CHAPTER 64

CHEMICAL INJURIES

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PERSPECTIVE

During the past century, there has been a dramatic increase in the number of chemicals produced. Worldwide, there are more than 5 million known chemicals, with an additional 10,000 to 20,000 new chemicals developed each year. Furthermore, an estimated 500,000 unique shipments of hazardous materials occur daily throughout the United States, resulting in thousands of exposures to hazardous materials annually.1 These chemicals, which include acids, alkalis, and other highly reactive substances, not only are found throughout industry but also are ingredients in many household products. Exposure to these substances can result in injuries to many organs, including the eyes, skin, and lungs.

Despite myriad potential exposures to chemicals each day, the number of actual exposures is relatively low, largely because of sound industry practices and state and federal regulations. The Superfund Amendments and Reauthorization Act contains extensive provisions for emergency planning.

A hazardous material (hazmat) is defined as any substance, including gases, solids, or liquids, that has the potential to cause harm to people or the environment. The Hazardous Substances Emergency Events Surveillance (HSEES) system collects information on chemical exposures from 14 states. According to the 2007-2008 HSEES report, more than 15,000 chemical events occurred in the United States during this 2-year span. The manufacturing sector accounted for nearly half of all chemical exposures in the United States. Transportation, communication, and other public utilities accounted for nearly one third of all exposures. Employees working with the chemicals were the most likely to be injured, followed by the general public.1 Both the current and the past HSEES reports can be found online at www.atsdr.cdc.gov/HS/HSEES/annual2008.html.

The most commonly released hazardous substances are volatile organic compounds, herbicides, acids, and ammonia. Various household products, such as cement, drain cleaners, and gasoline, are also potentially quite hazardous, and exposure can result in severe disability or death.

PATHOPHYSIOLOGY

Most chemical agents cause skin damage by producing a chemical reaction rather than a hyperthermic injury. Certain chemicals can generate significant heat production via an exothermic reaction. Nonetheless, the majority of dermal injuries result from direct damage to the skin rather than from a hyperthermic injury. The type of chemical reaction produced depends on the properties of the individual agent. In general, however, the degree of damage is directly correlated with the toxic agent’s concentration and duration of exposure. Several other factors also contribute to the degree of injury—for example, areas of the body where the skin is particularly thin are more at risk than areas of the body where the skin is thicker. Skin that is particularly thin or broken can contribute to more severe injury.

When acidic compounds interact with skin, protein denaturation and coagulative necrosis ensue. This coagulative necrosis produces an eschar, which limits the depth to which the acid can penetrate. Despite this eschar formation, acidic burns can, nonetheless, produce profound burns. Various acids produce eschars with characteristic colors. For example, nitric acid burns result in a yellow eschar, whereas sulfuric acid burns result in a black or brown eschar. Hydrochloric acid and phenol burns produce a white to gray-brown eschar.

Unlike the coagulative necrosis produced from most acids, alkalis produce saponification and liquefactive necrosis of body fat. Because there is no eschar to limit penetration, alkali burns tend to penetrate deeper into the tissues, which results in significant tissue damage.

COMMUNITY PREPAREDNESS AND HAZMAT RESPONSE

Hazardous materials are found in residential, urban (e.g., manufacturing), and rural (e.g., agricultural) settings. Furthermore, because these substances are often transported on highways and railroads, a hazmat exposure could potentially occur in virtually any community. First responders, paramedics, and members of the hazmat response team must work together to identify toxic chemicals and assess hazardous environments. Placards, shipping papers, United Nations chemical identification numbers, and markings on shipping containers help identify the offending agent. In some cases, chemical analysis may be required to assist in the identification of the agent. The Chemical Transportation Emergency Center (CHEMTREC) in Arlington, Virginia, maintains a 24-hour telephone hotline (1-800-424-9300) to assist in the rapid identification and management of chemical agents. In addition, regional poison control centers (1-800-222-1222) provide specific health information regarding individual chemicals.

