

MEDICAL MANAGEMENT OF CHEMICAL CASUALTIES

PULMONARY AGENTS

**U.S. ARMY MEDICAL RESEARCH
INSTITUTE OF CHEMICAL DEFENSE**



USAMRICD
PROTECT, PROJECT, SUSTAIN



OBJECTIVES

- **Historical perspective**
- **General issues related to toxic exposure**
- **Agents**
 - source
 - mechanism of injury
 - clinical effects
 - therapy

HISTORY

- **1899** Hague Convention bans CW
- **1914** WWI begins - August
- Battle of the Marne - stalemate
- Both sides explore options to break stalemate
- Professor Fritz Haber suggests chlorine

22 APRIL 1915

- Chlorine gas used by Germany
- at Ypres, Belgium
- against the French
- 6,000 cylinders (168 tons)
- along a 7,000 m front
- reported 5,000 casualties
- both sides unprepared

HISTORY

- **19 DEC 1915** Phosgene gas by Germany
 - at Ypres, Belgium against the British
 - mass casualties 2 days later

- **19 MAY 1916** Diphosgene by Germany
 - decomposes to phosgene + chloroform
 - chloroform attacks mask filters

WW I CHEMICAL CASUALTIES

Chlorine and Phosgene produced **80%** of the **fatalities** from chemical agent exposure in WW I

RELEVANCE

- **Chlorine, Phosgene - used in industry**
 - mass produced and transported
 - industrial accidents
 - domestic terrorism
- **Related compounds**
 - organofluoride polymers (PFIB)
 - oxides of nitrogen
 - HC smoke (zinc oxide)

EXPOSURE SURFACE

Route

Surface Area

-
- Ingestion / parenteral ---
 - Ocular 0.0002 m²
 - Percutaneous 2 m²
 - Respiratory 50-150 m²

ANATOMY - PHYSIOLOGY

- **Nasopharynx**
 - humidifies, filters
 - bypassed when exercise increases MV
- **Central airways** (mouth to 2 mm airways)
 - flow is from smaller to larger area, laminar = QUIET
- **Peripheral airways** - (2 mm to alveoli)
 - geometric increase in cross-sectional area
 - Brownian motion

AGENT DISTRIBUTION

- **Aerosols**

- solid particles or liquid droplets suspended in air
- distribute in lung by particle size
- produce effects at site of deposition
 - 5 to 30 μ - nasopharynx
 - 1 to 5 μ - tracheobronchial level (central)
 - < 1 μ - alveolar level (peripheral)

AGENT DISTRIBUTION

- **Gas/vapor**
 - distributes uniformly throughout the lung
 - Effects due to solubility and reactivity
 - High - **central effects**
 - Low - **peripheral effects**

PROTECTIVE MECHANISMS

- **Aerosols**
 - Solubilized, absorbed, removed by cough, sneeze, specialized cells or mucociliary transport
- **Gases**
 - Reactivity - cough and sneeze act as warning
 - Mucociliary damage increases risk of infection

CLINICAL EXAMPLES

Site of Action

Agent

Central Airways

Mustard

Peripheral Airways

Phosgene

Combined

Chlorine

PHYSICAL ASSESSMENT

SITE

SYMPTOMS

SIGNS

Nasopharynx

Sneeze, pain

Erythema

Central

Oropharynx

Painful swallow

Inflammation

Larynx

Choking

Hoarse, stridor

Trach/bronchi

Pain, cough

Wheezes, rhonchi

Peripheral

Small airways
and alveoli

Dyspnea

Rare crackles

Tight chest

Clinical Considerations

- **These agents cause pulmonary edema**
 - damage alveolar-capillary membrane
- **Latent Period**
 - symptom onset may be delayed hours to days
 - objective signs appear later than symptoms
- **Sudden Death may occur**
 - laryngeal obstruction (edema/spasm)
 - bronchospasm

Clinical Considerations

- **Infectious Bronchitis / Pneumonitis common**
 - usually occurs **3-5 days** post-exposure
 - fever, elevated WBC, infiltrates NOT always infection
 - prophylactic antibiotics NOT indicated
- **Effects exacerbated by exertion**
 - compensatory mechanisms overwhelmed
 - strict rest, even if asymptomatic
- **No specific therapy exists**

