PHOSGENE

Information on Options for First Aid and Medical Treatment

Last revised February 2006
Check Phosgene Panel website (www.phosgenepanel.org) for most updated copy

Legal Disclaimer and Notice

This document is presented by the American Chemistry Council's Phosgene Panel to assist persons already sophisticated and experienced in first aid and medical treatment of phosgene exposure. The document is intended to assist such readers in their understanding of various options related to first aid and treatment. It is intended that the document will facilitate in-depth dialog and analysis concerning the issues presented. Readers are encouraged to consider information presented in the document as they evaluate and develop their own programs and procedures.

The development of protocols to address phosgene exposure can assist companies and health care providers in their provision of timely and helpful first aid and medical treatments. Although this document may be used to facilitate the development of such protocols, the material herein is very clearly not proposed, and is not to be interpreted, as a specific standard or protocol. This document is not intended to be a substitute for in-depth training or specific requirements, nor is it intended to define or create legal rights or other obligations. The document is not intended as a "how-to" manual, nor is it a prescriptive guide. Because this document is necessarily general in nature, each reader has an independent obligation to evaluate whether information and options contained in the booklet are appropriate based on the particular factual circumstances of the individual.

Although the information provided is provided in good faith, and believed accurate based upon information available to preparers of the document, neither the American Chemistry Council (ACC), its Phosgene Panel (Panel), nor their individual member companies, nor any of their employees, subcontractors, consultants, or other assigns, makes any warranty or representation, either express or implied, with respect to the accuracy or completeness of the information contained herein; nor do these organizations or individuals assume any liability or responsibility for any use, or the results of such use, of any information, procedure, conclusion, opinion, product or process disclosed in this document.

New information may be developed subsequent to publication that may render the document incomplete or inaccurate. ACC and the Panel assume no responsibility to amend, revise or update the document to reflect any such information that becomes available after its publication. Notwithstanding, because this document may be revised periodically, the reader is advised to visit the Panel's website at "phosgenepanel.org" to obtain the most current version.

Table of Contents	
Title	**Page**

Introduction

This document is presented by the American Chemistry Council's Phosgene Panel (Panel). Member companies of the Panel are:

- BASF Corporation
- BayerMaterial Science
- Davey Process Technology
- DuPont
- GE Advanced Materials
- Great Lakes Chemical Corporation (a Chemtura Corporation)
- IsoChem
- PPG Industries, Inc.
- Rubicon
- The Dow Chemical Company

The Panel wishes to acknowledge the contributions provided by the Phosgene Medical Experts Group (PMEG) and the International Isocyanate Institute (III) to assist in this effort.

Background

The value of a reference resource to provide clinicians with information on the evaluation and treatment of individuals with phosgene exposure has long been recognized. In 1982, the *International Symposium on Phosgene Induced Edema: Diagnosis and Countermeasures* was held with the papers from this symposium later published. In 1994, the physicians of the Phosgene Panel of the then Chemical Manufacturers Association (CMA) now called the American Chemistry Council (ACC) compiled a booklet, *Phosgene Pulmonary Exposure Information*, in order to assist other physicians who may be called upon to evaluate and treat patients after phosgene exposure. The information was compiled from review of relevant medical literature and from consultations with occupational physicians experienced in the evaluation and treatment of phosgene-exposed patients. This information was updated with the revised version of that document newly titled: *Phosgene: Information for Emergency Responders and Health Care Providers*, released in 2002. III released two documents in 1999 - *Critical Review of the Medical Management of Acute Phosgene Poisoning* by WF Diller and *Options for the Medical Management of Phosgene Poisoning* by D Pallapies and WF Diller. Review articles on this topic have been published periodically including the 2001 paper - *Phosgene Exposure: Mechanisms of Injury and Treatment Strategies* in the *Journal of Occupational and Environmental Medicine.*

In 2003, the PMEG was created. The PMEG is an *ad hoc* group which consists of physicians from various countries with knowledge and actual experience with phosgene inhalations. One of the goals of the PMEG was to develop an updated document on phosgene exposure evaluation and treatment. The PMEG offered its work to the Panel and this document is a result of these efforts.

Overview

Patients transiently exposed only to phosgene gas generally have not demonstrated a significant risk of transporting phosgene vapors on their bodies or clothing to other locations in concentrations sufficient to contaminate other individuals (i.e., "secondary contamination"). Patients whose clothing or skin is contaminated with liquid or gaseous phosgene or solvents containing phosgene, however, can secondarily contaminate themselves, or rescue and medical personnel, by direct contact or through off-gassing phosgene. To reduce risks of secondary contamination, the absence of off-gassing can be verified prior to transport through proper use of a phosgene badge or detector tape. Appropriate removal and disposal of contaminated clothing reduces potential risks in phosgene exposure cases.

Phosgene is a severe pulmonary toxicant. Signs of pulmonary edema (such as shortness of breath, cyanosis, expectoration, cough) do not usually appear for hours after even severely toxic exposures. (**Note**: Because of this potential delay in the signs and symptoms of pulmonary edema, a patient may initially present in apparently perfect health even after the inhalation of a life-threatening phosgene dose.)