Contingency Plan

The contingency plan for hazmat management is divided into two parts: initiation of the site plan and evacuation. Initiation of the site plan begins after the specific offending agent has been identified and the surrounding environment has been assessed. Only after the substance has been identified can the risks to the public and the environment accurately be identified. First responders should be trained to recognize the potential for a hazmat incident and should establish a perimeter. The hazmat
technicians are specifically trained in the use of personal protective equipment (PPE), establishing entry into a hazmat scene, victim rescue, and determining the type and extent of a hazmat emergency. A central command post should be used to coordinate the activities of the hazmat team with those of the emergency medical services personnel, firefighters, police officers, and other relevant personnel.

Coping with Hazmat Incidents

In dealing with a hazmat incident, two distinct processes occur simultaneously. First, the scene is secured, which involves containing the substance, extinguishing fires, and controlling other environmental hazards. The second process involves treatment, which begins with decontamination. The exact decontamination depends on the specific agent and route of exposure. In general, all decontamination should be performed before arrival in the emergency department. Individuals who are not exposed to the hazardous material are kept away from the scene to prevent subsequent exposure.

At the outset of any contamination event, the offending agent may not be known. Therefore first responders and those having direct contact with ill patients must wear appropriate PPE. Once the first responder is dressed appropriately, decontamination begins by removing the patient’s contaminated clothes. Dry (anhydrous) chemicals can be brushed off the patient’s skin, followed by copious irrigation with water delivered under low pressure. Ideally, the contaminated water will be contained on the scene for appropriate disposal. Liquid chemicals can be copiously irrigated directly. If decontamination was indicated and not performed on the scene, the patient should be decontaminated before entering the ED. The primary and secondary survey can occur simultaneously with decontamination.

Although the exact requirements for PPE among hospital personnel are somewhat controversial, at a minimum, all personnel involved with decontamination should wear chemical-resistant clothing with a hood, boots, eyewear, at least two layers of gloves, and some form of respiratory protection.

MANAGEMENT

The initial management of the chemically burned patient involves removing the individual from the hostile environment. All clothing is promptly removed and placed in plastic bags, if not already done. Dry chemical agents, such as lye, should be brushed away before hydrotherapy is instituted. The priority of decontamination is to progress from cleansing of contaminated wounds to eyes, mucous membranes, skin, and hair.

Chemical burns continue to destroy tissue until the causative agent is inactivated or removed. Therefore the more quickly the agent is removed from the skin, the less severe the injury. Prompt treatment results in a return of the skin pH to normal or near-normal conditions.

Hydrotherapy

Hydrotherapy involves the application of large amounts of water or saline to the affected skin. Gentle irrigation of a large volume of water under low pressure for a prolonged time dilutes the toxic agent and washes it out of the skin. High-pressure irrigation should not be used because it is possible to drive the chemical deeper into the skin. Furthermore, the use of high-pressure irrigation can result in splattering of the chemical into the eyes of the patient or rescuer.

Elemental metals (e.g., sodium) may produce profound exothermic reactions when combined with water. To minimize the exothermic reaction from such compounds, mineral oil is applied to the skin first, if it is immediately available. However, hydrotherapy should not be delayed while waiting for mineral oil. In addition, some have argued that phenol (carboxylic acid) should not be irrigated with water owing to concern for enhanced skin penetration after exposure to water. However, the use of a substance that has both hydrophobic and hydrophilic properties (i.e., polyethylene glycol [PEG]) has not been proven to exhibit clear benefit over water alone; therefore hydrotherapy should not be delayed while waiting for PEG. If PEG solution is used for decontamination, the molecular weight of the preferred solution should be 200 to 400 daltons, which is different from the molecular weight of the PEG solution used for colonoscopy preparations.

After exposure to strong alkalis, prolonged hydrotherapy is especially important to limit the severity of the injury. In experimental animal models, the pH of chemically burned skin does not approach a normal concentration unless continuous irrigation has been maintained for more than 1 hour, and the pH often does not return to normal for 12 hours despite hydrotherapy. In contrast, with hydrochloric acid skin burns, the pH usually returns to normal within 2 hours after initiation of hydrotherapy. The mechanism by which sodium hydroxide (NaOH) maintains an alkaline pH despite treatment is related to the byproducts of its chemical reaction to skin. Alkalis combine with proteins or fats in tissues to form soluble protein complexes or soaps. These complexes permit passage of hydroxyl ions deep into the tissue, limiting their contact with the water diluent on the skin surface. On the other hand, acids do not form complexes, and their free hydrogen ions are easily neutralized.

