lewisite (L)]
- [Smokes] [isocyanates] [PFIB] [oxides of nitrogen]
Overview

Chemical-agent Damage to Respiratory System

- **Central** effects (in larynx, trachea, and bronchi) predominate
  - Mustard (H, HD)
  - Lewisite (L)
  - [Chlorine (CL)]

- **Peripheral** effects (in small airways and alveoli) predominate
  - Phosgene (CG)
  - Perfluoroisobutylene (PFIB)
  - Nitrogen oxides (NOₓ)
  - HC smoke, isocyanates, many others
Overview

“Blood” Agents (Cyanogens)

- Hydrogen cyanide (AC)
- Cyanogen chloride (CK)
Overview

Blister Agents (Vesicants)

- Sulfur mustard (H, HD)
- Nitrogen mustard (HN₁, HN₂, HN₃)
- Lewisite = chlorovinylidichloroarsine (L)
- Mustard / Lewisite mixtures (HL, HT, TL)
- Phosgene oxime (CX)
- [Riot-control agents]
- [T-2 mycotoxin]
Overview

Nerve Agents (Anticholinesterases)

- Tabun (GA)
- Sarin (GB)
- Soman (GD)
- GF
- VX
“Official” Chemical Agents II: Incapacitating Agents

- **Purpose:** Temporary incapacitation
- **CNS stimulants**
  - Amphetamines, cocaine, caffeine, nicotine, strychnine, metrazole
- **CNS depressants**
  - Barbiturates, opioids, antipsychotics, benzodiazepines
- **Psychedelics**
  - LSD-25, psilocybin, ibogaine, harmine, MDMA (“ecstasy”), PCP
- **Deliriants**
  - Anticholinergic glycolates (BZ, Agent 15)
Overview

Physical Forms of Chemical Agents

- Solid
- Liquid
- Gas
- Vapor
- Aerosol
Overview

Persistence

- Dependent on several factors
  - Agent volatility (determined by chemical structure)
  - Temperature
  - Wind
  - Agent-surface interactions
- “Nonpersistent” agents (usually gone within 24 hours)
  - GA, GB, GD, CL, CG, AC, CK
- “Persistent” agents
  - VX, L, HL, “thickened” nerve and blister agents (e.g., TGD, THD)
Exposure and Absorption

- **Exposure** (contact with agent) does not necessarily lead to **absorption** (penetration of epithelial barrier)

- Two types of **effects** from exposure and absorption:
  - **Local**
    - (effects are at the site of contact)
  - **Systemic**
    - (absorption and subsequent systemic distribution produce effects at sites distant from contact site)
Routes of Exposure and Absorption

- Absorption through skin (*percutaneous* absorption)
- Absorption through lungs (*inhalational* absorption)
- Absorption through eyes (*ocular* absorption)
- Absorption through the gut (*enteral* absorption)
- Absorption by injection (*parenteral* absorption)
  - *Intravenous* absorption
  - *Intramuscular* absorption
Overview

Toxicity (Potency) of Liquid Agents

- **ED$_{50}$**: Effective Dose for 50% of exposed individuals
- **ID$_{50}$**: Incapacitating Dose for 50% of exposed individuals
- **LD$_{50}$**: Lethal Dose for 50% of exposed individuals

**ID$_{50}$** for liquid HD: 770 mg / 70-kg man

**LD$_{50}$** for liquid HD: 3000-7000 mg / 70-kg man
Toxicity of Vapors or Gases

The $C_t$ concept: Concentration $\times$ time

- $1 \text{ mg} / \text{m}^3 \times 8 \text{ min} = 8 \text{ mg-min} / \text{m}^3$
- $8 \text{ mg} / \text{m}^3 \times 1 \text{ min} = 8 \text{ mg-min} / \text{m}^3$
- $4 \text{ mg} / \text{m}^3 \times 2 \text{ min} = 8 \text{ mg-min} / \text{m}^3$
- $2 \text{ mg} / \text{m}^3 \times 4 \text{ min} = 8 \text{ mg-min} / \text{m}^3$
Toxicity of Vapors or Gases

- **ECt\(_{50}\)**: Effective Ct for 50% of exposed individuals
- **ICt\(_{50}\)**: Incapacitating Ct for 50% of exposed individuals
- **LCt\(_{50}\)**: Lethal Ct for 50% of exposed individuals

**Ct\(_{50}\)** assesses external dose, not internal dose

- **ICt\(_{50}\)** and **LCt\(_{50}\)** therefore affected by
  - Route of exposure
  - Respiratory rate and depth, skin moisture, etc.
Toxicity of HD Vapor

- **HD vapor in eyes:**
  - $\text{ICT}_{50} = 200 \text{ mg-min / m}^3$

- **Inhaled HD vapor:**
  - $\text{ICT}_{50} = 200 \text{ mg-min / m}^3$

- **HD vapor on skin:**
  - $\text{ICT}_{50} = 1000-2000 \text{ mg-min / m}^3$
Toxicity of HD Vapor

- **HD vapor in eyes:**
  - Permanent injury: $> 800 \text{ mg-min/ m}^3$

- **Inhaled HD vapor:**
  - $LCT_{50}$: 1000-1500 mg-min / m$^3$

- **HD vapor on skin:**
  - $LCT_{50}$: 10,000 mg-min / m$^3$
Comparative Toxicity of CW Agents

Ct$_{50}$ (mg-min/m$^3$)
Medical Response to CW Threats

**Crisis Management**

- Exposure
- Onset of Signs and Symptoms

**Pre-exposure**
- Latent Period (seconds to days)

**Primary Prevention:**
- The most important phase!
  - Military intelligence
  - Detection in nearby areas
  - True pretreatment
  - Skin protectants
  - Protective clothing
  - Mask
  - Soldier training *(what to do)*
  - Soldier education *(why to do it)*
  - Command emphasis!

**Secondary Prevention:**
- After failure of 1° prevention
  - Continued 1° prevention
  - Early diagnosis
  - Early decontamination
  - Evacuation as appropriate
  - Treatment to prevent or minimize later effects as possible

**Tertiary Prevention:**
- After failure of 1° / 2° prevention
  - Continued 1°/2° prevention
  - Intervention to ameliorate existing clinical effects and to prevent or minimize sequelae
    - General supportive care
    - Specific antidotal therapy
    - Antidotal enhancement*

*Given before exposure
A Framework for Learning about Chemical Agents

- **Overview**
  - History / background
  - Physicochemical properties
  - Toxicokinetics (ADBE) [how the body handles the agent]
  - Toxicodynamics (mechanism of action) [how the agent “handles” the body]
  - Clinical presentation / diagnosis: ASBESTOS
  - Management
    - Protection, general supportive treatment, and antidotal treatment
    - Decontamination and evacuation
“ASBESTOS”: A Systematic Approach to the Patient

- **Agent(s):** Type and toxicity (remember LD₅₀)
- **State(s):** Solid? Liquid? Gas? Vapor? Aerosol?
- **Body site(s):** Where exposed / Route(s) of entry? [absorption]
- **Effects:** Local? Systemic? [distribution]
- **Severity:** Mild? Moderate? Severe? [effects and exposure]
- **Time course:** Onset? Getting better/worse? Prognosis?
- **Other diagnoses?:** Instead of? [DDx] In addition to?
- **Synergism:** Combined effects of multiple exposures or insults?
Summary: “Official” Chemical Agents

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