Based on available sources, there appears to be no proven antidote available to counteract the effects of phosgene. On this basis, treatment consists of supportive measures and therapeutic agents aimed at modulating the inflammatory process.

Substance Information

Phosgene ($COCl_2$), CAS 75-44-5

Synonyms: carbonic acid dichloride, carbonic dichloride, carbon oxychloride, carbonyl chloride, chloroformyl chloride

Phosgene is a colorless, fuming liquid below 8°C (47° F) and a colorless, nonflammable gas above 8°C (47° F).

Phosgene is often used as a solution in organic solvents. At low concentrations, its odor has been described as similar to that of green corn or newly mowed hay. At high concentrations, its odor can be sharp and suffocating. Phosgene is hydrolyzed slowly by moisture to form hydrochloric acid.

Phosgene is used as an intermediate in the manufacture of many chemicals, including isocyanates, polycarbonates, dyes, crop protection products and pharmaceuticals.

Routes of Exposure

Inhalation

Inhalation is the major route of phosgene exposure. Because hazardous exposures can occur even at low concentrations, by the time an individual is aware of the chemical's odor, injury may be imminent or already underway. Irritant effects on the eyes and upper airways can be mild and transitory, and may be delayed. Additionally, olfactory fatigue at low doses occurs quickly and may result in prolonged asymptomatic exposures with delayed pulmonary effects.

At temperatures above 8°C (47°F), phosgene is a gas that is heavier than air and may cause asphyxiation in poorly ventilated, low lying or enclosed spaces.

Skin/Eye Contact

When phosgene gas contacts moist or wet skin or eyes, it may cause irritation and reddening. Liquid phosgene may cause severe burns. Contamination with phosgene in solvent solution may cause significant off-gassing and continuous exposure of the victim or secondary exposure of others.

Ingestion

Ingestion of phosgene is less likely because phosgene is a gas at room temperature. No information was identified about the sequelae of swallowing phosgene-containing solvents.

Mechanism of Phosgene Injury

After human inhalation of phosgene, two different reactions have been noted to occur:

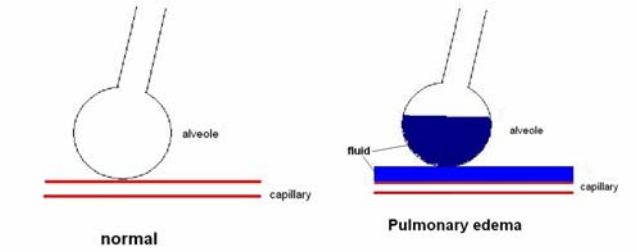
1. Slow and slight HYDROLYSIS with the formation of HCl. In cases of higher-concentration exposures, this may cause irritation of the eyes, nose, and throat, with burning sensation, cough and chest oppression. Signs and symptoms have been reported to appear soon after the inhalation. These vary according to the inhaled phosgene concentration, and usually regress after a few hours. Some experts suppose that this mechanism also plays a causal role for the formation of pulmonary edema.

Mechanism of Phosgene Injury (cont.)

2. Direct ACYLATING REACTIONS with nucleophilic structures of cells and their products. While the upper respiratory tract is largely protected by a mucous layer, this dangerous reaction mainly damages the terminal bronchioli and alveoli. As a consequence, the permeability of the blood-air barrier is altered, and fluid is excreted first into the interstitial space between capillary and alveoli. This increases the distance to be crossed by oxygen to reach the blood, and thus encourages hypoxemia. In the further course of the edema formation, flooding of the alveoli has been identified ("pulmonary edema"). While the whole process starts immediately with phosgene inhalation, clinically obvious signs and symptoms have not typically appeared before a critical volume of extravascular fluid has accumulated. Evidence indicates the length of this "clinical latency period" is inversely related to the inhaled phosgene dose: the higher the inhaled dose, the shorter the latency period. Available information suggests that the pulmonary edema generally reaches its maximum 24-30 hours after exposure and may last for several days.

The above mechanisms activate the inflammatory cascade resulting in the FORMATION OF REACTIVE OXYGEN SPECIES adversely impacting alveolar and capillary integrity, resulting in a compromised blood air-barrier and a dose-dependent pulmonary edema.

Picture 1: Development of pulmonary edema:

