

Toxic inhalational injury: gas, vapor and vesicant exposure

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The tragic events of September 2001 serve as a stark reminder that this country is vulnerable to terrorism and needs to be prepared for possible future events. This article focuses on the toxic inhalation effects of several groups of chemical agents that could be employed by terrorists. In the modern era, chemical agents were first used on the European battlefields of World War I, when chlorine, phosgene, and mustard release caused large numbers of injuries and deaths. In spite of international treaties, wartime use of chemical weapons continued throughout the twentieth century. Most recently, Iraq's use of mustard in its war against Iran, as well as its use of mustard and tabun to subdue its own Kurdish population in 1988, has been amply documented [1–4]. Furthermore, the nefarious release of the nerve agent sarin into Japanese subways in 1995 by Aum Shinrikyo, an apocalyptic religious sect, underscores the vulnerability of urban civilian populations when terrorists obtain chemical agents [5,6]. Unquestionably, the widespread availability of a host of chemical agents, whether designed to kill, injure, or incapacitate large numbers of people indiscriminately or manufactured for industrial and agricultural use, guarantees ongoing risk to civilian populations [7,8]. The potential for mass casualties is illustrated by the Bhopal, India chemical plant disaster in which more than 2500 people died from the accidental release of chlorine and methylisocyanate into the surrounding residential area [9]. Difficulty in manufacturing or obtaining chemical weapons means that terrorist groups may turn to commercially produced toxic agents used in industry or agriculture and attempt to deploy them as weapons (Table 1) [7,8]. State-sponsored terrorism is especially

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Table 1
 Characteristics of selected chemical agents that may pose a risk of inhalational lung injury

Agent	Ease of Manufacture and Precursor Availability	Agent Persistence	Lethality	Government Accounting Office Observations ^a
Choking Agents				
Chlorine (CL)	Industrial product. No precursors required.	Not persistent	Low	Likely agent because of availability as a commercial product.
Phosgene (CG)	Industrial product. No precursors required	Not persistent	Low	Likely agent because of its commercial availability
Nerve Agents				
Tabun (GA)	Not readily available manufacturing instructions, but precursors available.	Intermediate	High	Likely agent because of availability of precursor chemicals and relative ease of manufacture.
Sarin (GB)	Relatively easy to manufacture. Moderately difficult to manufacture. Precursor chemical covered by Chemical weapons Convention (CWC).	Not persistent	High	Likely agent because of demonstrated use by Aum Shinriko, although restrictions on precursors could create difficulties for production.
Blood Agents				
Hydrogen cyanide (AC)	Industrial product. Precursor chemicals covered by CWC.	Very low	Low	Likely agent because of its availability as a commercial product. Precursor availability may be a problem.
Cyanogen chloride (CK)	Not easily produced. Available as commercial product.	Low	Low to moderate	Likely agent, although precursor availability may be a problem.

Blistering Agents

Sulfur mustard (HD)	Easy to synthesize. Large quantity buys of precursor chemical without detection difficult. Precursors are covered by CWC.	Intermediate to high	Can incapacitate because of blistering. Can also produce death if inhaled or a toxic dose is absorbed.	Not likely agent because of difficulty in obtaining precursor materials and moderate production requirements.
Lewisite (L, HL)	Moderately difficult to manufacture and moderately difficult to acquire precursor chemicals.	Intermediate to high	Can incapacitate because of blistering. Can also produce death if inhaled or if a toxic dose is absorbed.	Not likely agent because of difficulty in obtaining precursor materials and production requirements.

^a Government Accounting Office observations are based on a research synthesis of discussions with experts in chemical warfare, science, intelligence, law enforcement, and medicine and of an analysis of manuals, handbooks, textbooks, studies, and reports on chemical agents.

Note: The following assumption are used:

1. Dosage and concentration are maximized for an interior environment.
2. The venue is high-profile event where a large population has gathered.
3. The terrorists have competence (first-year graduate student in chemistry) and motivation to obtain and implement the dispersion of agents.
4. The interior environment has an accessible heating, ventilation, and air conditioning distribution system.