CHLORINE - Civilian Uses

- Chlorinated lime (bleaching powder)
- water purification
- disinfection
- synthesis of other compounds
 - synthetic rubber
 - plastics
 - chlorinated hydrocarbons
- Don't try this at home! (bleach + ammonia)

CHLORINE - Physical Properties

- gas at STP (bp = -34 degrees C)
- 2.5 times heavier than air
- green-yellow color
- acrid, pungent odor

CHLORINE - Mechanism of Injury

- **Reaction 1: generation of HCL**



- **Reaction 2: oxygen free radical generation**



CHLORINE - Tissue Effects

- **Topical rather than systemic**
- **In central airways - from HCl**
 - necrosis, sloughing
- **In peripheral airways**
 - oxygen free radicals
 - react with sulfhydryl groups, disulfide bonds
 - damage to alveolar-capillary membrane

CHLORINE - Clinical Effects

Mild Exposure

- suffocation, choking sensation
- ocular, nasal irritation
- chest tightness, cough
- exertional dyspnea

Moderate Exposure

- above sx + hoarseness, stridor
- pulmonary edema within 2-4 hours

CHLORINE - Clinical Effects

- **Severe Exposure**
 - severe dyspnea at rest
 - may cause pulmonary edema within 30-60 min
 - copious upper airway secretions
 - sudden death may occur from laryngospasm

CHLORINE - Therapy

- **Supportive care only**
 - oxygen
 - positive pressure ventilation
 - with PEEP to keep PaO₂ > 60 torr
 - bronchodilators
- **Bacterial superinfection common (3-5 days out)**
 - follow serial cultures
 - prophylactic antibiotics not indicated
- **No long-term sequelae (uncomplicated cases)**

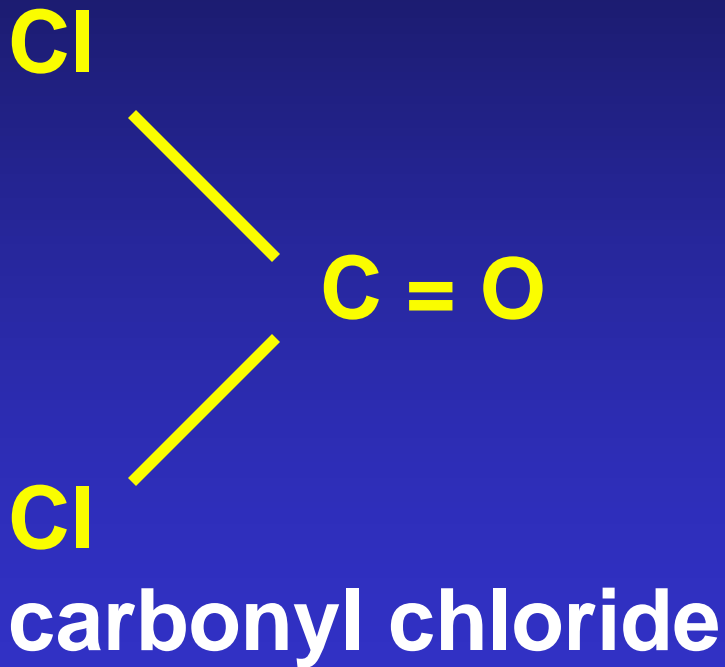
CHLORINE EXPOSURE

- 36 y/o female
- 2 hrs post exposure
- resting dyspnea
- diffuse crackles
- PaO₂ 32 torr (room air)
- CXR:
 - diffuse edema
 - w/o cardiomegaly

PHOSGENE - Uses/Sources

- **Chemical industrial production**
 - isocyanates (foam plastics)
 - herbicides, pesticides
 - aniline dyes
- **Combustion of chlorinated hydrocarbons**
 - plastics
 - Carbon tetrachloride
 - Methylene chloride (paint stripper)
 - degreasers

PHOSGENE - Physical Properties



Gas at STP (bp = 7.6 deg C)