Water is the agent of choice for decontaminating dermal burns from either acidic or alkali substances. The deleterious effects of attempting to neutralize acid and alkali burns were first noted in experimental models in 1927. In nearly every instance, animals with either acid or alkali burns that underwent initial irrigation with water survived longer than animals treated with chemical neutralizers. The striking difference between the results of these two treatment methods is attributed to the additional trauma of the heat generated by the neutralization reaction superimposed on the existing burn. Although the same effect may occur when certain chemicals come in contact with water, large volumes of water tend to limit the exothermic reaction.

However, scientists are beginning to question the belief that neutralization of an alkaline burn of the skin with acid does indeed increase tissue damage because of the exothermic nature of acid-base reactions. Using an animal model with 5% topical acetic acid (i.e., household vinegar), researchers demonstrated that the application of acetic acid to alkaline burns resulted in rapid neutralization of the tissue and reduction of the tissue injury in comparison with water irrigation alone. However, these data are preliminary and limited, and therefore irrigation with water alone is acceptable.

Ocular Injury

Chemical burns to the eye require emergent management. Alkali burns are more common than acidic burns, and unilateral involvement is more common than bilateral involvement. Common causes include inadvertent handling of chemicals with resultant splash injury, exploding batteries, airbag deployment, and intentional assaults. Alkali burns can initially appear trivial, but because of an interaction with lipids in the corneal epithelial cells, a coagulative necrosis results, and deep penetration through the corneal stroma can ensue. The injury can occur rapidly; for example, anhydrous ammonia can penetrate into the anterior chamber in less than 1 minute, resulting in complete blindness.

Similar to cutaneous burns, ocular burns are classified into four grades, with grade IV being the most severe. Grade I and II burns are associated with hyperemia, conjunctival ecchymosis, and
defects in the corneal epithelium. Grade III and IV burns are associated with deeper penetration and therefore are associated with mydriasis, a gray discoloration of the iris, and early cataract formation.

Grade II burns are differentiated from grade I burns by the hazy appearance of the cornea in the former. Blood vessel thrombosis in the anterior chamber occurs in both grade III and grade IV burns, and as a result, limbus ischemia occurs. The degree of ischemia differentiates grade III from grade IV burns: ischemia occurs in less than half of the limbus in grade III, whereas ischemia occurs in more than half of the limbus in grade IV. In addition, grade IV burns are associated with necrosis of the bulbar and tarsal conjunctiva and significant limbal ischemia.5,6

Treatment

When a chemical injury to the eye is suspected, copious irrigation is started immediately. At the scene, it is recommended that the victim submerge the eyes in running tap water and continuously open and close the eyes with the head turned such that the affected eye is lower than the unaffected eye to minimize any contamination into the unaffected eye. In the emergency department, tap water irrigation can be continued during preparation for a more definitive irrigation system. The repeated application of topical anesthetics such as proparacaine can decrease pain and facilitate irrigation. Hydrotherapy can also be accomplished by connecting intravenous tubing to a bag containing normal saline or lactated Ringer’s solution. The initial therapy consists of continual irrigation of the eye with 2 L of normal saline during the first 30 minutes. A Morgan lens can be used for irrigation, although there is a theoretic risk of trapping the chemical between the conjunctiva and the Morgan lens, thereby increasing the burn. If a Morgan lens is used, we recommend replacing the lens between saline applications. After 2 L has been infused, litmus paper is inserted into the conjunctiva to determine the pH; irrigation is continued until the pH is at a near-physiologic level (pH of 7.4).

Chemical burns are likely to require more irrigation than acidic burns. For very severe acid or alkali burns, prolonged irrigation may be needed regardless of a normal ocular pH. It is important to also evert the upper eyelid and visually inspect the area for any lodged particulate matter, which may be hidden. A slit-lamp examination with fluorescein staining should be performed to assess for any corneal abrasion. Although of undetermined benefit, ocular antibiotics can be considered after decontamination if a corneal abrasion is present.

