

Florida Poison Information Center/Jacksonville
At Shands Jacksonville
University of Florida Health Science Center
1-800-222-1222

Phosgene

History

Phosgene gas, also known as carbonyl chloride, is a synthetic and colorless irritant with a somewhat musty odor that is heavier than air. It first developed a worldwide reputation during World War I, when it was used in chemical warfare. Phosgene was the principal agent used, accounting for approximately 80% of the 100,000 gas-induced casualties.^{1,2,3} Today, phosgene gas most commonly arises from welding and from the combustion of volatile substances including organochloride compounds (i.e. polyvinyl chloride and isocyanates).⁴ These substances are found commonly in many household products such as solvents, paint removers, dry cleaning fluids, home and office furnishings, floor coverings and electrical insulation.

Mechanism of Action

Because of its poor water-solubility, phosgene gas is inhaled deeply into the lungs where it slowly hydrolyzes to form hydrochloric acid and carbon dioxide. This reaction occurs within minutes, however, clinical symptoms may be delayed for more than twenty-four hours after exposure. The reaction and the subsequent extent of pulmonary damage are dependent on exposure concentration and duration. Hydrochloric acid proceeds to cause epithelial damage and necrosis in bronchi, small bronchioles and capillaries. This leads to increased permeability of the alveolar and capillary basement membranes with resultant pulmonary edema.⁵ The damage is associated with disruption to Type I pneumocytes, which can be followed by damage to Type II pneumocytes, causing interstitial necrosis and/or alveolar collapse.⁶ Phosgene also binds to cellular enzymes causing hepatic and renal necrosis.⁷

Concentrations as little as 3 to 5 parts per million (ppm) can cause acute, mild irritant symptoms. Exposure to 25 ppm is extremely dangerous and can be fatal for even short periods of time. Exposure to 50 ppm is usually rapidly fatal without the appropriate medical intervention.^{8,9}

Symptoms

Signs and symptoms of acute phosgene gas exposure include irritation to the eyes, skin, respiratory and gastrointestinal systems. They are dependent on both the exposure concentration and duration.

In addition to the acute irritant symptoms, non-cardiogenic pulmonary edema can develop within minutes and up to 72 hours, leading to progressive respiratory insufficiency and ARDS. The respiratory symptoms may be accompanied by hypovolemia, hypotension, and hemoconcentration. The development of these delayed symptoms is usually preceded by a relatively asymptomatic period. The length of the latent period is thought to be inversely proportional to the severity of the initial symptoms. In several cases, infectious pneumonitis develops 3 to 5 weeks after exposure.¹⁰ Mortality is also rare, however, in such cases it occurs within 24 to 48 hours after exposure.

Testing

There exists no specific laboratory test for phosgene gas exposure, however, various means of monitoring pulmonary status should be undertaken. These include a chest x-

ray, oxygen saturation, arterial blood gas (if deemed necessary), and volume status assessment (initially via vital signs and examination of mucous membranes). Chest x-ray typically shows signs of pulmonary edema with enlargement of the hila as the earliest finding (4 to 8 hours after exposure) and/or ill-defined patchy infiltrates.¹¹

Medical Management

Decontamination: Initially, the patient should be removed from the exposed environment and stripped of his/her clothes. If any area of the skin or eyes has been exposed, thorough irrigation with tepid water should be performed. In areas where direct skin contact has occurred, one should perform a thorough rinse and wash with soap and water.

Pulmonary support should initially be maintained by oxygen therapy as needed. If the patient continues to be hypoxic, intubation may be necessary with or without positive-end-expiratory pressure. Pulmonary edema should be managed with special attention to maintain a net negative fluid balance. Diuretics should be avoided since the pulmonary edema is not secondary to fluid overload. If necessary, hemodynamics should be monitored through a central line or Swan-Ganz catheter.

Antibiotics should not be started empirically, but instead should be reserved for the cases in which there is clinical evidence of pneumonia or bronchitis. Both bronchodilators and steroids are effective in relieving bronchospasm and inflammation secondary to irritant effects of phosgene gas.

Specific treatments have been studied in the past include the use of hexamethylenetetramine (HMT) and N-acetylcysteine (NAC). HMT, once considered a specific antidote, has been proven only to be effective if administered in a prophylactic manner. There has been no evidence of benefit from HMT in acute phosgene exposure.^{7,11} NAC is thought to “trap” phosgene and convert it to a less harmful metabolite. It has also been postulated that NAC’s antioxidant properties play a role in the decrease in direct toxicity to pulmonary parenchyma. There are, however, no good in vivo studies of reduction of morbidity and mortality with the administration of NAC.^{12,13}

Disposition: Because of the risk of developing delayed non-cardiogenic pulmonary edema, patients should be admitted for close observation for at least 24 hours after phosgene gas exposure, with or without multiple irritant symptoms.

References

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