Modified from Combatting terrorism. Need for comprehensive threat and risk assessments of chemical and biological attacks. Washington (DC): National Security and International Affairs Division, US government Accounting Office; 1999.

problematic, because nations with the resources to manufacture and distribute weapons of mass destruction covertly may make them available to groups that use terrorism to further their political or economic goals. Past use and current threats mandate that the United States health care system be ever vigilant and prepared to treat large numbers of casualties that result from terrorist acts.

Classification of chemical warfare agents

Chemical warfare agents are classified by wartime use and physiologic action. Toxic agents are designed to cause bodily injury or death, whereas incapacitating agents temporarily disable their victims. The standard physiologic classification of chemical agents includes four groups: (1) nerve agents, (2) vesicants (blistering agents), (3) lung-damaging agents, and (4) blood agents. Nerve agents act by interfering with transmission of nerve impulses in the central, peripheral, and autonomic nervous systems. Organophosphate insecticides are chemically related to the nerve agents, and accidental exposure leads to similar symptoms and toxicity. Blistering agents cause direct toxic injury to the skin, mucous membranes, and airways. Lung-damaging agents may also irritate the eyes and mucous membranes but primarily cause pulmonary injury and edema. The blood agents interfere with cellular oxidative phosphorylation and cause direct cell death. Finally, a fifth group, incapacitating agents used primarily for riot control, are sometimes subcategorized as irritant agents and vomiting agents, depending on their primary physiologic effect [10].

Principles of toxic inhalation injury

Inhalation of toxic agents may produce injury anywhere along the respiratory tract, from nose to alveoli. The type of damage depends on toxin properties and on host factors. Toxic substances may be inhaled in the form of gas, fumes, dust, mist, aerosol, or smoke. The intensity of the exposure, particle size, and water solubility of the agent are important determinants of injury. The intensity of exposure depends on the concentration of toxin in the atmosphere as well as on the duration of exposure. Particle size determines whether the agent will gain access to the respiratory tract and, after entry, where it will be deposited. Particles smaller than 10 microns may reach the lower respiratory tract, but particles generally must be smaller than 5 microns to reach the alveoli. Host factors including the ability to respond appropriately to exposure, the availability of medical care, and underlying medical conditions are obviously critical in determining the magnitude of injury inflicted by chemical agent exposure [11].

Vesicants

Vesicants or blister-producing agents include the sulfur and nitrogen mustards, lewisite, and phosgene oxide. Sulfur mustard [bis-(2-chloroethyl) sulfide], the most important agent in this group, is an oily liquid with low volatility that smells faintly of garlic or horseradish. The liquid form is lipophilic and readily penetrates the skin, most textiles, and rubber. Its freezing point is 54°F, limiting its toxicity and battlefield usefulness in cold environments. At temperatures between 100°F and 120°F, sulfur mustard rapidly vaporizes and becomes a major inhalation hazard. Mustard vapor, with a density 5.4 times greater than air, tends to hug the ground and settles into low-lying areas, a major problem for entrenched troops.

Sulfur mustard was first used on the battlefield in July 1917 and was responsible for 80% of the chemical casualties during World War I. Although banned by the 1925 Geneva Protocol and by other international treaties, mustard gas has been used on multiple occasions since 1918. For example, the Italians used mustard against the Ethiopians in the 1930s, Japan used mustard against the Chinese during World War II, Egypt allegedly used it in Yemen in the mid 1960s, and Iraq employed mustard against its own ethnic Kurdish population, as well as against the Iranians during the Iran-Iraq War (1982-1988) [2,3]. It is estimated that 45,000 Iranians were injured or killed from mustard exposure during the war [1,12].