Some experimental settings have found benefit from the application of N-acetylcysteine or cysteine to eyes subjected to chemical injury.7 These collagenase inhibitors are thought to prevent loss of the corneal stroma by limiting the amount of collagenase released from the injured tissue. In one retrospective study, the application of steroids, ascorbate, citrate, and antibiotics resulted in improved outcomes in grade III, but not grade IV, burns compared with steroids and antibiotics alone.8 It is hypothesized that the citrate suppresses neutrophils and inhibits collagenase, thereby reducing the inflammatory response. Ascorbate has been hypothesized to promote new collagen deposition. Topical antibiotics (e.g., sulfacetamide, gentamycin, and ciprofloxacin) are recommended for any corneal injury, but this practice is not supported by strong evidence. Mobility of the eye should be encouraged to minimize the formation of adhesions (symblepharon). With the exception of the antibiotics, there are insufficient data at this time to recommend use of any of the pharmaceutical agents mentioned in this paragraph as part of routine practice.

Immediate ophthalmologic consultation and close follow-up are indicated for all significant exposures. Patients with grade I and II injuries can often be managed as outpatients, but patients with higher-grade injuries should be admitted to the hospital. All but the mildest burns should be treated with a long-acting cyclopregic, a mydriatic. After discussion with an ophthalmologist, a carbonic anhydrase inhibitor may be used for 2 weeks (or until the pain disappears). These medications decrease the potential for pupillary constriction, increased intraocular pressure, and early glaucoma. Procedures such as amniotic membrane patching, anterior chamber paracentesis, and corneal transplant have been used for chemical injuries to the eye, and these are undertaken by the ophthalmologic consultant.

Hydrofluoric Acid

Hydrofluoric acid (HF) is an acidic aqueous solution made from the element fluorne. It is commonly used in the petroleum industry to manufacture high-octane gasoline. It is also commonly used in the production of microelectronics and for etching glass, removing rust, and cleaning cement and bricks. Absorption of HF can occur after exposure to the lung, skin, and eyes. In an 11-year review of all HF deaths reported to the Occupational Safety and Health Administration, four deaths resulted strictly from dermal exposure, and five deaths resulted from both inhalational and dermal exposure. Seven of these deaths were associated with inadequate medical therapy, and all of the cases were associated with unsafe workplace practices.6 HF solutions with a concentration exceeding 50% will produce near immediate pain, whereas burns from more dilute concentrations can be delayed for hours.

HF is unique in its mechanism of action. Despite being an acid, it is capable of causing a liquefactive necrosis, similar to alkanis. However, the free fluoride ion is actually responsible for most of the damage associated with HF exposure. The free fluoride ion scavenges cations, such as calcium and magnesium, thereby resulting in systemic hypocalcemia and hypomagnesemia. In addition, free fluoride ions can inhibit sodium, potassium–ATPase (Na+,K+-ATPase) and the Krebs cycle. The combination of cellular destruction and inhibition of Na+,K+-ATPase can also result in hyperkalemia, a preterminal finding. As a result of the numerous electrolyte disturbances, QT prolongation, hypotension, and ventricular arrhythmias can occur. The severity of injury depends on the concentration of the substance and the duration of exposure.

Inhalational Exposure

Inhalation of HF is rare, and it almost always occurs in the industrial setting. Patient outcomes vary considerably depending on the concentration and duration of exposure to HF. Inhalation and skin exposure to 70% HF can result in pulmonary edema and death within 2 hours. However, delayed pneumonitis and adult respiratory distress syndrome can also occur, and once symptoms occur, they can be present for months. Pneumonitis can be severe and require ventilatory support.

Gastrointestinal Exposure

Gastrointestinal exposure is rare; it can produce symptoms ranging from nausea, vomiting, and abdominal pain to life-threatening fluoride toxicity.

Ocular Exposure

Despite the fact that HF is an acid, exposure of the eye to HF can result in a severe burn with penetration and necrosis of the structures throughout the anterior chamber. As with other ocular injuries, immediate and copious irrigation of the eye is indicated. Systemic absorption is possible.
Dermal Exposure

Dermal exposure is perhaps the most common route of injury. Relatively dilute solutions of HF (0.6-12%) are available to the general public in the form of rust removal and aluminum cleaning products. During handling of containers in which HF is stored, contamination of inadequately protected fingers and hands often results in a chemical burn injury. The HF skin burn has a distinct characteristic: the exposure causes progressive tissue destruction. Intense pain can occur quickly or be delayed for several hours, but it can persist for days if untreated. The skin at the site of contact develops a tough coagulated appearance. Eschar formation can occur. If untreated, the burn can progress to an indurated, whitish appearance with vesicle formation. In the digits, HF has a predilection for subungual tissue. Severe untreated burns can progress to full-thickness burns and can even result in loss of digits.

