JOINT TRAUMA SYSTEM CLINICAL PRACTICE GUIDELINE (JTS CPG)

Inhalation Injury and Toxic Industrial Chemical Exposure (CPG ID: 25)

There are multiple toxic industrial chemicals that act on the respiratory tract. This CPG reviews the most common toxic industrial chemicals related in pulmonary injury

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First Publication Date: 23 Feb 2007 | Publication Date: 25 Jul 2016 | Supersedes CPG dated 07 Jun 2008

TABLE OF CONTENTS

PURPOSE

There are multiple toxic industrial chemicals that act on the respiratory tract. This CPG reviews the most common toxic industrial chemicals which lead to pulmonary injury.

More information is available from the CDC:

- http://www.bt.cdc.gov/agent/agentlistchem-category.asp
- Textbook of Military Medicine http://www.bordeninstitute.army.mil/published_volumes/biological_warfare/biological.html

Patients with both burn and inhalation injury have significantly increased morbidity and mortality compared to those with burn injury alone.[1] The current CPG is intended to review relevant information in the care of patients with inhalation injury and more specifically toxic industrial chemicals. Also included is a brief overview of the management strategies for these patients. We intend to inform caregivers with the goal of reducing some of the complications of inhalation injury.

GENERAL SMOKE INHALATION INJURY

Smoke inhalation injury occurs from several agents. Thermal injury and chemical injury are the primary initial toxicities. Chemical injury occurs from several materials of combustion and pyrolysis.[2] Highly water soluble irritants such as acrolein, sulfur dioxide, hydrogen chloride and ammonia, and intermediate water soluble irritants such as chlorine and isocyanates are produced. Poorly water soluble irritants are oxides of nitrogen and phosgene. Simple asphyxiants which displace oxygen include carbon dioxide and methane, and chemical asphyxiants which inhibit mitochondrial activity and reduce hemoglobin carrying capacity include carbon monoxide, cyanide, and hydrogen sulfide. Treatment is generally supportive. Some require antidotes. Most critically ill patients require unique ventilation techniques used for Acute Respiratory Distress Syndrome (ARDS).

TOXIC INDUSTRIAL CHEMICAL INHALATIONAL INJURY

In general, the treatment of ARDS secondary to toxic industrial chemicals is similar to that for smoke inhalation injury. The care is supportive with a focus on:

- Airway management
- Lung-protective ventilation strategies
- Aggressive pulmonary toilet, and
- Avoidance of volume overload or rapid fluid infusion that might worsen pulmonary edema secondary to capillary leak.

PATIENTS REQUIRING MECHANICAL VENTILATION (MV) SECONDARY TO TOXIC INDUSTRIAL CHEMICAL INHALATION

Patients requiring Mechanical Ventilation (MV) secondary to toxic industrial chemicals inhalation, in particular chlorine, are at a higher risk of developing ventilator-associated pneumonia and should be monitored closely. The treatments in this CPG are primarily based on animal experiments. Evidence for clinical use in humans is limited.

CHLORINE

Chlorine (Cl_2) (Appendix A) is used commonly in industry. It is a commonly found in industrial and transportation accidents and are sometimes used in weapons such as IEDs. Chlorine dissolves in water to form hydrochloric and hypochlorous acids.

Chlorine has intermediate water solubility. Just after exposure the patient develops mucosal irritation (tearing, skin burning, drooling), but after large or sustained exposure the patient may develop cough, shortness of breath, and chest pain due to alveolar injury. If the patient develops pulmonary toxicity, it may worsen over days.

Treatment is primarily skin decontamination, supplemental oxygen, beta agonists and ARDS ventilatory techniques.[3] Inhaled corticosteroids (e.g. fluticasone) improved secondary outcomes in severely toxic animal models.[4] Clinical data on the efficacy of corticosteroids after human exposure to lung-damaging agents are inconclusive as the number of well-structured controlled studies is small and the indications for administration of corticosteroids are unclear.[5] Prone positioning mechanical ventilation maybe effective.[6] Nebulized bicarbonate has not reliably improved outcomes.[3,5,7,8]

PHOSGENE

Phosgene (Carbonyl chloride, $COCl_2$) has a sweet, pleasant smell of mown hay. It is poorly water soluble, not noxious and does not prompt escape from the location by the victim. It was used in WWI as a chemical weapon. It is produced from the combustion of chlorinated hydrocarbons (welding, fires) and from synthesis of solvents (degreasers, cleaners). The primary symptom is delayed ARDS (up to a day after exposure), which can be very severe. The mechanism of toxicity is release of hydrochloric acid and reactive oxygen species and free radicals in the lung epithelial layers. Decontamination is typically not needed once the patient leaves the exposure. Treat with observation, supplemental oxygen and ARDS ventilation techniques.