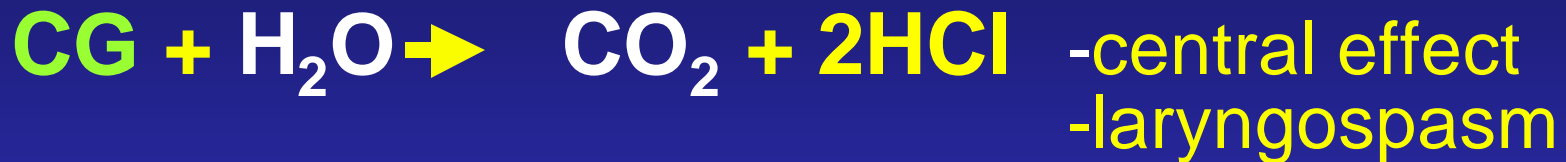
3.4 times heavier than air

colorless

odor of new mown hay

PHOSGENE - Mechanism of Injury

- **Reaction 1:** hydrolysis, generation of HCl



- **Reaction 2:** acylation, X = NH, NR, O, S



PHOSGENE - Clinical Effects

- **Mild Exposure**
 - mild cough
 - dyspnea
 - chest tightness
- **Moderate Exposure**
 - above symptoms
 - ocular irritation, lacrimation
 - smoking tobacco produces bad taste

PHOSGENE - Clinical Effects

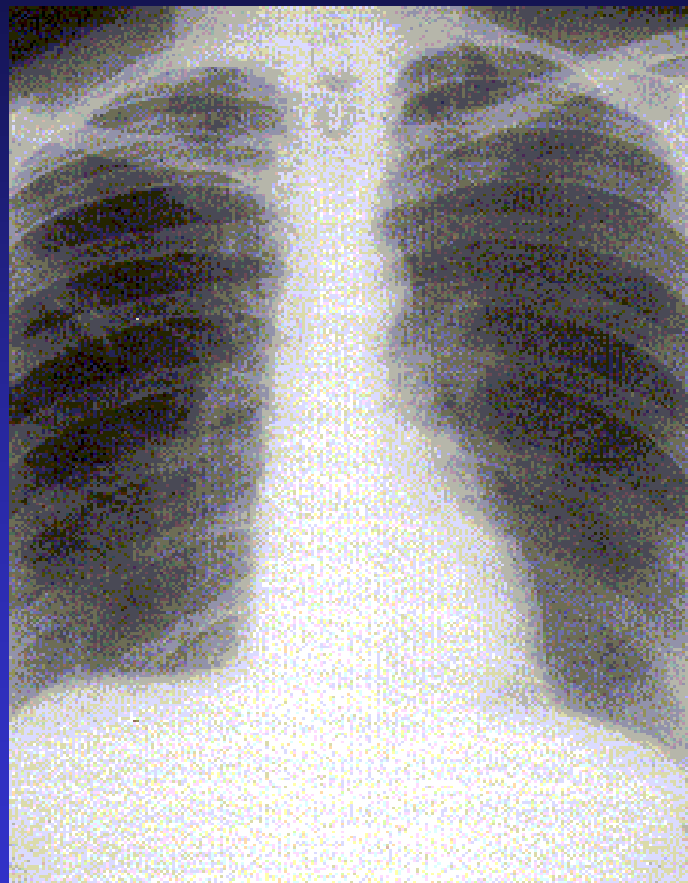
- **Severe Exposure**
 - severe cough, dyspnea
 - onset of pulmonary edema **within 4 hours**
 - may produce laryngospasm
- **Latent Period**
 - s/s onset more rapid with higher exposures
- **Exacerbated by exercise**

PHOSGENE - Therapy

- **Supportive care**
 - strict bed rest
 - O₂, PPV with PEEP to maintain PaO₂
 - IV fluids for hypotension (3rd spacing)
 - bronchodilators for bronchospasm
 - surveillance cultures
 - antibiotics when indicated
- **No long-term sequelae (uncomplicated)**