Initial Therapy

The initial treatment of HF skin exposure is immediate irrigation with copious amounts of water for at least 15 to 30 minutes. Most exposures to dilute solutions of HF respond favorably to immediate irrigation. Severe pain or any pain that persists after irrigation denotes a more severe burn that requires detoxification of the fluoride ion. Detoxification is accomplished when an insoluble calcium salt is formed.

All blisters are removed because necrotic tissue may harbor fluoride ions; the fluoride ions can then be detoxified through topical treatment, local infiltrative therapy, or intra-arterial infusion of calcium. Calcium gluconate (2.5%) gel is the preferred topical agent. This gel is often not available in hospital pharmacies, but it can be made by mixing 3.5 g of calcium gluconate powder in 150 mL of a water-soluble lubricant (e.g., glycerin-hydroxyethyl cellulose lubricant [K-Y Jelly]). The gel is secured by an occlusive cover (e.g., powder-free latex glove). Because the skin is impermeable to calcium, topical treatment is effective only for mild, superficial burns.

Infiltration Therapy

Subcutaneous. Infiltrative therapy is necessary for treatment of deep, painful HF burns. Calcium gluconate is the agent of choice and can be administered by either direct infiltration or intra-arterial injection. A common technique involves injecting 0.5 mL/cm² of 10% calcium gluconate subcutaneously through a 27- or 30-gauge needle. The use of an equal volume mixture of 5% calcium gluconate and 0.9% normal saline has been shown to reduce irritation of tissues and decrease subsequent scarring. Patients treated in this manner should be hospitalized for observation and toxicologic consultation.

Despite its wide acceptance, the infiltration technique has disadvantages, especially in treating digits. A regional nerve block is recommended because the injections may be very painful. Removal of the nail to expose the nail bed is required if subungual tissue is involved. Vascular compromise can occur if excessive fluid is injected into the skin exposure sites, and unbound calcium ions have a direct toxic effect on tissue. Because of these disadvantages with subcutaneous infiltration, intra-arterial infusion of calcium is now recommended in most instances.

Intravenous and Intra-arterial. Patients with pain refractory to local or subcutaneous calcium administration may benefit from regional anesthesia, either in the form of an intravenous infusion (e.g., Bier block), or intra-arterial. Various dilute solutions of calcium have been used, but perhaps the most commonly used solution is a mixture of 10 mL of solution of 10% calcium gluconate in 40 to 50 mL of normal saline infused over 4 hours. If more than 6 hours has elapsed since the time of HF exposure, tissue necrosis cannot be prevented, even though pain relief can be achieved up to 24 hours after exposure.

The intra-arterial infusion technique has potential disadvantages. Arterial spasm or thrombosis may result in significant skin loss. The intra-arterial procedure is more costly because it requires hospitalization for the use of the infusion pump and the monitoring of serum calcium concentrations if repeated infusions are used.

Systemic Toxicity

HF binds calcium and magnesium ions with strong affinity. Systemic manifestations of fluoride toxicity are at least partly related to hypocalcemia and include abdominal pain, muscle fasciculations, nausea, seizures, ventricular dysrhythmias, and cardiovascular collapse. Consequently, patients with significant HF exposure require hospitalization to monitor for cardiac dysrhythmias for 24 to 48 hours. Hypocalcemia can occur after significant exposure to HF and is corrected with the intravenous administration of a 10% calcium gluconate infusion. Calcium chloride can be used, but its administration requires central access. In addition, fluoride ion accumulation has cardiac and neurotoxic effects. Burns as small as 2.5% of the total body surface area have proven fatal in concentrated HF exposure.