Toxicity and clinical course

The vesicants all cause severe skin, eye, and mucous membrane irritation. Unlike lewisite and phosgene oxide, which cause immediate irritation, the onset of symptoms from mustard exposure may be delayed up to 24 hours depending on the intensity of exposure and weather conditions. After contact, mustard rapidly penetrates the skin, becomes fixed to underlying tissue, and cannot be removed. For this reason decontamination is effective only if done immediately after exposure (ie, before absorption). Mustard irreversibly alkylates DNA, RNA, and protein, causing cell death. The median lethal dose (LD₅₀) is 100 mg/kg, 1 to 2 teaspoons of liquid, which is an amount sufficient to cover approximately 25% of the body surface area. In World War I, the lethality rate was less than 3% and almost entirely the result of pulmonary complications, although serious skin and eye injuries from mustard were extremely debilitating and required long convalescent periods. The average length of hospitalization for mustard casualties during that conflict was 42 days. Unprotected skin, eyes, and the respiratory tract are the sites most commonly affected by mustard. Eye exposure may result in a range of symptoms including itching, tearing, burning, foreign body sensation, lid edema, pain, and corneal injury. Skin injury ranges from mild erythema to blister formation and, uncommonly, to full-thickness damage with deep bullae or ulcer formation. Nausea and vomiting, probably caused

by a cholinergic effect of mustard, are common, beginning about the same time that the initial skin lesions develop. Ingestion of mustard can cause desquamation and necrosis of the gastrointestinal tract lining. Pulmonary toxicity occurs when mustard vapor is inhaled. The nasopharynx and proximal airways are exposed to the highest concentrations of mustard vapor, and therefore symptoms such as hoarseness, cough, and wheezing usually occur first, within 4 to 6 hours of exposure. Repetitive exposures or higher concentrations cause more inflammation and extend the injury deeper into the lower airways. The inflammatory reaction may take several days to evolve fully and, when severe, causes hemorrhagic bronchitis or necrosis sufficient to form pseudomembranous casts of the tracheobronchial tree and acute airway obstruction. Mustard inhalation injury is commonly complicated by infection, both bronchitis and pneumonia. Pneumonia, in fact, was the major cause of mortality following mustard vapor inhalation in American troops in World War I. Long-term effects on the respiratory tract include recurrent infections, stenosis of the airways, reactive airway dysfunction syndrome (RADS), bronchiolitis obliterans, bronchiectasis, and respiratory neoplasia (Table 2) [13–18]. Extremely intense exposure may cause bone marrow suppression within 3 to 5 days, resulting in an initial leukocytosis followed by a neutropenia that reaches a nadir around day 10. This bone marrow suppression increases the risk of infection in patients with underlying pulmonary injury [18–23].

Treatment

Despite more than 80 years of experience, there is still no specific antidote for mustard. Decontamination within 1 or 2 minutes following exposure is the only effective means to minimize tissue damage from mustard. Mustard chemical burns are painful, prone to infection, and slow to heal. Standard burn management includes intravenous fluid administration, necrotic tissue

Table 2
Potential respiratory manifestations following inhalation of mustard vapor

Acute	Chronic
Sore Throat, hoarseness	Rhinopharyngitis
Laryngospasm, Laryngeal Edema	Bronchiectasis
Upper airway mucosal necrosis, cough, dyspnea	Recurrent pneumonias
Bronchospasm, Hypoxemia	Reactive airways dysfunction Syndrome
Pseudomembranes	Chronic bronchitis
Lower airway obstruction	Pulmonary fibrosis
Bronchitis	Tracheobronchial stenosis
Pneumonitis	Respiratory tract neoplasia
Secondary pneumonia	
Pulmonary edema (rare)	

Data from Refs. [13–19, 21–23, 25].