HYDROGEN SULFIDE

Hydrogen sulfide (H_2S) smells like rotten eggs and is a chemical irritant. Exposures occur in waste management, petroleum, natural gas industries, and asphalt and rubber factories. The gas acts like cyanide and inhibits cytochrome oxidase, preventing mitochondrial oxygen use and cellular respiration. At lower doses, H_2S causes skin and mucous membrane irritation. At high concentrations, it produces a “knockdown” effect, a sudden loss consciousness. At these concentrations it can produce seizure, myocardial ischemia, keratoconjunctivitis, and upper airway and pulmonary injury. Treat with skin irrigation, supplemental oxygen, removal from exposure, intravenous sodium nitrite (300 mg), and supportive care.[2] Inhalation of sodium nitrite is associated with methemoglobinemia and hypotension. Infuse it over 5-7 minutes.

AMMONIA

Ammonia (NH_3) is a common industrial and household chemical used as a fertilizer, refrigerant, cleaning agent. NH_3 has a pungent odor. It is also used in plastic and explosive synthesis. NH_3 is transported under pressure in liquid form at sub-zero temperatures. It reacts with water upon release, to form ammonium hydroxide (NH_4OH), a strong base, which produces mucosal irritation (tearing, skin irritation, eye pain and burns), severe upper airway irritation, and alkali skin burns. High concentrations or prolonged exposure duration (patient unconscious in a closed room) can produce tracheobronchial and pulmonary inflammation. It can produce respiratory failure within 2-5 minutes of exposure. Treat with skin and eye irrigation, alkali burn skin care, supplemental oxygen, ARDS ventilatory techniques, and supportive care.[3]

OTHER COMMON CHEMICAL TOXINS RELATED TO INHALATIONAL EXPOSURES

CYANIDE

Cyanide (CN) is released in structural and vehicle fires and in occupational settings of chemical or synthetic material combustion. It is used in manufacturing of pesticides and synthetic materials, metal extraction, and in chemical laboratories. Cyanide inhibits mitochondrial cytochrome oxidase thereby halting cellular respiration and aerobic metabolism. Early or mild effects are mostly neurologic (dizziness, headache, nausea, and anxiety). Late or severe effects are coma, seizure, respiratory depression, hypotension, and tachycardia. ARDS and pulmonary edema can occur in severe cases. Coma precedes apnea, and then hypotension develops.

The triad of severe toxicity is hypotension, altered mental status, and lactic acidosis (commonly > 8 mmol/L).[9] Treat with oxygen, mechanical ventilation, and rapid administration of an antidote. Hydroxocobalamin, the most commonly available antidote (sold as Cyanokit®), binds to CN to form cyanocobalamin, which is nontoxic and excreted in the urine. The standard dose of 5 g is infused intravenously over 15 minutes. A second dose of 5 g can be administered in patients with severe toxicity or poor clinical response. It is generally regarded as safe. Red discoloration of the skin and urine is common which may interfere with colorimetric assays. Hydroxocobalamin has been compared to sodium nitrite (300 mg) and sodium thiosulfate (12.5 g), prior treatment options, and was found to be superior with less toxicity and the latter two therapies are now not recommended for severe cyanide toxicity.[10] Treatment with nitrites carries significant risk of hypotension and methemoglobinemia, which can further jeopardize tissue oxygen delivery.