Formic Acid

Formic acid is a caustic organic acid used in industry and agriculture. It causes cutaneous injury by inducing a coagulative necrosis. Systemic toxicity occurs after absorption and is manifested by acidosis, hemolysis, and hemoglobinuria. Hemolysis is the result of the direct effect of formic acid on the red blood cells. Copious wound lavage should be instituted immediately. Acidosis (pH < 7.30) should be treated with sodium bicarbonate. Mannitol may be used to expand plasma volume and promote osmotic diuresis in patients with hemolysis. Exchange transfusion and hemodialysis may be needed in patients with severe formic acid poisoning.

Anhydrous Ammonia

Anhydrous ammonia is a colorless, pungent gas used extensively as a fertilizer in the agricultural setting. It can also be used in the manufacture of explosives, petroleum, plastics, and synthetic fibers. In addition, the “dry cook” or the “Nazi” method of methamphetamine production uses anhydrous ammonia as an amphetamine precursor. As a result of the use of this new method, there has been an increasing number of anhydrous ammonia burns associated with illicit methamphetamine production. In one study the incidence of anhydrous ammonia exposure from methamphetamine production was three times greater than that from agricultural production.

The sudden release of liquid ammonia can cause injury through two distinct mechanisms. First, anhydrous ammonia has an extremely low temperature (−33° C) and freezes any tissue it touches. Second, the ammonia vapors readily dissolve in the moisture in skin, eyes, oropharynx, and lungs to form hydroxyl ions that cause chemical burns by liquefaction necrosis, which can result in full-tissue skin loss. The severity of injury is directly related to the concentration and duration of ammonia exposure. In general, acute exposure to anhydrous ammonia produces the greatest injury to the proximal airway rather than the distal airway.

Treatment consists of prompt irrigation of the eyes and skin with water and management of inhalation injury. If necessary, the airway should be secured through standard intubation methods with a large-diameter tube to prevent distal airway obstruction.
from sloughing of mucosa. After intubation, lower airway injury is managed with positive end-expiratory pressure ventilation.

Cement

Cement is a solid material composed of salicylates and calcium aluminates. When dry cement is combined with water, hydrolysis occurs, resulting in a solution of basic lime hydrate. This solution has a pH of 10 to 12. As hydrolysis continues, however, the pH can increase up to 14, which is comparable to the pH of sodium or potassium hydroxide or lye.

There are three types of cement burns. The most common burn is a chemically abrasive form, and heat-related or blast-induced burns can also occur. Heat-related and blast-induced burns are more common in the industrial setting and are associated with severe burns, often involving the respiratory tract.

The treatment of a cement burn attempts to eliminate the toxic component via copious irrigation after all clothes have been removed. Early excision and grafting are often necessary.14

Phenol and Derivatives

Phenols are used industrially as starting materials for many organic polymers and plastics. They are widely used in the agricultural, cosmetic, and medical fields. Because of their antiseptic properties, they are also used in many commercial germicidal solutions. A number of phenol derivatives (e.g., hexylresorcinol and resorcinol) are more bactericidal than phenol.

Phenol (carbolic acid) is an aromatic acid alcohol. Both phenol and its derivatives are highly reactive, corrosive poisons that damage cells by inducing cell wall disruption, protein denaturation, and coagulative necrosis. Their characteristic odor usually signals their presence. After penetrating the dermis, phenol produces necrosis of the papillary dermis. This necrotic tissue may temporarily delay its absorption. Therefore when skin comes in contact with phenol, treatment is instituted immediately. The exposed area is irrigated with large volumes of water delivered under low pressure. Because dilute phenol solutions are more rapidly absorbed through skin than concentrated solutions, gentle swabbing of the skin surface with sponges soaked in water should be avoided. Any hair, including a beard or mustache, that has come in contact with a phenol is removed as soon as possible because the phenol can become trapped in hair.

In animal studies, it was found that exposure to as little as 0.625 mg of phenol per kilogram could be lethal.3 Systemic toxicity of phenol primarily affects the central nervous system (CNS) and cardiovascular system. In the CNS, toxicity can manifest as stimulation, lethargy, seizures, or coma. Conduction disturbances can be either tachycardic or bradycardic in nature. Marked hypotension may occur as a result of central vasomotor depression, in addition to a direct toxic effect on the myocardial cells and small blood vessels. Hypothermia and metabolic acidosis can also occur.

