Inhalational Poisoning

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Triphosgene (bistrichloromethyl carbonate (BTC), $c_3cl_6o_3$)

- Safer substitute for phosgene.
- Solid crystal and less water soluble.
- Decompose >200^0c to phosgene gaseous form.
- Aqueous phosgene rapidly hydrolyzes to CO2, and Hcl.

- Exposure by the oral route is highly unlikely.
- Diller and zante (1982) performed an extensive literature review of human effects from phosgene inhalation exposure and found that a great majority of data were anecdotal or rough estimates and, thus, did not contain reliable exposure concentrations and/or durations.

- Cases of acute phosgene toxicity associated with two large-scale releases of phosgene in Germany and Japan have been reported.
- In Hamburg, Germany, on May 20, 1928, 11 metric tons (24,640 pounds) of "pure" phosgene escaped from a storage tank, resulting in a large-scale exposure to the airborne gas (Hegler, 1928; Wohlwill, 1928, both cited in U.S. EPA, 1986c).

- A total of 300 people—some located as far as 6 miles from the site reported illness within a few days of the release. Of those, 10 died as a result of the exposure.

- One hospital reported admitting 195 victims on the night of May 20. Of those, 17 were very ill, 15 were moderately ill, and the rest were only slightly affected.
- Autopsy of six of the fatalities revealed abnormalities primarily in the lungs. Occasional lesions of the kidney, liver, and heart were observed.

- In November 1966, phosgene was accidentally released from a factory in Japan (Sakakibara et al., 1967, cited in WHO, 1997).
- A total of 382 people were reported poisoned, 12 of whom were hospitalized.

- Signs and symptoms of exposure in the 12 hospitalized patients included headache, nausea, cough, dyspnea, fatigue, pharyngeal pain, chest tightness, chest pain, and fever.
- Seven patients showed evidence of pulmonary edema, as revealed by chest x-ray 48 hours postexposure.

- One patient reported lacrimation and redness of the eyes.
- Phosgene is a highly reactive gas capable of damaging a variety of biological macromolecules in an oxidant-like fashion.
- Mechanism of action is by Acylation and Hydrolysis.

- Phosgene reacts with nucleophilic moieties, such as the amino, hydroxyl, and sulfhydryl groups of tissue macromolecules.
- Acylation causes destruction of proteins and lipids, irreversible alterations of membrane structures, and disruption of enzyme and other cell functions.

- Exposure to phosgene depletes lung nucleophiles, particularly glutathione, and restoration of glutathione seems to protect against phosgene-induced injury (Sciuto and Moran, 1999; Sciuto et al., 1998, 1995; Schroeder and Gurtner, 1992; Jaskot et al., 1991; Sciuto and Gurtner, 1989).

- For several days after acute phosgene exposure, tissue levels of antioxidant enzymes, such as glutathione reductase and superoxide dismutase, increase as part of the lungs' response to injury (Jaskot et al., 1991).

- Hydrolysis to HCl is the probable cause of immediate inflammation and discomfort after phosgene exposure at concentrations greater than 3 ppm.
- Pulmonary cellular glycolysis and oxygen uptake following phosgene exposure are depressed and, thus, leads to a corresponding decrease in the levels of intracellular adenosine triphosphate and cyclic adenosine monophosphate (Sciuto et al., 1996; Kennedy et al., 1989; Currie et al., 1985).

- Interventions that increase intracellular cyclic adenosine monophosphate, such as treatment with

1. Phosphodiesterase inhibitors (e.g.,aminophylline),
2. Beta-adrenergic agonists (e.g., isoproterenol), or
3. cyclic adenosine monophosphate analogs,

- Pre-exposure injections of cyclophosphamide, significantly reduces circulating neutrophil counts, and decrease neutrophil migration to the lungs and limit phosgene-induced edema and mortality (Ghio et al., 1991)
- Acyltransferase activity in alveolar type II cell microsomes (which is necessary for the synthesis of pulmonary surfactant) was shown to be inhibited in rabbits after high doses of phosgene (Frosolono and Passarelli, 1978).