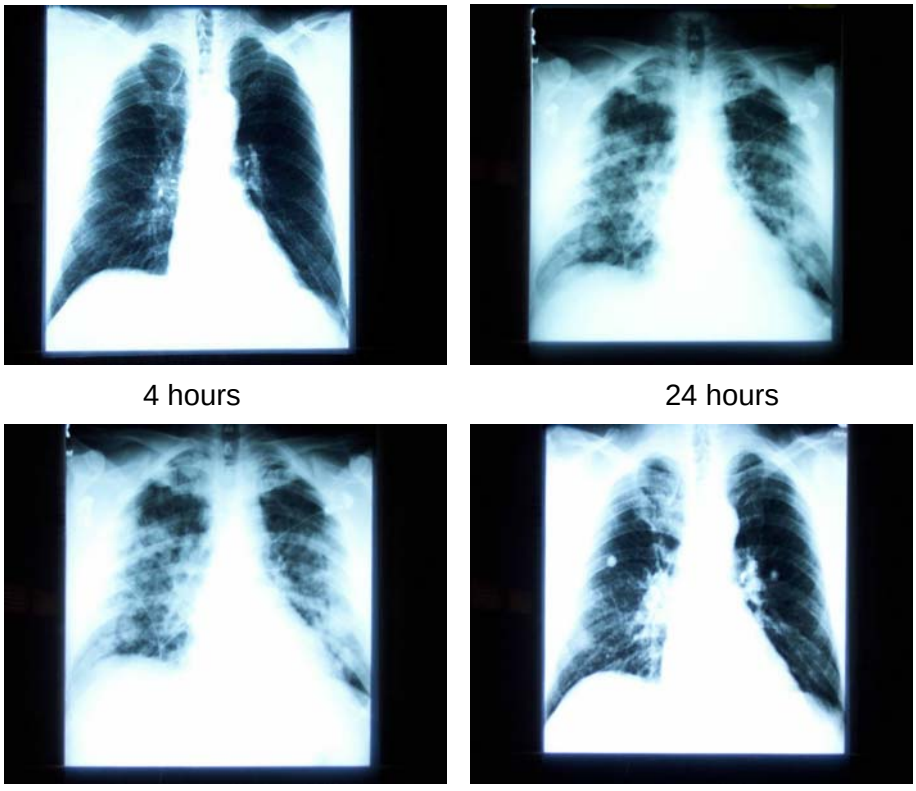


Clinical signs of toxic pulmonary edema include:

- respiratory distress;
- cyanosis;
- increasing cough;
- crackles on auscultation; and,
- discharge of frothy liquids ("foam") from nose and mouth.

Mechanism of Phosgene Injury (cont.)

Picture 2: Sequential radiographs demonstrating development and resolution of pulmonary edema after a severe phosgene exposure: Although the exact exposure dose in this case was unknown, the x-ray findings indicate that a severe exposure took place. Initial treatment included early administration of high-dose aerosolized corticosteroids, high-dose intravenous corticosteroids, and hospital admission after 4 hours. Hospital treatment was continued with high-dose aerosolized and intravenous corticosteroids, but no mechanical ventilation.



4 hours | 24 hours

40 hours | 108 hours

Photographs reprinted courtesy of W. Steffens

4 hours: Slightly blurred hili, clinically some wheezing.

24 hours: Full blown pulmonary edema with opacities all over the lungs.

40 hours: Further deterioration of pulmonary edema.

108 hours: Pulmonary edema resolved, patient survived.

Last revised February 2006
Check Phosgene Panel website (www.phosgenepanel.org) for most updated copy

Exposure-Effect Relationships

The unit for phosgene concentration in air is "part per million," abbreviated "ppm." The "inhalation dose" is the product of exposure concentration (in ppm) and exposure time (in minutes), thus ppm x min (or ppm-min).

As a consequence of the different underlying mechanisms of phosgene injury caused by exposure via inhalation, the health effects depend both on the inhaled phosgene concentration and inhalation dose.

Phosgene Concentration*	**Reported Effects**
> 1.5 ppm	Odor recognition
> 3.0 ppm	Irritation of eyes, nose, throat, bronchi

Inhalation Dose of Phosgene	**Reported Effects****
< 25 ppm-min	No detrimental effect
25 – <50 ppm-min	Subclinical biochemical lung alterations
50 – 150 ppm-min	Subclinical pulmonary reactions
> 150 ppm-min	Overt alveolar pulmonary edema
> 300 ppm-min	Possible lethality
~ 500 ppm-min	50% mortality rate (LCT_{50})

* This is the concentration to which an individual is actually exposed. Associated reported effects may vary by individual.

** Represents dose-effect relationships based on commonly reported responses and accurate assessment of inhalation dose (i.e., not badge readings only). Individual effects may vary.

Estimation of inhaled dose:

If a badge reading or other measurements are available, the inhalation dose may be **estimated** from breathing zone concentration and time of exposure (e.g., badge dosimetry reading).

Note: Although a badge reading is useful information, it does not necessarily represent the actual inhaled dose. Other factors, such as use of personal protective equipment (PPE), breath holding, relationship (distance) of badge to mouth/nose and source, etc., may affect the amount of phosgene inhaled. Also, badge readings may vary depending on the manufacturer of the badge, the comparator used, the reader of the badge, and certain environmental conditions like humidity, as well as the presence of other gases (e.g., hydrogen chloride or chloroformates).

Potential Sequelae:

If a patient who develops pulmonary edema survives the initial 48 hours after exposure, available reports support the conclusion that recovery is likely although prolonged symptoms of impaired lung function have been reported.

Clinical Features

The clinical picture after phosgene exposure may vary significantly according to the inhaled phosgene concentration and the individual inhalation dose as well as specific medical issues relevant to the exposed individual. Thus, a wide range of scenarios is conceivable. This demonstrates why estimating inhalation dose in ppm-min is important to the choice of medical support provided to the patient.