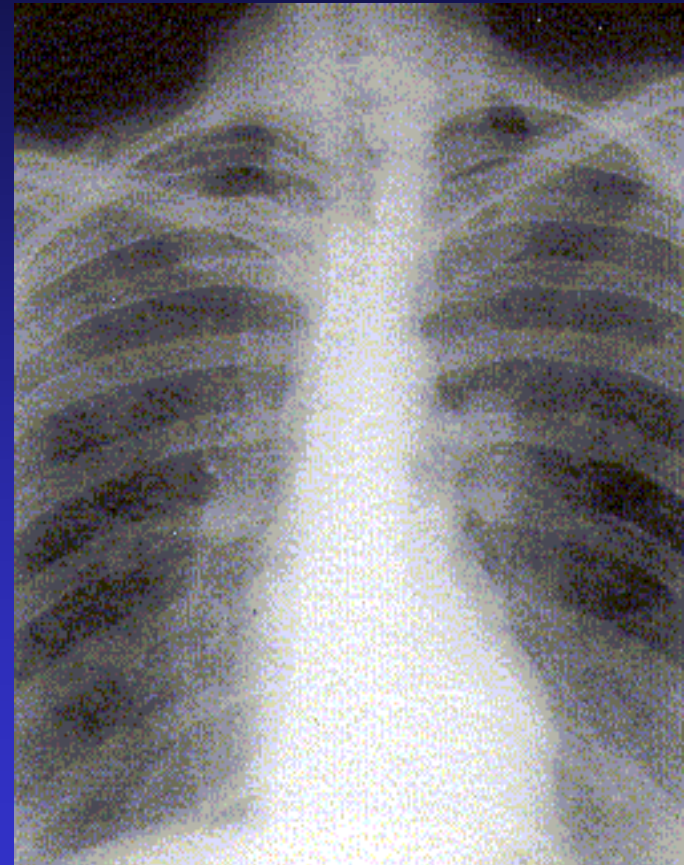
PHOSGENE - Case 1

- 40 y/o male
- 2 hrs post exposure
- mild dyspnea
- normal physical exam
- PaO₂ 88 torr (room air)
- CXR: normal



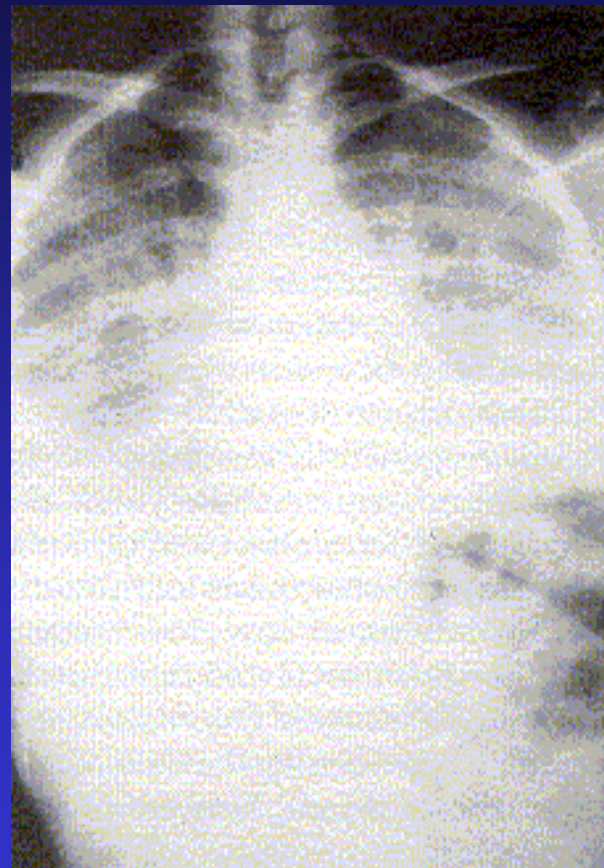
PHOSGENE - Case 1

- 7 hrs post exposure
- mod. dyspnea at rest
- few crackles
- PaO₂ 64 torr (room air)
- CXR: mild interstitial edema
- survived w/o sequelae



PHOSGENE - Case 2

- 42 y/o female
- 2 hrs post exposure
- rapidly inc. dyspnea
- PaO₂ 40 torr (room air)
- CXR: infiltrates -
 - perihilar
 - fluffy
 - diffuse interstitial
- death 6 hrs post exp.