3 phases of presentation after inhalation

- Initial Bio protective phase
- Symptom-free latent period
- Terminal phase characterized by pulmonary edema (schneider and diller, 1989; diller, 1985)

- In the initial phase, high concentrations (>3 ppm) may result in frequent, shallow respiration and decreased respiratory vital capacity and volume.
- Arterial CO2 pressure increase and decreased blood pH.

- In the second phase,- several hours postexposure, clinical signs and symptoms are generally lacking (schneider and diller, 1989; diller, 1985).
- Histologic examination reveals the beginnings of an edematous swelling, with blood plasma increasingly entering the pulmonary interstitium and alveoli.

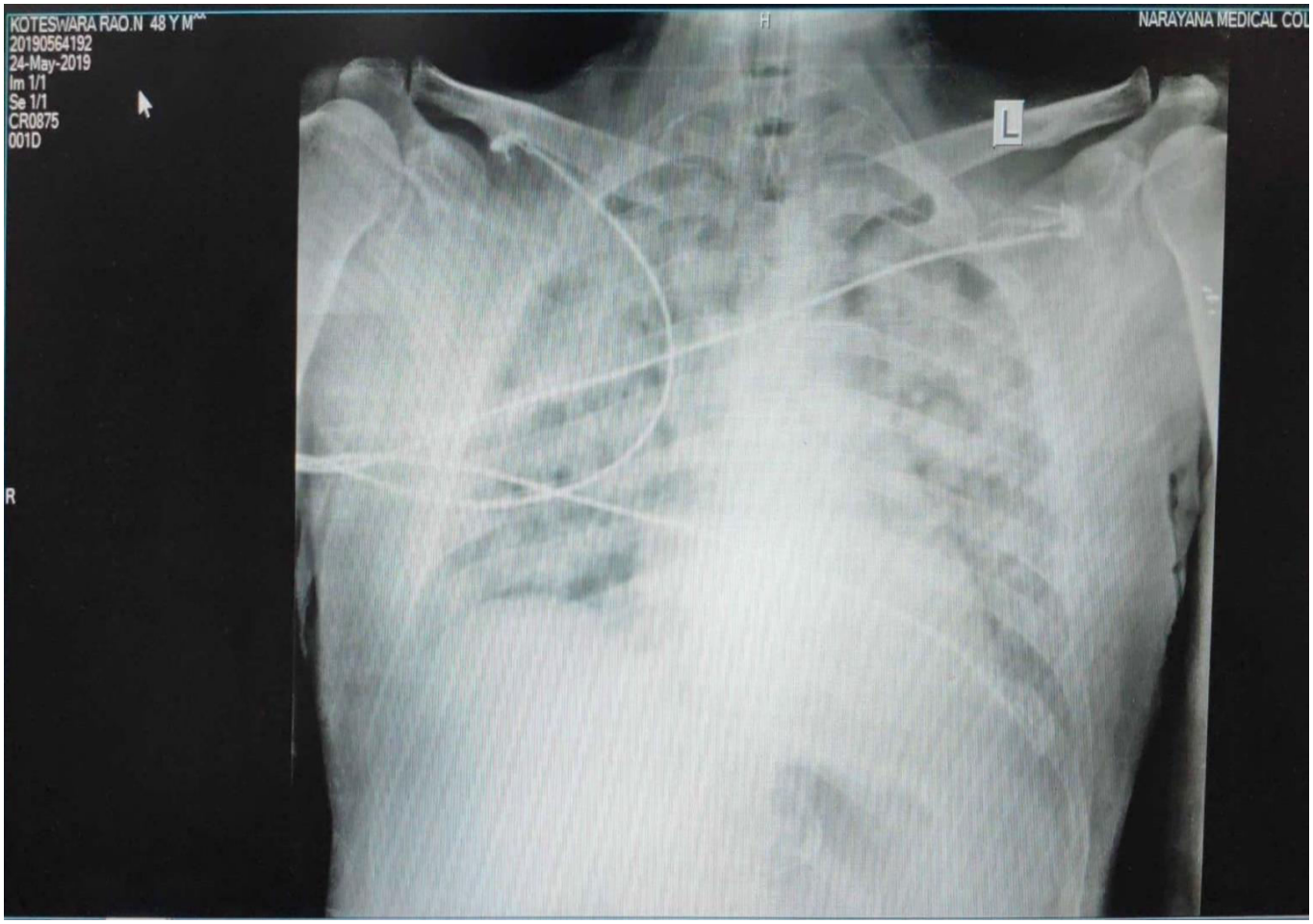
- Damage to the alveolar type 1 cells and a rise in hematocrit.
- In exposed humans, the individual is unaware of these processes; thus, this phase is termed the **“clinical latent phase.”** The length of this phase varies inversely with the inhaled dose.