Sample of observed scenarios:

- odor recognition without further signs and symptoms, *e.g.*, after the inhalation of 2 ppm x 1 min (or a dose of 2 ppm-min)
- odor recognition and early eye and upper airways irritation, *e.g.*, after an inhalation of 5 ppm x 3 mins (or a dose of 15 ppm-min)
- odor recognition, no upper airways irritation, but pulmonary edema 8 hrs after phosgene inhalation, *e.g.*, after an inhalation of 2 ppm x 80 min (or a dose of 160 ppm-min)
- odor recognition, significant upper airways irritation, pulmonary edema 7 hours after phosgene inhalation, *e.g.*, after an inhalation of 5 ppm x 50 min (or a dose of 250 ppm-min)
- odor recognition, severe upper airways irritation, pulmonary edema after 4 hours, death after 24 hrs, *e.g.*, after an inhalation of 20 ppm x 40 min (or a dose of 800 ppm-min)
- no odor recognition, no upper airways irritation, but pulmonary edema after 5 hours and death after 30 hours, *e.g.*, after an inhalation of 1 ppm x 600 min (or a dose of 600 ppm-min)

<u>The above scenarios support the following conclusions:</u>

- Odor recognition, upper airways irritation, pulmonary edema and death may be independent from each other.
- Odor recognition is an unreliable warning mechanism.
- Upper airways irritation does not necessarily precede pulmonary edema or death.
- Observed signs and symptoms of pulmonary edema will usually be delayed by several hours.
- The length of the “latency period” can provide some insight as a prognostic indicator: the shorter the latency period, the worse the prognosis is likely to be.

The development of pulmonary edema is a progressive process initiated with the actual inhalation. Currently, there is no known specific diagnostic test to accurately predict the future development of pulmonary edema**.** However, the presence of sub-clinical changes which could signal edema’s future development may be demonstrated earlier in the process by technical examinations including blood-gas analysis, measurement of oxygen saturation and chest X-rays.

Emergency Response, Medical Monitoring, Medical Treatment and Discharge

Emergency Response Actions:

Decontamination

Patients transiently exposed only to phosgene gas generally have not demonstrated a significant risk of transporting phosgene vapors on their clothing or bodies to other locations in concentrations sufficient to contaminate other individuals (i.e., secondary contamination). However, patients whose clothing or skin is contaminated with liquid or gaseous phosgene, or solvents containing phosgene, can continue inhaling and/or secondarily contaminate other people by direct contact or through off-gassing phosgene. To reduce the risk of secondary contamination, the absence of off-gassing can be verified prior to transport through proper use of a phosgene badge or detector tape.

Patients who are able and cooperative may assist with their own decontamination as long as their efforts do not result in undue stress or exertion (see below). If the exposure involved liquid phosgene or solvents containing phosgene, and if clothing could be contaminated, completely removing and double-bagging the clothing for proper disposal mitigates potential risk of continued exposure.

Exposed skin and hair are generally flushed with plain water as a decontamination activity. For example, a number of practitioners flush exposed skin and hair with lukewarm water for at least 15 minutes. Some further injuries can be reduced by protecting the exposed individual's eyes during flushing of skin and hair.

Exposed or irritated eyes are typically irrigated with plain water or saline as a decontamination activity. For example, a number of practitioners irrigate exposed or irritated eyes for at least 15 minutes.

In some cases, an exposed individual will be wearing contact lenses. Decontamination can be facilitated by removing the lenses, assuming the lenses are easily removable without providing additional trauma to the eye.

In cases of a severe exposure, severe symptoms or suspicion of imminent or manifest pulmonary edema, the decontamination period has been shortened to 3 to 5 minutes to allow for prompt initiation of any needed medical assistance and transport to a higher level of care. However, failure to take steps necessary to protect the victim(s), emergency responders, ambulance attendants and equipment from contamination with phosgene and other compounds can result in even further injury to the initially exposed individual and everyone else involved.

Physical stress or exercise after significant phosgene exposure can contribute to further injury to exposed individuals based on animal experiments which have shown that physical activity increases both the rapidity of development and the severity of lung edema.

Emergency Response, Medical Monitoring, and Discharge (cont.)

Medical Assessment and Treatment:

Triage

Although individual triage processes may differ based on specific facts and circumstances, the following information provides one example of initial triage procedures used by some practitioners:

- Some authorities believe that: (1) patients with an inhalation dose of <50 ppm-min can be discharged if symptom-free (see patient discharge information); and that (2) all other patients (inhalation dose 50 ppm-min or greater, unknown inhalation dose or significant symptoms) receive medical monitoring such as that outlined in the section below. This monitoring is generally done initially in the Emergency Room (ER) and later in the intensive care unit (ICU) or medical unit where close monitoring can be done.

Note: Some authorities take the approach that medical monitoring is instituted at levels as low as 25 ppm-min.

Medical Monitoring:
Medical monitoring may include items such as the following:

- Standard intake history;
- History of possible exposure;
- Frequent vital signs (recurring checks);
- Physical exam (with specific emphasis on the respiratory system - auscultation);
- Pulse oximetry monitoring;
- Chest X-ray (posterior-anterior and lateral); and,
- Baseline blood work (e.g., including complete blood count, electrolytes, liver and kidney functions).