débridement, pain control, and split-thickness skin grafting as necessary. Ocular irritation or injury occurs in 85% of exposed patients. In addition to conjunctivitis and lid involvement, visual acuity may be decreased by corneal edema and vesication. After necrotic tissue is sloughed, recovery occurs in most cases over several weeks. Initially, the eyes should be irrigated copiously with water, and corneal abrasions should be treated with a cycloplegic agent and antibiotic ointment [24]. Upper airway symptoms, such as rhinorrhea and cough may respond to warm humidified air and antitussives. Bronchodilators may be useful when wheezing or bronchospasm is evident. In severe injury, intubation may be necessary to protect the airway from acute obstruction caused by laryngeal edema and spasm. Intubation also facilitates pulmonary toilet by allowing the suctioning of necrotic and inflammatory debris from the airways. Therapeutic flexible bronchoscopy and rigid bronchoscopy were successfully used in the management of the acute and chronic airway complications associated with sulfur mustard exposure in some of the Iranian casualties brought to Europe for treatment between 1984 and 1990 [17]. Hypoxemia commonly results from ventilation perfusion mismatching caused by airway edema, bronchospasm, and mucosal sloughing with obstruction. Secondary infection of the vulnerable respiratory tract is heralded by fever, sputum production, and new pulmonary infiltrates on chest radiograph (Box 1) [20–22,25].

The other vesicants (ie, lewisite and phosgene oxide) cause similar clinical syndromes, but there are important differences that fall beyond the scope of

Box 1. Treatment of acute respiratory disorders following mustard exposure

Antitussives

Warm humidified air

Supplemental oxygen

Postural drainage

Chest percussion

Inhaled bronchodilators—consider steroids for bronchospasm

Antibiotics only for confirmed infections

Early intubation to facilitate pulmonary toilet and for protection of airways before development of severe laryngeal spasm or edema

Mechanical ventilation to facilitate pulmonary toilet; apply positive end-expiratory pressure to reduce atelectasis; support ventilation

Rigid or flexible bronchoscopy—therapeutic lavage, removal of pseudomembranes, treatment of strictures

Data from Refs. [17,21,22,25].

this article. The interested reader is referred to comprehensive reviews of these agents [10,22].

Lung-damaging agents

Chemical agents that directly attack lung tissue and primarily cause pulmonary edema are classified as lung-damaging agents (choking agents). This group of chemicals includes phosgene, diphosgene, chlorine, and chloropicrin. Given their historical significance and widespread use in industry, only chlorine and phosgene are reviewed in this article. All these agents are highly volatile and produce vapors that are readily inhaled.

Chlorine

At ambient temperatures, chlorine is a pungent greenish-yellow gas. Its density is greater than air, and therefore it tends to settle in low-lying areas. Because its odor threshold is below the toxic level, the pungent odor tends to provide adequate warning of the presence of chlorine. Chlorine species are highly reactive, and tissue injury may result from exposure to chlorine and its metabolites—hydrochloric acid, hypochlorous acid, and oxygen free radicals. Industrial production of chlorine started just before World War I, and the German Army first used it on the battlefield in April 1915 at Ypres, Belgium. One hundred sixty tons of gas was released from cylinders strategically placed upwind from the entrenched Allied positions and killed as many as 5000 soldiers. The allies responded in kind and used chlorine gas against the Germans just 5 months later in September 1915. Today, chlorine is widely used in the manufacture of paper, metal, pharmaceuticals, and textiles. Large quantities of chlorine are regularly stored at industrial sites and transported on interstate highways and rail lines. Toxic exposure can occur as a result of transportation mishaps, inadvertent industrial release, and even home accidents [26]. Since 1916 there have been more than 200 significant industrial accidents involving chlorine [27,28].

Clinical manifestations

Chlorine is highly water-soluble and exerts toxic effects on the nose and upper airway as well as the lung. Immediate symptoms, including lacrimation, nasal irritation, and a burning sensation of mucous membranes, are followed by hoarseness, cough, a choking sensation, chest pain, and dyspnea. Exertional dyspnea may be especially prominent. Copious thin secretions and laryngeal spasm can contribute to acute respiratory collapse. In patients with more intense exposures, fulminant pulmonary edema may develop within 30 minutes. Pulmonary function tests following acute exposure may show either restrictive or obstructive defects. Longitudinal

studies following chlorine exposure have shown decreases in forced expiratory volume in 1 second (FEV₁), increased bronchial hyperresponsiveness, and the development of RADS in some individuals. It seems, however, that most survivors do not have any long-term pulmonary symptoms or decrement in lung function [11,28–34].

