Chapter 1

LUNG-DAMAGING AGENTS: TOXIC INDUSTRIAL CHEMICALS

Summary

NATO Codes: CG, Cl

Signs and Symptoms: Central effects: eye and airway irritation, dyspnea; peripheral effects: chest tightness and *delayed* pulmonary edema.

Field Detection: Joint Chemical Agent Detector (JCAD). The M18A2 Chemical Agent Detector Kit and the M93 series Fox Reconnaissance System will detect small concentrations of CG; however, they will not detect Cl.

Decontamination: *Vapor:* fresh air; *liquid:* copious water irrigation.

Management: Termination of exposure, ABCs of resuscitation (airway, breathing, circulation), enforced rest and observation, oxygen with or without positive airway pressure for signs of respiratory distress, other supportive therapy as needed.

Overview

Over 1,800 toxic industrial chemicals (TICs) are used in industry, stored at industrial sites, and transported on the world's road and rail systems. Some of these chemicals were deployed as chemical warfare agents during the First World War, killing and injuring thousands, and can have the same deadly consequences

today if released during an accident or through terrorist sabotage. Death from exposure to TICs is more frequent when they are inhaled. Inhaling a TIC in the form of a gas, vapor (gas coming from a liquid), or aerosol (liquid or solid particles suspended in a gas) can cause a sudden closure of the larynx (laryngospasm), causing the victim to choke and collapse. TICs can also cause damage to the tissues of the upper airways, resulting in swelling, scarring, and airway narrowing, which can restrict breathing. TICs can damage lung tissues, allowing body plasma and other fluids to leak into the lung air sacs (alveoli), causing pulmonary edema and death from asphyxiation.

Lung-damaging TICs are typically heavier than air and hang close to the ground when released. They tend to evaporate and disperse very quickly, depending on temperature and wind conditions (Table 1-1). If the TIC is in liquid form at room temperature, it will tend to give off a vapor. Vapors can become trapped in clothing fibers and "off-gas" to affect anyone nearby with no respiratory protection. Although skin decontamination after vapor exposure is not a high priority, clothing should be removed and the underlying skin decontaminated with soap and water.

Table 1-1. Physiochemical Characteristics of Toxic Industrial Chemicals

Agent	Molecular Weight	Boiling Point	Freezing Point	Distinctive Odor
Phosgene (CG)	99	7.6°C	−128°C	Newly mown hay
Hydrogen chloride (HCl)	36.46	−85°C	−114°C	Pungent
Ammonia	17.03	−33.4°C	−77.7°C	Sharp, intensely irritating
Perfluoroisobutylene	Polymer	214°C –217°C	257°C –263°C	None
Oxides of nitrogen (NOx)	28.1	−196°C	−210°C	Irritating
White phosphorus smoke	123.895	280°C	44.1°C	Garlic-like

Exposure to TIC lung-damaging agents can occur on and off the battlefield. The care provider must know how to identify the signs and symptoms and provide appropriate life-saving support to those exposed to these agents.

Understanding the Respiratory System

The respiratory system can be divided into two compartments, the central airway and the peripheral airway (Figure 1-1). Understanding these compartments can greatly simplify the treatment problem-solving process.

The *central airway compartment* includes the nasopharynx (nose), oropharynx (mouth), larynx (vocal cords), and the trachea and bronchi (airway from the throat into the lungs). Tissues in this area are very moist and thin and can be damaged by TICs.

The *peripheral lung compartment* includes the lung sacs

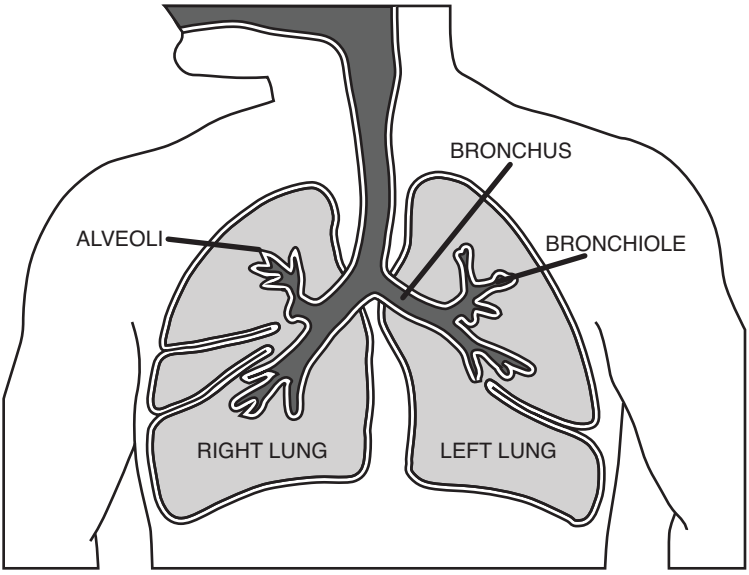

Figure 1-1. Central airway (dark gray) and peripheral airway (light gray).