NOTE: If pulmonary edema is anticipated (particularly after an inhalation dose >150 ppm-min or a strong suspicion thereof), intensified medical monitoring is important. Such monitoring may include items such as the following:

- Baseline arterial blood gases (ABG);
- Continuous pulse oximetry;
- Vital signs (consistent with intensive care unit protocols);
- Frequent chest auscultation;
- Serial chest x-rays;
- Chest x-ray post-exposure; and,
- Admission to a facility with intensive level care capabilities.

The earliest signs of pulmonary edema on chest x-ray are generally reported as enlarged, blurred hilar area and ill-defined patches or strip shadows in the central lung area. (See Picture 2).

Emergency Response, Medical Monitoring and Discharge (cont.)

Patient Discharge:

Because of the potential for delayed effects, patients with phosgene exposures deemed to be significant have historically been observed for up to 48 hours. Before discharging any patient, the practitioner must determine that, following appropriate inquiry, the totality of the evidence provides justification to conclude that the patient's presence in the monitoring facility is no longer necessary. Some authorities generally indicate that patients with an exposure dose of 50 ppm-min or greater or with unknown inhalation; who (1) have a normal examination **and** (2) no signs or symptoms of toxicity after observation for 8 hours **and** (3) no signs of acute pathologic findings (specifically any signs of pulmonary edema) on chest x-rays 8 hours after exposure, may be discharged with appropriate discharge instructions. If any one of these criteria is not met, additional medical monitoring is used to help identify delayed effects. A number of practitioners will observe patients for at least 24 hours under such circumstances.

Upon discharging a patient after initial evaluation or from a hospital ER, the provision of written discharge instructions can minimize risks of potential confusion and other difficulties. Discharge instructions may include items such as the following:

- Information on signs/symptoms of concern;
- Whom to contact for concerns;
- Follow-up instructions;
- Recommendations to avoid heavy physical exertion for specified period; and,
- Recommendations to avoid exposure to cigarette smoke for specified period.

Note: The use of spirometry can help practitioners monitor the patient's respiratory functioning after discharge. Because the spirometry evaluations can indicate serious unforeseen complications, their use following discharge is especially relevant in cases of significant phosgene exposure.

Notice: Based on available information, there appears to be no proven antidote available to counteract the effects of phosgene. On this basis, treatment consists of supportive measures addressing symptoms and potential inhaled dose. Treatment options are primarily based on animal studies and anecdotal experiences. Therefore, the health care professional is to recommend specific treatment on a case-by-case assessment based on factors including, but not limited to, his/her own professional judgment, local medical practice, and availability of medical technologies. Symptoms, possible inhaled dose, preexisting medical conditions, and clinical findings from medical monitoring are key components in this decision-making process. The following are options available for consideration (see also Appendix B for abbreviated sample guide).

Note: If no badge has been worn (or there is other reason for large uncertainty), a number of practitioners assume that in all cases of inhalation of phosgene, a significant inhalation has occurred, and the patient is observed and/or treated accordingly.

Emergency Response, Medical Monitoring and Discharge (cont.)

Initial Treatment:

- Irritation of eyes can sometimes be adequately treated by thorough rinsing (decontamination). If irritation continues, the eyes can be checked for corneal abrasion/burns. An ophthalmologist may be consulted if ocular signs and symptoms continue.
- Cough may respond to a non-narcotic anti-tussive.
- Wheezing/bronchospasm may respond to aerosolized B_2-selective adrenergic agonists, e.g. terbutalin, salbutamol or isoproterenol, as per standard treatment for asthma.
- Oxygen administration, particularly at 100%, has been speculated to cause adverse effects, and therefore is not generally recommended. However, oxygen by mask or nasal cannula may be helpful if a patient is experiencing dyspnea, wheezing, or sustaining low pulse oximetry readings.
- Anxiety is a normal reaction to the often dramatic circumstances of a phosgene accident. A calming, informative talk with medical personnel likely will help. In patients who manifest moderate to severe anxiety, a light sedative may be considered.

Note: Potential risks can be reduced by keeping patients under medical supervision until signs and symptoms abate significantly (see medical monitoring and patient discharge information).

Note: Persistent or increasing signs and symptoms of respiratory impairment, including the appearance on auscultation of wheezing without a previous history of wheezing or asthma, may signal the appearance of pulmonary edema.

Treatment Options:

Early Treatment

Based on available information, there appears to be no specific proven antidote against phosgene-induced lung injury. However, clinical experience seems to indicate that early treatment of suspected pulmonary injury due to significant phosgene exposure may be more effective than the treatment of clinically overt pulmonary edema.

A stepwise type of early therapy, depending on the suspected phosgene inhalation dose, has been used for a dose as low as 50 ppm-min. In some cases, this stepwise therapy was sometimes considered at doses >25 ppm-min. Early treatment, along with the medical monitoring summarized above, is the procedure for a number of practitioners.

Note: Based on information available, there is not consensus on the exact exposure level at which treatment is warranted, hence practices vary according to medical protocols and individual circumstances.

Steroids administered as soon as possible after an inhalation have been reported to mitigate the inflammatory response and prevent blood vessel leakage. Options previously used include inhaled, oral or intravenous administration. One of the factors to consider in determining routes and timing of delivery is the presence of the local resources (e.g., emergency response personnel, level of training, local scope of practice, transport time to a clinical facility, etc.).