CARBON MONOXIDE

Carbon monoxide (CO) is released from the combustion of carbon containing compounds with combustion engines and cooking stoves in enclosed spaces. CO has a high affinity for hemoglobin and displaces oxygen when present. This displacement of oxygen ultimately leads to decreased oxygen delivery at the tissue and mitochondrial level.[11] Symptoms of CO toxicity include confusion, stupor, coma, seizures, and myocardial infarction.[12] CO levels are traditionally measured using a cooximeter, in a blood gas lab; however, this testing may not always be available and a high index of suspicion must be present as elevated CO may be present despite normal PaO2 and SpO2 readings. Newer non-invasive CO-oximetry may allow for early diagnosis and better monitoring.[13] Treatment of CO poisoning involves producing 100% oxygen, shortening the half-life of CO binding to hemoglobin to about 45 minutes. Hyperbaric oxygen therapy (HBO) has been used to reduce the half-life to about 20 minutes.[14] Logistical factors have limited the utilization of HBO and a systematic review found that not enough evidence exists at this point to determine definitively whether HBO reduces adverse neurologic outcomes after CO poisoning.

FIRE SUPPRESSANTS

Chemical fire suppressants are released in military vehicle fires. The most common is HFC227 (HFC-227EA, heptafluoropropane). It replaced bromotrifluoromethane (one of many “Halons”) in military vehicles.[15] These “virgin Halons” were banned by the EPA in 1994.[16] HFC227 is inert, a simple asphyxiant, and no cases of combustion related toxicity have been published or reported to the EPA or OSHA.[17,18] HFC227 can convert to hydrogen fluoride in small amounts during a fire, and; treatment is supportive, similar to other chemical exposures resulting in inhalation injury.[3] "Hydrogen fluoride (HF) as a byproduct of combustion with standard fire suppression systems may cause severe inhalation injury. Exposure to HF may result in rapidly progressive or fatal respiratory failure despite minimal external evidence of injury. Patients present typically with shortness of breath, cough, or hypoxia; there must be a high level of suspicion. Treatment is supportive. If hypocalcemia is present, administer nebulized calcium gluconate (1.5 ml of 10% Ca Gluconate in 4.5 ml water) every 4 hours until normalization of serum calcium. In the absence of significant burns, consider steroids if symptoms do not improve. Bronchopneumonia can develop within the first week."

PERFORMANCE IMPROVEMENT (PI) MONITORING

INTENT (EXPECTED OUTCOMES)

All patients who suffer severe toxic or chemical inhalation injuries will receive appropriate supportive care including intubation and mechanical ventilation when indicated.

PERFORMANCE/ADHERENCE MEASURES

- All patients with severe toxic or chemical inhalation injuries received appropriate supportive care, including intubation and mechanical ventilation.
- Appropriate evaluation of the posterior pharynx and mucosal inflammation of the airway using standard bronchospic assessment.

DATA SOURCE

- Patient Record
- Department of Defense Trauma Registry (DoDTR)

SYSTEM REPORTING & FREQUENCY

The above constitutes the minimum criteria for PI monitoring of this CPG. System reporting will be performed annually; additional PI monitoring and system reporting may be performed as needed.

The system review and data analysis will be performed by the Joint Trauma System (JTS) Director and the Joint Trauma System (JTS) Performance Improvement Branch.

RESPONSIBILITIES

It is the trauma team leader's responsibility to ensure familiarity, appropriate compliance and PI monitoring at the local level with this CPG.

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APPENDIX A: CHLORINE INHALATION

Stratify chlorine toxic patients into no symptoms, mild, moderate and severe. Treatment and observation periods can be tailored based on the severity of symptoms.

1. **No symptoms.** If no symptoms, then may be discharged if initial assessment (respiratory examination, vital signs, and pulse oximetry) is normal.
2. **Mild** (minimal symptoms, coughing, normal pulse oximetry, and no increased respiratory effort). Obtain chest radiograph, administer inhaled beta agonists, and observe for up to 6 hours. Most patients can be discharged.
3. **Moderate** (hypoxia, increased respiratory effort, normal chest radiograph) - Obtain chest radiograph, administer beta agonists, and admit for at least 12 hours. Consider inhaled steroids (fluticasone 200 mcg or similar agent) twice a day, early endotracheal intubation for increased respiratory effort, and inhaled ipratropium.
4. **Severe** (hypoxia, respiratory distress, often require intubation). Perform early endotracheal intubation with 8.0 tube to allow for bronchoscopy, obtain chest radiograph, administer beta agonists, and admit to ICU. Administer humidified oxygen and inhaled steroids (fluticasone 200 mcg or similar agent) twice a day. Consider inhaled ipratropium if not improving. If unable to administer inhaled steroids or if patient has significant bronchoconstriction consider intravenous steroids.