(alveoli) distributed throughout the lung tissue. During normal respiration, inhaled gasses fill the alveoli and then move slowly through their walls. The gasses then move through the thin walls of the blood vessels (capillaries) surrounding the alveoli and into the blood. TICs can damage the walls of alveoli and the capillaries surrounding them, allowing blood plasma and cells to leak into the air space of the alveoli.

Lung-Damaging Agents

TICs are numerous. Those that pose a frequent threat to the service members in the field are listed below. Though the list is not complete, casualties from other lung-damaging agents are managed the same way as these examples. In low doses, highly reactive TICs have a greater effect on the central airway; other TICs act on both airways; and still others that are not as reactive in the central airway travel deeper into the respiratory tract and destroy alveoli tissues in the peripheral airways (Table 1-2). Any TIC inhaled in large doses will cause damage to both central and peripheral airways.

Centrally Acting TICS

Ammonia is highly caustic and reactive gas used for cleaning, industrial refrigeration, and numerous other legitimate industrial

Table 1-2. Toxic Industrial Chemicals Compartment of Action

Agent	Central	Peripheral
Phosgene (CG)	Large dose	Yes
Oxides of nitrogen (NOx)	Large dose	Yes
HC smoke	Large dose	Yes
Ammonia	Yes	Large dose
Chloride (Cl)	Yes	Yes
Perfluoroisobutylene	Large dose	Yes

processes, as well as for processing some illicit drugs. It is a good example of a TIC that, in low doses, is primarily centrally acting. It rapidly forms a strong base (alkali) when it contacts the moist tissues of the central airway compartment. The alkali burns and destroys the tissues it contacts. The victim may suddenly go into laryngospasm and collapse. The tissues of the compartment become swollen. Scar tissue may form along the airway. Damaged tissue in the airway may die and slough off, obstructing the airway.

Sulfur mustard (HD) is an example of a chemical agent produced solely for warfare that acts on the central airway compartment when inhaled. HD will cause tissue to slough off in large sheets, known as pseudomembranes, which block the airway. The various resulting degrees of airway obstruction cause hoarseness or wheezing, or prevent casualties from breathing, sneezing, or coughing.

Peripherally Acting TICs

Phosgene (CG) is a major industrial chemical used in many manufacturing processes. More importantly, it is released from heating or burning many common chemicals or solvents. Carbon tetrachloride, perchloroethylene (a degreasing compound), methylene chloride (used in paint removal), and many other compounds break down to phosgene with flame or heat. Also, common substances such as foam plastics release phosgene when they burn. A soldier presenting with shortness of breath in the absence of a chemical attack or other obvious cause should be questioned carefully about whether he or she has been near any burning substances or chemical vapors that were near flame or other hot materials (eg, a heater with open coils).

Perfluoroisobutylene (PFIB) is given off when Teflon (DuPont, Wilmington, DE) burns at high temperatures, such as in a vehicle fire. Teflon is used to line the interior of many military vehicles, particularly armored vehicles and aircraft. Closed-space fires in these vehicles release PFIB. Survivors of vehicle fires who are short of breath should be questioned about their exposure to the smoke.

Oxides of nitrogen (NOx) are components of photochemical smog that can be produced by the burning of gunpowder

or industrial waste. These substances can build up to high concentrations where artillery is fired and there is inadequate ventilation. Soldiers who become short of breath after heavy firing should be suspected of exposure to this lung-damaging agent.

HC smoke is a mixture of equal amounts of hexachloroethane, zinc oxide, and approximately 7% grained aluminum or aluminum powder used in the military for obscuration. The zinc oxide can cause lung damage if inhaled in toxic amounts. Appropriate precautions, such as wearing protective masks, must be taken when HC smoke is used.