Treatment Options:

Early Treatment (cont.)

Various doses and routes have been utilized for the administration of steroids. When it is deemed appropriate and immediately available, an inhaled steroid at its maximum dose has been given by some practitioners. Another option that has been used is the IV administration of 250 – 1,000 mg of methylprednisolone as soon as possible.

Note: These options are opinion-based, not evidence-based, especially for exposures <150 ppm-min. The decision on treatment, therefore, like other issues presented in the document, should be left to the attending physician.

After the inhalation of a large phosgene dose (>150 ppm-min) or the suspicion thereof (e.g., facial contamination with phosgene in solution), severe or therapy-resistant irritation of upper airways, or sustained drop of oxygen saturation, it may be critical that all possibilities to combat impending pulmonary edema be used immediately. According to anecdotal clinical observations and/or information from animal experiments, the following therapeutic measures are included in a number of clinical protocols used by Phosgene Panel member companies and may assist practitioners in development of their own procedures.

Steroids: The early use of corticosteroids via the most readily available route, inhaled, oral and/or intravenous, may provide increased chance to reach directly the alveolar epithelium as well as the pulmonary capillary endothelium. If the intravenous route is readily available, then an IV dose of methylprednisolone or equivalent has been given. Additionally and/or if the IV route is not available, then an inhaled steroid at its maximum dose is an option. Oral prednisone may be considered, if the inhaled and/or IV steroid is not available.

- **Positive airway pressure ventilation** by mask (End-expiratory Positive Airway Pressure (EPAP) or Continuous Positive Airway Pressure (CPAP)) has been shown to reverse alveolar collapse and arterio-venous shunts.)

- **Terbutaline or aminophylline(IV/PO)/theophylline (PO)**

  Terbutaline has been used as an early treatment option similar to treatment protocols for asthma. As an alternative, practitioners can also consider aminophylline(IV/PO)/theophylline (PO). For a rapid effect, aminophylline has been initiated intravenously as per treatment protocol for asthma. Because of the therapeutic and toxicity issues associated with use of aminophylline, the use of blood level monitoring helps practitioners reduce potential risks when this option is employed.

  Note: Terbutaline and aminophylline are reported to suppress the synthesis of lipoxygenase mediators, known inflammatory mediators triggered by phosgene exposure. Caution is advised when considering the provision of aminophylline/theophylline and terbutaline together because of possible synergistic side effects.

Treatment Options:

Early Treatment (cont.)

- **N-Acetyl Cysteine (NAC)** has been reported to restore the glutathione lung antioxidant defense system. Therefore, it has been postulated that it may be beneficial in significant phosgene exposure cases. However, bronchoconstriction has been reported to be prompted by inhaled NAC.
- **Leukotriene Receptor Antagonists (PO, also available as aerosol combined with steroid).** A variety of agents with high safety profiles is currently available for the treatment of asthma and may be considered in moderate to severe phosgene exposures. Animal toxicology studies have demonstrated that leukotriene-mediated capillary permeability is a factor in phosgene-induced pulmonary edema. These medications are of interest to some practitioners based on the agents' pharmacologic effects. Experience with their use in treatment of phosgene exposures is very limited and has not been compiled.

Treatment of Manifest Pulmonary Edema

Frequently reported signs and symptoms of overt pulmonary edema include progressive dyspnea, cyanosis, rales (crackles) on auscultation and copious discharge of frothy fluid from mouth and nose. Resources available at hospital intensive care units are needed by patients with these signs and symptoms. Once pulmonary edema has developed as a result of phosgene inhalation, the general treatment approach is basically that of an acute respiratory distress syndrome (ARDS). Animal experiments and some anecdotal clinical observations report favorable results after the following treatment methods:

- **Steroids:** Even though the exact benefits of large-dose steroid treatment has not been definitively proven in human exposures to phosgene, many practitioners use this therapy in cases resulting in pulmonary edema. One common approach is to administer methyprednisolone 1 g IV, repeated every 8-12 hours if needed.
- **Intubation and Mechanical Ventilation**: In some cases, intubation and mechanical ventilation with PEEP (positive endexpiratory pressure) as indicated for progressive respiratory failure have been required. To minimize ventilator-associated lung damage, the volume, pressure and oxygen concentration (FiO_2) levels are adjusted to appropriate amounts. Consultation with a clinician experienced in the management of ARDS is beneficial when readily available.
- **Therapies outlined in Early Treatment section (above).**

Other Treatment Options

- **ECMO (Adult Extracorporeal Membrane Oxygenation):** ECMO, which is available only in select tertiary care centers, provides for external blood oxygenation and reintroduction of oxygenated blood via a veno-venous or arterio-venous circuit. This treatment alternative merits consideration in patients who are refractory to other interventions. In geographies where this treatment option is available, potential complications can be reduced by resolving referral arrangements in advance, and consulting with ECMO staff for early notification, treatment and referral criteria for severely exposed individuals.

Treatment of Manifest Pulmonary Edema (cont.)

Information and location of ECMO-capable facilities can be found at the Extracorporeal Life Support Organization (ELSO) at the following outside website: http://www.elso.med.umich.edu/.