Treatment

The initial response to toxic chlorine exposure should be to remove the individual from the source immediately and then perform a thorough decontamination. Decontamination consists of removal of all clothing followed by copious flushing of the skin with soap and water. Contact lenses, if present, should be taken out. Removal of residual surface chlorine eliminates additional vapor formation and further pulmonary exposure. Treatment for acute chlorine inhalation is primarily supportive, because no antidote is available. Strict bed rest is recommended for toxic inhalation casualties with moderate-to-severe exposure, because strenuous activity may hasten the onset of pulmonary edema [11,18]. Severe exposures may require intubation for protection of the upper airway when laryngeal edema or spasm is clinically suspected. Mechanical ventilation and positive end-expiratory pressure (PEEP) may be necessary in the treatment of the respiratory failure caused by pulmonary edema. Aggressive use of bronchodilators should be used to treat associated bronchospasm, and careful surveillance with prompt treatment of secondary bacterial infections should be routine [29,35].

Treatment of chlorine gas inhalation injuries with corticosteroids is supported by several animal studies and by anecdotal human experience. A study by Gunnarsson et al [35] demonstrated that pigs treated with nebulized beclomethasone-dipropionate (20 µg/kg) immediately following exposure to chlorine gas had better lung compliance and oxygen delivery 6 hours after injury, than did controls. Additionally, a more recent study looked at the timing of treatment with inhaled budesonide in chlorine-exposed pigs. Four groups of 6 pigs were exposed to 400 ppm of chlorine gas for 20 minutes each and then randomly assigned to receive inhaled budesonide immediately, or at 30 minutes or 60 minutes after exposure, or to control. The two groups that were treated with nebulized budesonide immediately or 30 minutes after exposure had better pulmonary compliance and arterial oxygen tension during the 5 hours of the study than the group treated at 60 minutes or the control group, which did not receive inhaled corticosteroids [36]. Reports of efficacy of systemic corticosteroid use in humans with chlorine exposure are at best, anecdotal [37–40]. The use of inhaled sodium bicarbonate to neutralize the hydrochloric acid generated by chlorine inhalation has been described but is of unproven benefit [41]. In the absence of intervening complications, the adverse effects of chlorine inhalation lung injury should resolve in 3 to 5 days.

Phosgene

Phosgene is another chemical agent that was used on the battlefields of Europe during World War I. Today, phosgene is widely used in the production of dyes, pesticides, and plastics. It is a white gas that is heavier than air and has the distinct odor of sweet, newly mown hay. Unfortunately, the odor threshold, 1.5 ppm, provides insufficient warning of gas exposure. With relatively low water solubility, phosgene tends to spare the nose and upper airway, exerting its toxic effects mainly on the respiratory bronchioles and alveoli. Hydrochloric acid is released when phosgene interacts with water, leading to damage of the alveolar–capillary interface and subsequent pulmonary edema. Low-concentration exposures to phosgene gas generally cause mild cough, chest discomfort, and dyspnea. Higher concentrations can lead to the development of more severe cough, laryngospasm, and pulmonary edema. Sudden death following very intense exposures has been attributed to laryngospasm and upper airway obstruction. Symptoms normally begin within a few hours of exposure. There are reports of some individuals, however, who do not develop symptoms for 24 to 72 hours. The delayed and insidious onset of symptoms may lead to a patient's being evaluated and prematurely discharged from a medical facility only to become acutely ill later. Therefore it is recommended that patients be closely observed for at least 12 to 24 hours [11,18,42].