TICs That Act Both Centrally and Peripherally

Chlorine (Cl) is a good example of a combination agent, one that acts on both airway compartments in low doses. It is widely used in industry for manufacturing plastics and lubricants and purifying water. It was the first chemical agent used effectively on the First World War battlefield against unprotected military troops, but its effectiveness as a weapon was greatly reduced once protective masks became widely available to soldiers. Chlorine turns to hydrochloric acid when it contacts the moisture of the airway; it then causes chemical burns to the tissue. It produces signs and symptoms seen with exposure to both central and peripherally acting agents. Its action serves as a reminder that although central compartment damage may seem like the primary concern in some patients (eg, they are coughing and wheezing), the medic must always treat casualties as if they could develop peripheral compartment symptoms, and take seriously any patient complaints about feeling chest tightness or having breathing difficulty.

Detection

Chlorine and ammonia have their own distinctive odors. Phosgene smells like newly cut grass, newly mown hay, or green corn. It is important to remember that odor is not a reliable detection method. Smelling the gas exposes the individual to potentially toxic inhalation effects. There are no specific field detection devices for these compounds.

Protection

The military protective mask, if fitted with a C2A1 filter canister, or the Joint Service General Purpose Mask with M61 filters will protect against Cl, CG, PFIB, NOx, and HC smoke in the open battlefield. Specific filters, or the use of a self-contained breathing apparatus, are mandated for other TICs, such as ammonia. Masks do not protect against carbon dioxide, and they are not be effective in environments where the TIC displaces oxygen, creating a low oxygen environment (at or below 19.5% fraction of expired oxygen [FiO_2]). Masks should only be used in these environments for escape purposes. A self-contained breathing apparatus is recommended.

Toxicity

The median lethal concentration (LCt_{50}) of phosgene is approximately half the LCt_{50} of chlorine. Since only half as much phosgene is required to kill half of an exposed group, phosgene is thus twice as potent as chlorine. PFIB is ten times more toxic than phosgene. Table 1-3 lists the Occupational Safety and Health Administration standards for exposure limits in parts per million.

Table 1-3. Occupational Safety and Health Administration Standards for Toxic Industrial Chemical Exposure Limits

Agent	Concentrated Exposure Limits (ppm)
Phosgene (CG)	0.1
Chloride (Cl)	5
Ammonia	50
Perfluoroisobutylene	0.01
Oxides of nitrogen (NOx)	25
White phosphorus smoke	1

Toxicodynamics: Mechanisms of Action

Central compartment. Centrally acting TICs such as ammonia and HD form strong acids or bases (alkali) when in contact with the water in the central airway tissues, and then destroy these tissues. Damaged tissues will swell and can slough into the airway and restrict breathing.

Peripheral compartment. Phosgene is the most studied peripheral compartment agent. It causes pulmonary edema, which is life threatening. Less is known about the other compounds; however, they are believed to be very similar.

Phosgene causes effects in the lung by inhalation only. It does not affect the lung when absorbed through the skin, injected, or orally ingested. When inhaled, phosgene travels to the very end of the smallest airways, the bronchioles, and causes damage to these airways. Additionally, it damages the thin membrane that separates the smallest blood vessels (the capillaries) and the air sacs (the alveoli) by reacting with the proteins and enzymes in the membranes. These membranes usually separate the blood in the capillaries from the air in the alveoli, but when the membranes are damaged, they cannot perform this function. Blood, or at least plasma (the liquid part of the blood), can leak through the damaged membrane into the alveoli. When plasma leaks into the alveoli, the air sacs become full of fluid, and air cannot enter them. Therefore, exchange of oxygen from the air into the blood is hindered, and the casualty suffers oxygen deprivation. The extent of oxygen deprivation depends on the extent of the phosgene exposure and the number of alveoli filled with plasma. The mechanism is similar to what happens with drowning, in that the alveoli fill up with fluid; however, in this instance, it is fluid from the blood, not from an external source. For this reason, phosgene poisoning is sometimes referred to as "dry land drowning."

Clinical Effects

Centrally acting agents. Immediately or shortly after exposure to these gasses or vapors, the casualty can develop laryngospasm, though not in all exposures. As the airways become irritated

and damaged, the individual will sneeze and experience pain in the nose (nasopharynx inflammation) and may develop painful swallowing (oropharynx inflammation); hoarseness, a feeling of choking, and noise with exhalation (larynx inflammation); and pain in the chest, coughing, and wheezing during breathing (trachea and bronchi inflammation). If the exposure has been enough to cause the TIC to reach the peripheral compartment, peripheral effects can follow. Scarring of the central airway can create permanent airway narrowing depending on the agent involved and the dose received.