- **N-Acetyl Cysteine (NAC):** There is a single anecdotal case report of a phosgene-induced pulmonary edema dissipating after this therapy. The reported dosage in this case was 4-7 g IV. However, the value of this treatment in this clinical setting has not been proven, and there have been reports of significant side effects in patients receiving IV NAC for other reasons. In evaluating whether a discontinuation of the infusion is required, practitioners can pay particular attention to the presence of flush reactions. Again, the decision to use this regimen should be based on its risk/benefits.

- **Ibuprofen:** Various animal studies have been conducted which indicate that ibuprofen at very high doses may have a beneficial effect on treating phosgene-induced lung injury. However, since there are no reports specifically demonstrating that ibuprofen is beneficial in the treatment of phosgene exposures of humans, and since it has not been proven useful in the treatment or prevention of ARDS, ibuprofen is not routinely recommended. Regardless, some practitioners may consider ibuprofen for severe phosgene exposures.

Miscellaneous Approaches Raising Issues

In addition to the previously mentioned treatment options, there are some remaining approaches sometimes discussed in phosgene-exposure contexts. Based on information available to the PMEG, benefits from the following treatments have not been adequately demonstrated, or their application raises other issues, that may lead some practitioners to reconsider their use:

- **Diuretics:** Toxic pulmonary edema is different from cardiopulmonary edema and therefore the use of diuretics to treat pulmonary edema after phosgene exposure has not been demonstrated to achieve desired results.

- **Overinfusion:** Experience of the PMEG indicates that it is advantageous to manage fluids and electrolytes conservatively (especially if pulmonary edema is present or a possibility). Overinfusion and the use of crystalloid IV fluids should be avoided. If volume expansion is necessary, colloid solutions have been used previously by some practitioners with some success.

- **Antibiotics:** Though pulmonary superinfection may occur, past experiences with using prophylactic antibiotics have not proven to be beneficial, therefore the prophylactic administration of antibiotics is generally not recommended by practitioners.

- **Phlebotomy:** Phlebotomy has been tried in the past. However, based on information made available by others to the PMEG, members of the PMEG currently believe phlebotomy may cause more harm than benefit.

Other References

There are many references concerning the effects and medical treatment of phosgene exposure. Since this document provides only general guidance, readers are encouraged to evaluate other informational sources in order to prepare the most suitable first aid and treatment protocols and procedures for their own specific circumstances. Below are a few references which may be useful when formulating specific protocols:

Borak J and Diller WF, *Phosgene Exposure: Mechanisms of Injury and Treatment Strategies*, JOEM, Vol 43, Number 2, Feb 2001, pages 110-119.

Diller WF. *Critical Review of the Medical Management of Acute Phosgene Poisoning*, III project, 1999.

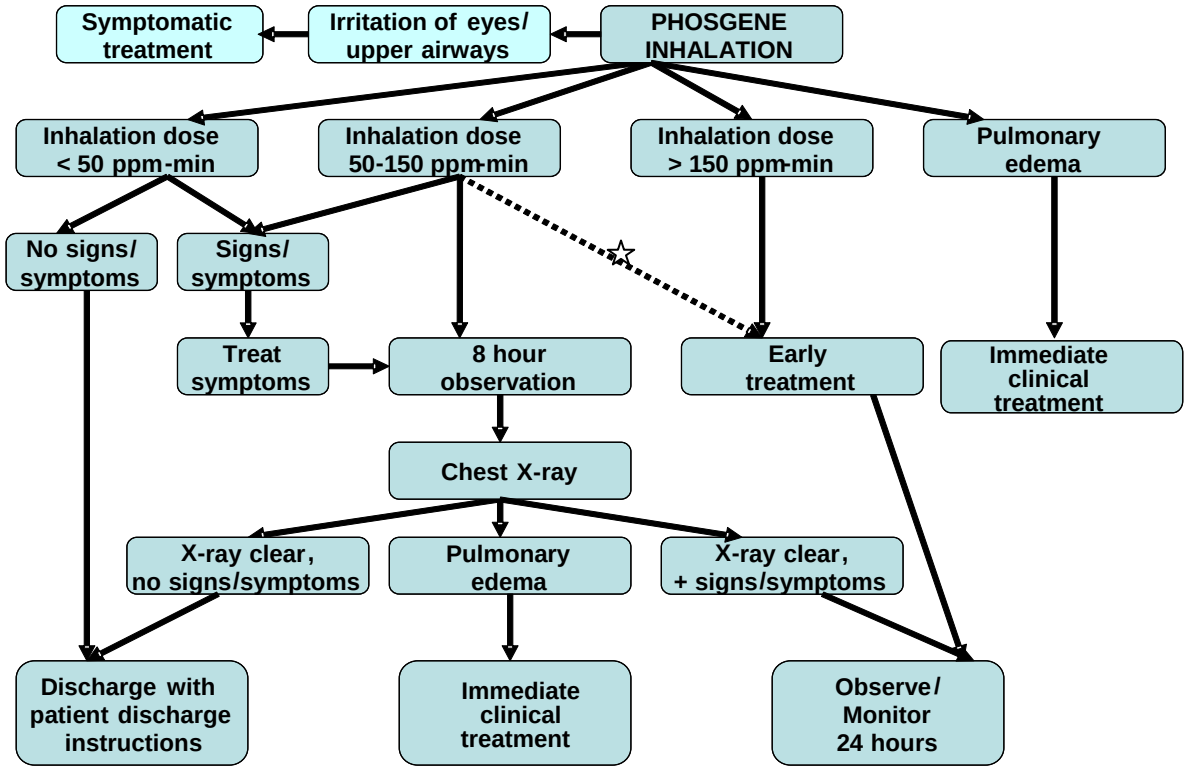
Pallapies D and Diller WF, *Options for Medical Management of Phosgene Poisoning*, III project, 1999.