PFIB

Organofluoride Polymers

- polytetrafluoroethylene (“Teflon”)
- many commercial uses
- used in armored vehicles, aircraft

Toxic Combustion By-Products

- perfluoroisobutylene (**PFIB**)
- pulmonary edema similar to phosgene

Teflon Pyrolysis - Clinical Effects

- **Teflon Pyrolysis at 450 degrees C**
 - symptoms mimic influenza
 - “polymer fume fever”
 - fever (104 degrees F)
 - chills, malaise, sore throat, chest tightness
 - spontaneous resolution
 - no sequelae

PFIB - Clinical Effects

Teflon Pyrolysis at **>800** degrees **C**

- liberates PFIB
- 10X more toxic than phosgene
- latent period of 1-4 hours
- followed by increasing dyspnea
- s/s of pulmonary edema
- usually recover within 72 hours, w/o sequelae

PFIB - Therapy

- **Supportive Care**
 - similar to treatment of phosgene

HC SMOKE

- **Obscurant smoke**
- **Zinc Oxide + Hexachloroethane**
- **Combustion Products:**
 - zinc chloride
 - phosgene
 - carbon tetrachloride
 - ethyl tetrachloride
 - hexachloroethane
 - chlorine
 - hydrogen chloride
 - carbon monoxide
 - hexachlorobenzene

HC SMOKE - Clinical Effects

- **Mild Exposure**
 - dyspnea
 - lab findings normal (monitor x 4-6 hours)
- **Moderate Exposure**
 - initial severe dyspnea, resolves spontaneously in 4-6 hrs
 - return of symptoms within 24-36 hours
 - CXR initially clear, later - dense infiltrates
 - hypoxia
 - bronchopneumonia may lead to **interstitial fibrosis**

HC SMOKE - Clinical Effects

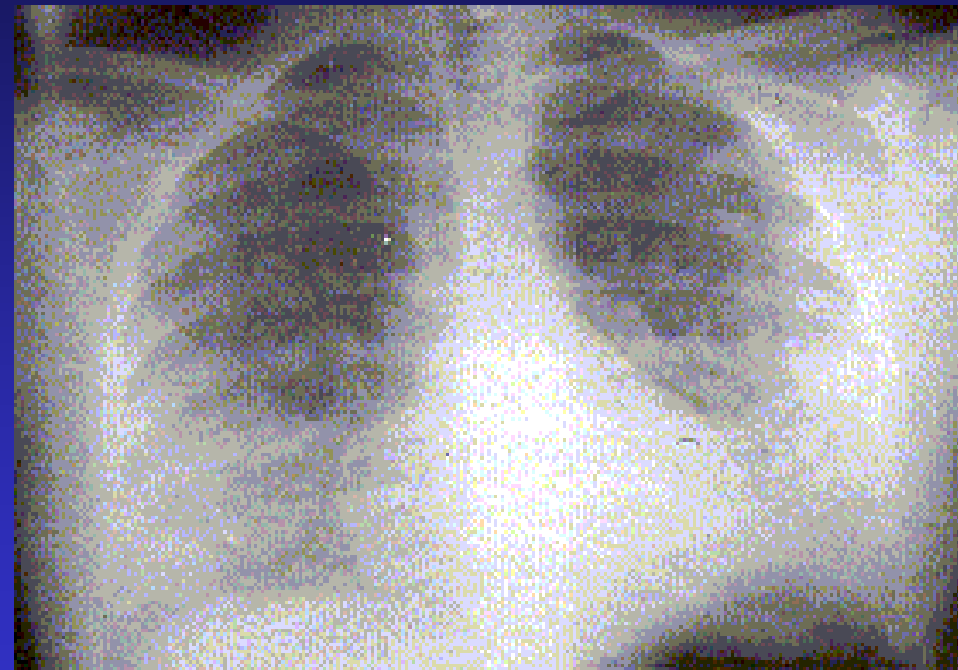
- **Severe Exposure**
 - rapid onset, severe dyspnea
 - paroxymal cough with bloody sputum
 - hemorrhagic ulceration of upper airway
 - rapid onset pulmonary edema
 - may have rapid onset laryngeal edema/spasm, death