Dilute solutions of phenol are used by plastic surgeons for chemical face peels. Phenols are usually mixed with water, soap, and croton oil. This solution can produce a partial-thickness burn of a predictable depth in a controlled manner. Phenols have been a standard for many years and are now being used for skin resurfacing to remove wrinkles, irregular pigmentation, and actinic keratosis. The concentration is kept sufficiently low to reduce the occurrence of systemic complications. It is interesting to note that higher concentrations of phenol result in a shallower burn depth because of increased coagulation of the keratin, thereby preventing deeper penetration. Histologic studies have demonstrated that 100% concentrations of phenol produce 35 to 50% less penetration than a 50% solution.

The physician performing phenol chemical peels should be concerned about the possibility of rapid phenol absorption. Even in a controlled setting, ventricular dysrhythmias occur as a result of the phenol application.15

Polyethylene Glycol Therapy

Experimental studies indicate that water alone is effective in reducing the severity of burns and preventing death in animals with skin exposed to phenol and its derivatives. The most effective treatment is undiluted PEG of molecular weight 200 to 400 or isopropanol (isopropyl alcohol).16 Adequate supplies of either PEG or isopropanol should be stocked in hospitals located near areas of phenol use and can often be found in the chemical section of hospital pharmacies. A quick wipe of the skin with PEG solutions reduces mortality and burn severity in experimental animals. These solutions can be used for phenol burns of the face because they are not irritating to the eyes. Decontamination with water should be performed until a PEG solution is obtained. Large amounts of water must be used, however, because small amounts are detrimental, enhancing dermal absorption of phenol. Removal of phenol should be undertaken in a well-ventilated room so that hospital personnel are not exposed to high concentrations of phenol fumes.

Treatment of Systemic Toxicity

The treatment of systemic symptoms is primarily supportive. Respiratory depression may require ventilatory support. Hypotension is initially treated with crystalloid fluids; if fluids are inadequate, vasopressors should be used. Metabolic acidosis can be treated with sodium bicarbonate until the pH is near 7.40. The alkalization can also help prevent hemoglobin precipitation in the nephron as a result of hemolysis. Benzodiazepines may be required to treat seizures caused by CNS stimulation.

Phosphorus

Phosphorus is a nonmetallic element that exists in three forms: elemental phosphorus, white phosphorus, and red phosphorus. White phosphorus, which is also referred to as yellow phosphorus, is widely used in munitions manufacturing, in fireworks, as an ingredient in methamphetamine production, and in fertilizers. Historically, it has also been widely used as a rodenticide. The autoignition temperature (the temperature at which spontaneous combustion can occur) is 30°C (86°F). When white phosphorus comes in contact with air at temperatures above the autoignition point, the phosphorus spontaneously oxidizes, forming phosphorus pentoxide. Phosphorus pentoxide can combine with small amounts of moisture in the air, forming phosphoric acid. In wounds, oxidation of phosphorus pentoxide will continue until it is removed through débridement, neutralized, or consumed.

Tissue injury from white phosphorus appears to have both thermal and chemical causes. The corrosive action of the phosphoric acid results in an exothermic reaction, thereby liberating heat and causing a thermal burn. The hygroscopic action of the phosphorus pentoxide, however, is also responsible for causing a chemical burn. Ultimately, a profound thermal injury can occur, which frequently results in a partial-thickness or full-thickness burn.

Metabolic derangements can also occur after white phosphorus exposure, including hypocalcemia and hyperphosphatemia. Conduction system disturbances, including bradycardia, QT prolongation, and ST and T wave abnormalities, can occur and are at least partially explained by electrolyte derangements. These electrocardiogram changes may explain the sudden early death that occasionally occurs in patients with relatively minor white phosphorus burns.
After oral ingestion of white phosphorus, three stages of toxicity are described, although only rarely do all three stages occur. The first stage is characterized by gastrointestinal tract irritation, including vomiting, abdominal pain, diarrhea, and gastrointestinal bleeding. The stool is occasionally described as being luminescent or “smoking.” Hypovolemic shock can result. As many as one third of patients who ingest significant quantities of white phosphorus will die during this stage. The first stage can last 8 to 24 hours. The second stage, which lasts 1 to 3 days, is a latent phase in which symptoms appear to improve. However, the third stage is characterized by multisystem organ failure, including hepatic failure, renal failure, and CNS depression. Renal failure is usually present at days 1 to 4, whereas jaundice typically manifests at days 3 to 5.