   ARDS. Perform similar ventilation strategies for ARDS, including increased PEEP and low tidal volumes. Evaluate daily for barotrauma. The patient may require high doses of sedatives to maintain synchrony with the ventilator.

IMPORTANT CAVEATS

A patient who is close to a large, dense chlorine exposure (IED detonated chlorine tank) or suffers a sustained exposure (unconscious in a chlorine filled room) may develop upper airway edema. In these cases, perform early intubation. Examine all exposed patients for eye, mucosal, and skin contamination which is manifested by corneal burns/abrasions, mucosal swelling, and skin erythema, blister, or burns. Decontaminate all symptomatic skin surfaces. Remove all exposed clothing. The trauma evaluation and treatment takes priority over the chlorine toxicity. Nebulized bicarbonate has not been reliably effective. It is made by mixing 1 ml of 8.5% sodium bicarbonate in 3 ml saline to create a 2% solution.

POST DISCHARGE FOLLOW-UP

If available, obtain pulmonary function tests with lung volume assessment and DLCO. If the PFT is abnormal, obtain high resolution pulmonary CT scan to assess or pulmonary fibrosis.

BACKGROUND AND CLINICAL EFFECTS

Chlorine is a gas with intermediate water solubility. It will induce mild irritant symptoms (tearing, pungent smell, upper airway irritation), but will also induce delayed pulmonary edema following a dense or sustained exposure. Chlorine dissolution into lung water generates hydrochloric acid and hypochlorous acid. The hypochlorous acid decomposes to HCl and nascent oxygen (O-). The nascent O- produces additional lung damage by free-radical formation. Chlorine was used in World War I as a chemical warfare agent.

- **Early effects.** Irritation of the eyes, nasal mucosa, upper airway, coughing, shortness of breath, and chest pain or burning
- **Late effects.** Pulmonary congestion and edema and then ARDS.

APPENDIX B: ADDITIONAL INFORMATION REGARDING OFF-LABEL USES IN CPGS

PURPOSE

The purpose of this Appendix is to ensure an understanding of DoD policy and practice regarding inclusion in CPGs of "off-label" uses of U.S. Food and Drug Administration (FDA)–approved products. This applies to off-label uses with patients who are armed forces members.

BACKGROUND

Unapproved (i.e., "off-label") uses of FDA-approved products are extremely common in American medicine and are usually not subject to any special regulations. However, under Federal law, in some circumstances, unapproved uses of approved drugs are subject to FDA regulations governing "investigational new drugs." These circumstances include such uses as part of clinical trials, and in the military context, command required, unapproved uses. Some command requested unapproved uses may also be subject to special regulations.

ADDITIONAL INFORMATION REGARDING OFF-LABEL USES IN CPGS

The inclusion in CPGs of off-label uses is not a clinical trial, nor is it a command request or requirement. Further, it does not imply that the Military Health System requires that use by DoD health care practitioners or considers it to be the "standard of care." Rather, the inclusion in CPGs of off-label uses is to inform the clinical judgment of the responsible health care practitioner by providing information regarding potential risks and benefits of treatment alternatives. The decision is for the clinical judgment of the responsible health care practitioner within the practitioner-patient relationship.

ADDITIONAL PROCEDURES

Balanced Discussion

Consistent with this purpose, CPG discussions of off-label uses specifically state that they are uses not approved by the FDA. Further, such discussions are balanced in the presentation of appropriate clinical study data, including any such data that suggest caution in the use of the product and specifically including any FDA-issued warnings.

Quality Assurance Monitoring

With respect to such off-label uses, DoD procedure is to maintain a regular system of quality assurance monitoring of outcomes and known potential adverse events. For this reason, the importance of accurate clinical records is underscored.

Information to Patients

Good clinical practice includes the provision of appropriate information to patients. Each CPG discussing an unusual off-label use will address the issue of information to patients. When practicable, consideration will be given to including in an appendix an appropriate information sheet for distribution to patients, whether before or after use of the product. Information to patients should address in plain language: a) that the use is not approved by the FDA; b) the reasons why a DoD health care practitioner would decide to use the product for this purpose; and c) the potential risks associated with such use.