*Peripherally acting agents***.** The *major effects* from phosgene and other peripherally acting agents *do not occur until hours after exposure***.** Immediately after exposure to these agents, the casualty will typically have an asymptomatic period of 30 minutes to 72 hours, but in most significant exposures the latent period is less than 24 hours. The duration and concentration of the exposure will determine the time to symptom onset. The casualty may notice irritation of the eyes, nose, and throat, but more commonly there are no effects during or immediately after exposure. HD signs are also delayed, but the damage is more in the central compartment.

The casualty with peripheral compartment damage who is developing pulmonary edema will notice shortness of breath (dyspnea) between 2 and 24 hours after exposure. Initially, this may be mild, and the eventual severity of the dyspnea depends on the amount of exposure. As the damage progresses, the dyspnea becomes more severe, and soon a cough develops. If the damage is severe, the casualty begins coughing up clear, foamy sputum, the plasma that has leaked into the alveoli.

Casualties with a very mild exposure to phosgene (or another of these compounds) will develop dyspnea 6 to 24 hours after exposure. They will notice it first after heavy exertion; however, later they become short of breath after any activity. With proper care, these casualties do well and recover completely.

A casualty with a severe exposure to phosgene (or another of these compounds) will notice shortness of breath within 4 to 6 hours after exposure. Increased difficulty breathing, even at rest, will occur, and even with intensive pulmonary care, the casualty may not survive.

The average exposure to a lung-damaging agent will fall between these two extreme cases. When the onset of dyspnea is greater than 6 hours after exposure, there may be progression to dyspnea at rest. However, with good pulmonary care beginning early after the onset of effects, the individual should recover completely.

Differential Diagnosis

Many TICs can be distinguished by their odor; they generally irritate the mucous membranes and can lead to dyspnea and pulmonary edema of delayed onset. In contrast, riot-control agents produce a burning sensation, predominantly in the eyes and upper airways, that is typically more intense than that caused by TICs and is unaccompanied by their distinctive odors. Nerve agents induce the production of watery secretions as well as respiratory distress; however, their other characteristic effects distinguish nerve agent toxicity from TIC inhalation injury.

The respiratory toxicity associated with vesicants is usually delayed but predominantly affects the central, rather than the peripheral, compartment. Vesicant inhalation severe enough to cause dyspnea typically causes signs of airway necrosis, often with pseudomembrane formation and partial or complete upper airway obstruction. Finally, pulmonary parenchymal damage following vesicant exposure usually manifests itself as hemorrhage rather than pulmonary edema.

Laboratory Findings

No commonly available laboratory tests exist for the specific identification or quantification of exposure to lung-damaging agents. However, an increase in the hematocrit may reflect the hemoconcentration induced by transudation of fluid into the pulmonary parenchyma from peripherally acting agents. Arterial blood gases may show a low PaO_2 or $PaCO_2$, which is an early, nonspecific warning of increased interstitial fluid in the lung.

Decreased lung compliance and carbon monoxide diffusing capacity are particularly sensitive indicators of interstitial fluid volume in the lung, but these are complex tests for hospital use only.

With peripherally acting agents, early findings on chest x-ray are hyperinflation, followed later by pulmonary edema without cardiovascular changes of redistribution or cardiomegaly. Ventilation profusion ratio (V/Q) scanning is very sensitive but is nonspecific and for hospital use only.

Medical Management

1. *Terminate exposure* as a vital first measure. This may be accomplished by physically removing casualties from the contaminated environment or by isolating them from surrounding contamination by supplying a properly fitting mask. Decontamination of any liquid agent on skin, and removal of clothing if vapors are trapped there, fully terminates exposure from that source.
2. *Execute the ABCs* (airway, breathing, circulation) of resuscitation as required. Establishing an airway is especially crucial in a patient exhibiting hoarseness or stridor; such individuals may face impending laryngeal spasm and require intubation. Establishing a clear airway also aids in interpreting auscultatory findings. Steps to minimize the work of breathing must be taken. Because of the always present danger of hypotension induced by pulmonary edema or positive airway pressure, accurate determination of the casualty's circulatory status is vital not just initially but also at regularly repeated intervals and whenever indicated by the clinical situation.
3. *Enforce rest.* Even minimal physical exertion may shorten the clinical latent period and increase the severity of respiratory symptoms and signs in a lung-damaging agent casualty. Physical activity in a symptomatic patient may precipitate acute clinical deterioration and even death. Strict limitation of activity (ie, forced bed rest) and litter evacuation are mandatory for patients suspected of having inhaled any of the edematogenic agents. This is true whether or not the patient has respiratory symptoms and whether or not objective evidence of pulmonary edema is present.
4. *Prepare to manage airway secretions and prevent/treat bronchospasm.* Unless superinfection is present, secretions in the airways