Treatment

Pulmonary edema is the most serious consequence of phosgene exposure. Symptoms and signs of pulmonary edema such as dyspnea, chest tightness, crackles on auscultation, and hypoxemia mandate close observation in an ICU, if available. Avoidance of exertion may reduce the risk of pulmonary edema following exposure to both chlorine and phosgene. With the onset of acute respiratory failure, the early institution of PEEP is recommended. Diuretics should be used with caution to avoid hypotension. Although controlled human trials of intravenous corticosteroids are lacking, some authors recommend them for severe phosgene inhalation injury [27,43]. Leukotriene receptor blockers, methylprednisolone, ibuprofen, and intratracheally administered *N*-acetylcysteine have been shown to mitigate lung injury in animal models of phosgene exposure [44–48]. The effects of phosgene, like chlorine, on the lung are short lived, and failure of a patient to improve within 4 to 5 days mandates a thorough search for other causes of pulmonary edema and possible superimposed infection [11,49].

Blood agents

Blood agents, such as hydrogen cyanide and cyanogen chloride, shut down oxygen metabolism at the most fundamental level—the cell. In addition

to potential warfare or terrorist use, the cyanides are encountered in manufacturing and as products of combustion. They are colorless, highly volatile liquids that act by combining with cytochrome a_3 to block oxidative phosphorylation and ATP production immediately. Even though the blood remains well oxygenated (hence the pink color), oxidative processes cease, and tissue hypoxia rapidly ensues. The brain is particularly vulnerable, and failure of the respiratory center is often the cause of death following high exposures. Hydrogen cyanide and cyanogen chloride both block oxidative phosphorylation and cause widespread tissue hypoxia; however, cyanogen chloride also produces distinct local irritant effects on the eyes, upper respiratory tract, and lungs. Exposure to cyanogen chloride may lead to severe inflammatory changes in the bronchioles and congestion and edema of the lungs. The symptom evolution of cyanide poisoning depends on the intensity and duration of exposure. Low-intensity exposures are likely to manifest as headache, vertigo, and nausea that resolve over minutes to hours following removal from the scene. Moderate toxicity is manifest by more pronounced central nervous system (CNS) dysfunction including confusion and weakness. Seizures and coma may ensue, and substantial residual CNS impairment may follow. High-intensity exposure may result in death within just a few minutes. Cyanide exposure initially stimulates respiratory drive, thereby increasing inhalation exposure, leading to a downward spiral of convulsions, apnea, cardiac arrest, and death.

Treatment

The first priority in managing the blood-agent victim is to terminate further exposure immediately and then to perform prompt decontamination that includes removal of all contaminated clothing and rinsing the exposed skin with soap and water. In the absence of significant symptoms, patients should be observed closely following any suspected exposure. Standard supportive therapy may be adequate for mild and moderate exposures, but severe exposure requires specific antidote therapy. Antidote therapy consisting of sequential administration of a nitrite followed by sodium thiosulfate should be instituted at the first signs of respiratory depression or CNS dysfunction. Nitrite displaces the cyanide moiety from cytochrome oxidase and results in the formation of methemoglobin, which has a higher binding affinity for cyanide than does cytochrome oxidase. The preferential binding of cyanide to methemoglobin yields cyanomethemoglobin and frees cytochrome oxidase to resume its critical role in aerobic metabolism. Nitrite was previously available in two forms. Amyl nitrite (for inhalation) is no longer part of the United States Army antidote kit because of the substantial risk of orthostatic hypotension and the difficulty in predicting the subsequent methemoglobin levels. Sodium nitrite, 10 mL of a 3% solution, should be administered intravenously over 5 to 15 minutes with careful monitoring of blood pressure to avoid hypotension. A second dose up to

half as large as the first dose can be given if needed. The goal is to see a clinical response while keeping methemoglobin levels below 35% to 40%. Above this level methemoglobin inhibits adequate oxygen carriage. Once cyanide is displaced from cytochrome oxidase by nitrite, it must be converted to a form that will be excreted. This conversion is accomplished by administering sodium thiosulfate. Sodium thiosulfate is administered as an intravenous injection of 50 mL of a 25% solution over a 10-minute period. A second treatment at half the dose may be required [50–53].