HC SMOKE - Therapy

- **Supportive care of**
 - acute tracheobronchitis
 - pulmonary edema
- **Steroids probably useful (acutely) for**
 - inflammatory fibrotic changes
- **long-term PFT follow-up**
 - 10-20% develop interstitial fibrotic changes

HC SMOKE EXPOSURE

- 60 y/o male
- 8 hrs post exposure
- mod. severe dyspnea
- diffuse crackles
- PaO₂ 41 torr (room air)
- CXR: dense peripheral infiltrates



HC SMOKE EXPOSURE

- 3.5 months later
- persistent, moderate dyspnea at rest
- PaO₂ = 61 mmHg (room air)
- biopsy: **diffuse interstitial fibrosis**

NITROGEN OXIDES

Nitrogen Dioxide (NO_2 , N_2O_4)

- high temp combustion
 - arc welding
- nitrate-based explosives
 - enclosed spaces
- diesel engine exhaust

NO_x - Clinical Effects

- **Symptoms similar to HC exposure**
 - may remit spontaneously
 - exacerbated by exertion
- **Long Latent Period**
 - may be asymptomatic for 2-5 weeks
- **Fibrotic changes may occur**
 - PFTs may show chronic airway obstruction

NITROGEN OXIDES - Therapy

- **Supportive Care**
 - similar to HC exposure
 - steroids may be beneficial

CG - EXPOSURE

February 3, 1917 - A chemist was working on a new chemical product. A syphon of **phosgene**, required for the synthesis of this substance, burst on his table at **1:00 p.m.** A yellowish cloud was seen by a second person in the room to go up close to the chemist's face, who exclaimed, "I am gassed," and both **hurried out of the room.** Outside, the patient sat down on a chair, looking pale and **coughing slightly.**

CG - EXPOSURE

2:30 p.m. - In bed at hospital, to which he had been taken in a car, having been **kept at rest** since the accident. Hardly coughing at all, pulse normal. **No distress** or anxiety and talking freely to friends for over an hour. During this time he was so well that the medical officer was not even asked to see the patient upon admission to the hospital.

CG - EXPOSURE

5:30 p.m. - Coughing, with frothy expectoration, commenced, and the patient was noticed to become bluish about the lips; his condition now **rapidly deteriorated**. Every fit of coughing brought up large quantities of clear, yellowish frothy liquid, of which about **80 ounces were expectorated in 1 and 1/2 hours**. His face became of a gray, ashen color, never purple, though the pulse remained fairly strong.

CG - EXPOSURE

He **died at 6:50 p.m.** without any great struggle for breath. The symptoms of irritation were very **slight at the onset**; there was then a **delay of at least 4 hours**, and the final development of **serious edema** up to death took little more than an hour though the patient was continually rested in bed.

Official History of The War
(1914-1918)

CG - EXERCISE PROHIBITION

“... men who have passed through a gas attack and have subsequently complained of only slight cough, nausea and tightness of the chest whilst resting in the trenches, have collapsed and even **died abruptly some hours later on attempting to perform some vigorous muscular effort.**”

Medical Manual of Chemical Warfare

SUMMARY

- **Inhaled toxic agent effects may be**
Central, peripheral, or combined
- **Latent period - “dose” dependent**
- **Onset of effect**
Symptoms occur *before* signs
< 4 hours - severe, often lethal exposure
> 4 hours - lethality less likely

SUMMARY - Therapy

- **Terminate exposure**
- **Resuscitate - ABCs**
- **Maintain strict bed rest**
- **Assess immediately *and* at 4 hours**
 - **If abnormal, assess for additional 24 to 36 hrs**

MEDICAL MANAGEMENT OF CHEMICAL CASUALTIES

ANY QUESTIONS?

U.S. ARMY MEDICAL RESEARCH INSTITUTE OF CHEMICAL DEFENSE



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