of lung-damaging agent casualties are usually copious and watery. They may serve as an index to the degree of pulmonary edema and do not require specific therapy apart from suctioning and drainage. Antibiotics should be reserved for those patients with an infectious process documented by sputum Gram staining and culture. Bronchospasm may occur in individuals with reactive airways, and these patients should receive theophylline or beta-adrenergic bronchodilators.

Steroid therapy is also indicated for bronchospasm as long as parenteral administration is chosen over topical therapy, which may result in inadequate distribution to damaged airways. Methylprednisolone, 700 to 1,000 mg, or its equivalent, may be given intravenously in divided doses during the first day and then tapered off during the duration of the clinical illness. Increased susceptibility to bacterial infection during steroid therapy mandates careful surveillance of the patient. There is some support in the literature for steroid use in those exposed to HC smoke (zinc/zinc oxide) and NOx, as these agents are theorized to reduce autoimmune reactions that can foster scar development and subsequent bronchiolitis obliterans. The literature does not give strong support for the use of steroids in the treatment of other toxic inhalants. Thus, steroids are not recommended in individuals without evidence of overt or latent reactive airway disease.

5. *Prevent and treat hypoxia*. Oxygen therapy is definitely indicated and may require supplemental positive airway pressure administered via one of several available devices for generating intermittent or continuous positive pressure. Intubation, with or without ventilatory assistance, may be required, and positive pressure may need to be applied during at least the end-expiratory phase of the ventilator cycle.
6. *Prevent and treat pulmonary edema*. Positive airway pressure provides some control over the clinical complications of pulmonary edema. Early use of a positive pressure mask may be beneficial. Positive airway pressure may exacerbate hypotension by decreasing thoracic venous return, necessitating intravenous fluid administration.
7. *Prevent and treat hypotension.* Sequestration of plasma-derived

fluid in the lungs may cause hypotension that may be exacerbated by positive airway pressure. Urgent intravenous administration of either crystalloid or colloid (in this situation) both appear equally effective. The use of vasopressors is a temporary measure until fluids can be replaced.

Triage

*Patients seen within 12 hours of exposure***.** A patient with pulmonary edema only is classified *immediate* if intensive pulmonary care is immediately available. In general, a shorter latent period portends a more serious illness. A *delayed* patient is dyspneic without objective signs and should be observed closely and retriaged hourly. An asymptomatic patient with known exposure should be classified *minimal* and observed and retriaged every 2 hours. If this patient remains asymptomatic 24 hours after exposure, he or she should be discharged. If exposure is in doubt and the patient remains asymptomatic 12 hours following putative exposure, consider discharge. An *expectant* patient presents with pulmonary edema, cyanosis, and hypotension. A casualty who presents with these signs within 6 hours of exposure generally will not survive; a casualty with the onset of these signs 6 hours or longer after exposure may survive with immediate, intensive medical care. If ventilatory support is not available but adequate evacuation assets are, these patients should have priority for urgent evacuation to a facility with adequate ventilatory resources.

Patients seen more than 12 hours after exposure. A patient with pulmonary edema is classified *immediate* provided he or she will receive intensive care within several hours. If cyanosis and hypotension are also present, triage the patient as *expectant*. A *delayed* patient is dyspneic and should be observed closely and retriaged every 2 hours. If the patient is recovering, discharge him or her 24 hours after exposure. An asymptomatic patient or patient with resolving dyspnea is classified *minimal***.** If the patient is asymptomatic 24 hours after exposure, he or she should be discharged. A patient with persistent hypotension despite intensive medical care is *expectant***.**

Return to Duty

If the patient has only eye or upper airway irritation and is asymptomatic with normal physical examination 12 hours after exposure, he or she may be returned to duty. If the patient's original complaint was dyspnea only, yet physical examination, chest x-ray, and arterial blood gases are all normal at 24 hours, he or she may be returned to duty. If the patient presented initially with symptoms *and* an abnormal physical examination, chest x-ray, or arterial blood gas, he or she requires close supervision but can be returned to duty at 48 hours if physical examination, chest x-ray, and arterial blood gases are all normal at that time.