Other agents

Irritant agents are also known as lacrimators because of their extreme local incapacitating effect on the eyes. These agents, used primarily by law enforcement officials to quell riots, may be dispersed as fine particulate smoke or in solutions as droplet aerosols. Examples include O-chlorobenzylidene malonitrile, chloroacetophenone (CN, Mace, General Ordnance Equipment Corp., Pittsburgh, PA), chloroacetophenone in chloroform, bromobenzylcyanid, and diebenz-(b,f)-1,4-oxazepine. Both O-chlorobenzylidene malonitrile and diebenz-(b,f)-1,4-oxazepine have a distinct, pepper-like odor and cause immediate eye pain, copious tearing, and nasal discharge. As unpleasant as these symptoms are, they are almost always self-limited, resolve in 5 to 10 minutes, and do not warrant specific treatment. When large particles or droplets are sprayed directly into the eyes, prompt irrigation with copious water may speed recovery. Exposure to high concentrations in a closed environment can cause both upper and lower airway irritation manifested by cough, wheezing, and chest pain. Rare cases of pulmonary edema have been reported following exposure to pepper spray. Inflammation and blistering of the skin may occur after a heavy or prolonged exposure [27,54].

Smokes are products of combustion, which have been used in wartime to conceal troops and equipment and confuse the enemy. Chemicals used to produce smokes include hexachloroethane, grained aluminum, zinc oxide mixture, petroleum oils, diesel fuel, red phosphorus, and white phosphorus. Most smokes are not extremely hazardous when they are encountered outdoors in usual concentrations. Petroleum oil smoke, as was used in the Gulf War conflict and again in Operation Iraqi Freedom, is thought to be the least toxic smoke and rarely causes illness or injury. Zinc oxide mixtures, on the other hand, often elicit nose, throat, and chest irritation. Moderate exposure to zinc oxide mixture can produce cough and severe dyspnea within 4 to 6 hours of exposure, although the chest radiograph may initially be normal. Respiratory symptoms may be accompanied by fever, and recovery normally occurs over days to weeks. Following exposure to extremely high levels of zinc oxide mixtures, sudden death may result from laryngeal edema and glottic spasm. A report of acute respiratory distress

syndrome developing in two soldiers who were exposed to zinc chloride smoke in a training accident underscores the potential for severe pulmonary toxicity. Although best supporting care, including steroids, was given, both patients died of severe respiratory failure (25 and 32 days after inhalation). Autopsy revealed diffuse microvascular obliteration, widespread occlusion of the pulmonary arteries, and extensive interstitial and intra-alveolar fibrosis [55]. Some reports suggest that systemic steroids may be beneficial in attenuating the progressive interstitial fibrosis seen in some patients following zinc oxide smoke injury [11,56].

Summary

Terrorism poses a clear and present danger to civilian populations. Although terrorist cells may gain access to traditional chemical weapons, there are literally thousands of other industrial chemicals to choose from. Common chemicals used on a daily basis in an industrialized society can be readily obtained from the local shopping center, rail yard, or from nearby industrial parks, and terrorists may choose to use these agents in an attack. The medical implications of a major incident involving the accidental or intentional release of a dangerous chemical are significant, and all health care facilities should have a plan in place to manage the casualties of such an event. This plan should include event recognition, crowd control, primary triage, emergency treatment, decontamination of injured and uninjured patients, and secondary triage [36,56,57]. Emergency health care providers should be prepared to respond to classic chemical agents such as mustard, chlorine, and phosgene and must also work carefully with law enforcement and public health agencies to keep abreast of new threats. The ability to recognize an event promptly, triage patients, decontaminate casualties, administer antidotes when available, and provide best supportive care will minimize the adverse outcomes.

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