- In the third clinical phase of phosgene toxicity (Schneider and Diller, 1989; Diller, 1985), the accumulating fluid in the lung results in the edema becoming apparent both directly and indirectly.
- Decreased gas exchange as the fluid gradually rises from the alveoli to the proximal segments of the respiratory tract.

- Agitated respiration may cause the protein-rich fluid to take on a frothy consistency.
- A severe edema may result in an increased concentration of hemoglobin in the blood and congestion of the alveolar capillaries.

- At sufficiently high exposure levels -cardiac failure due to pulmonary congestion.
- Peaks approximately 24 hours after an acute exposure and, assuming lethality does not occur, recedes over the next 3 to 5 days.

- Asthma-like symptoms months or even years after exposure to the material ceases.
- Non-allergenic condition known as Reactive Airway Dysfunction Syndrome (RADS)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- Criteria for the diagnosis of RADS include the

  - Absence of preceding respiratory disease, in a non-atopic individual,

  - Abrupt onset of persistent asthma-like symptoms within minutes to hours of a documented exposure to the irritant.

- A reversible airflow pattern, on spirometry, with the presence of moderate to severe bronchial hyperreactivity on methacholine challenge testing and the lack of minimal lymphocytic inflammation, without eosinophilia, have also been included in the criteria for diagnosis of RADS.
- Related to the concentration of and duration of exposure to the irritating substance.

- Industrial bronchitis- result of exposure due to high concentrations of irritating substance (often particulate in nature) and is completely reversible after exposure ceases.
- Dyspnea, cough and mucus production.

Management

- **Work up**
- CBP , Coagulation Profile
- RFT
- Serum Electrolytes
- Chest X-Ray
- ABG , ECG , 2D Echo

- **Treatment**
- Removal from the source, Irrigation of the eyes and skin as appropriate and Rest.
- O2 supplementation and Ventilation strategies
- Fluid therapy
- Bronchodilators , steroids and NAC
- FFP and Supportive therapy
- Prophylactic antibiotics are not indicated.

OTHER

- Overalls.
- PVC Apron.

ENGINEERING CONTROLS

- Local exhaust ventilation is required where solids are handled as powders or crystals; even when particulates are relatively large, a certain proportion will be powdered by mutual friction.
- Exhaust ventilation should be designed to prevent accumulation and recirculation of particulates in the workplace.

- Particulate dust filter.
- Acid vapour Type B cartridge/ canister.
- **EYE**
- Chemical goggles. " Full face shield.

HANDS/FEET

- Wear chemical protective gloves, eg. PVC.
- Suitability and durability of glove type is dependent on usage.
- Important factors in the selection of gloves include:

➢ Frequency and duration of contact,

➢ Chemical resistance of glove material

➢ Glove thickness and dexterity

- Select gloves tested to a relevant standard
- Gloves must only be worn on clean hands.
- After using gloves, hands should be washed and dried thoroughly.
- Application of a non-perfumed moisturiser is recommended.

THANK YOU