Medical Management Guidelines (MMG's) for Phosgene, ATSDR document, (no date available). (http://www.atsdr.cdc.gov/MHMI/mmg176.htm).

Phosgene Induced Edema: Diagnosis and Therapeutic Countermeasures, an International Symposium, Princeton Scientific Publishing Co. 1985.

Appendix A: Sample Flow Chart on Treatment Options

Notice: The following sample flow chart highlights how some practitioners process options described in the text based on estimated phosgene dose. While the flow chart is only a general example, readers can consider using it to develop their own treatment option flow chart, or evaluating their own decision-making based on specific circumstances. As with other parts of this document, health care professionals should recommend specific treatment on a case-by-case assessment based on factors including their own professional judgment, local medical practice, and availability of medical technologies.



☆ The dotted line indicates that treatment at levels as low as 50 ppm-min has been considered.

Note: Based on information available, there is not uniform consensus on the exact exposure level at which treatment is warranted, hence practices vary according to medical protocols and other individual circumstances.

Appendix B: Abbreviated Sample Guide

Sample Reference Guide

Notice: The following abbreviated guide is included to assist preparations necessary to efficiently evaluate and treat individuals exposed to phosgene, according to initial presentation and suspected severity of exposure. Because this is only an abbreviated sample based on the experiences of, and information available to, the PMEG, practitioners are strongly advised to also consider additional information including that provided in previous sections of this document, practitioners' and patients' own specific circumstances, and information outside this document relevant to the topics of discussion.

Decontamination	For all liquid phosgene exposure and massive phosgene gas exposure (See *Decontamination* section)	
Symptoms, Observations and Symptomatic Treatment	**Cough**	Non-narcotic anti-tussive
	Wheezing	Aerosolized B_2-selective adrenergic agonist as per standard treatment of asthma.
	Anxiety	Reassurance, light sedative if appropriate.
	Dyspnea	Humidified oxygen (4-6 liters/minute)
	Pulse Oximetry < 92%	Humidified oxygen (4-6 liters/minute)
Early Treatment for Phosgene Badge Reading or Suspected Exposure 50 - 150 ppm-min.	**Medical Monitoring**	E.g.: history, vital signs, physical exam, pulse oximetry
	Basic treatment and observations	See above
	Corticosteroids*	Delivery options: • Aerosolized: Maximal dosage according to the specific corticosteroid used and/or • Intravenous: 250 mg methylprednisolone or equivalent**.**

Continued on next page

*The efficacy of using corticosteroids has not been proven (see previous text for related information).

Appendix B: Abbreviated Sample Guide (Continued)		
Early Treatment for Badge Reading or Suspected Exposure > 150 ppm-min.	**Corticosteroids**	• Intravenous: 1000 mg methylprednisolone or equivalent • Aerosolized: maximal dosage according to the specific corticosteroid used and if immediately available **Note:** if intravenous and/or aerosolized corticosteroids are not available, oral or intramuscular application may be considered.
	EPAP/CPAP **(if any indications of early pulmonary edema exists)**	15 minutes per hour, up to 5 cm H_2O with $FiO_2 < 50$ % **Note**: This is for initial treatment only. Significant pulmonary edema may require mechanical ventilation with PEEP.
	Aminophylline/ Theophylline	Standard IV and/or PO loading and maintenance dosing as per standard treatment of asthma, **-- OR ---**
	Terbutaline	0.25 mg subcutaneously **(**SC) or as aerosol **Note**: Caution is advised when considering giving Aminophylline/ Theophylline and Terbutaline together because of possible synergistic side effects.
	N-Acetyl Cysteine	10 ml of a 20% solution via nebulizer
Continued on next page		

Appendix B: Abbreviated Sample Guide (Continued)		
Treatment of Pulmonary Edema	**Intubation**	As indicated for progressive respiratory failure
	Mechanical Ventilation with PEEP	Volume, pressure and FiO_2 should be adjusted to minimize ventilator associated lung damage. Consultation with a clinician experienced in the management of acute respiratory distress syndrome (ARDS) is advised.
	Corticosteroids IV	1,000 mg methylprednisolone equivalent every 8-12 hours
	Terbutaline	0.25 - 0.5 mg SC (max dose 0.5 mg every 4 hours)
	N-Acetyl Cysteine	10 ml of a 20% solution via nebulizer
	Duration	Duration of therapeutic interventions will require physician judgment regarding impact on clinical course.
	Additional Options	For additional treatment options, please refer to the text.