The out-of-hospital management involves the immediate removal of contaminated clothing, followed by submersion of the injured skin in cool water. Warm or hot water is avoided because white phosphorus becomes liquid at 44°C (111°F). Phosphorus particles are removed from the victim’s skin and submerged in water. The burned skin is covered with towels soaked in cool water during transport to the emergency department.

Red phosphorus can cause some gastrointestinal illness if consumed orally but is much better tolerated than white phosphorus that has been ingested.

After the patient arrives at the emergency department, the burned skin is washed copiously with normal saline. In the past, some advocated use of a suspension of 5% sodium bicarbonate, 3% copper sulfate, and 1% hydroxyethyl cellulose. Other, similar solutions containing copper sulfate have also been described. The use of 0.9% normal saline solution, however, has demonstrated better effects than copper-containing solutions. Although there are some conflicting recommendations in the literature, given that saline is probably at least as efficacious as copper sulfate solutions and has less associated toxicity, saline irrigation is the preferred irrigating solution.

Phosphorus particles can be identified with either ultraviolet light or copper-containing solutions. When a Wood’s lamp is used, the phosphorus will fluoresce under an ultraviolet light. Unlike copper-containing solutions, the use of a Wood’s lamp is not associated with any adverse or detrimental effects. The use of the copper-containing solutions causes the phosphorus particles to become coated with black cupric phosphate. These black particles are more easily identified and thus more easily removed. Copper sulfate also decreases the rate of oxidation of the phosphorus particles, thus limiting their damage to the underlying tissue. However, because the blackened particles can still cause tissue damage, they should be removed. If a copper solution is used, after 30 minutes of exposure to the burned skin the copper-containing solution must be thoroughly washed from the skin, thereby limiting the development of systemic copper toxicity.

After copious irrigation, decontamination, and treatment of associated electrolyte disturbances, definitive management of the skin burns is accomplished as with any other burn wound. Serum calcium and phosphate levels should be monitored for 24 to 48 hours.

### Nitrates and Nitrites

Both nitrates (NO$_3^-$) and nitrites (NO$_2^-$) are abundant in modern society. Both sodium nitrate and sodium nitrite are used in food preservatives. Nitrites also have many medicinal uses secondary to their vasodilatory properties. Nitrates are commonly used in electroplating, engraving, and metal casting. Nitrates are also commonly used as fertilizing agents. Exposure to either nitrates or nitrites has been associated with methemoglobinemia.

Reduced hemoglobin contains four heme groups, each with a ferrous (Fe$^{2+}$) ion. Methemoglobinemia results when the ferrous ion becomes oxidized to the ferric (Fe$^{3+}$) state. At physiologic levels, there is usually 1 or 2% methemoglobinemia in circulation at any given time. Cyanosis from methemoglobin occurs when methemoglobin concentrations exceeded 1.5 g/dL. Methemoglobin toxicity exists along a spectrum. Many patients with low levels are asymptomatic. When methemoglobin concentrations in non-anemic individuals exceed 20%, headache, anxiety, dyspnea, and tachycardia can occur. Confusion, lethargy, and acidosis typically occur with methemoglobin levels approaching 40 to 50%. Coma, seizures, hypotension, dysrhythmias, and death occur when levels exceed 70%. Patients can develop symptoms at lower methemoglobin percentages in the setting of anemia. However, in the setting of profound anemia, cyanosis may not be apparent. The diagnosis of methemoglobinemia should be sought in any cyanotic patient whose pulse oximetry displays a saturation of 85 to 88% that is unresponsive to oxygen (O$_2$) therapy and whose arterial blood appears chocolate brown in color. Asymptomatic patients are treated simply by removing the offending agent. For symptomatic patients without glucose-6-phosphate dehydrogenase (G6PD) deficiency, 2 mL of 1% methylene blue per kilogram is administered over 3 to 5 minutes. Symptoms typically improve within 20 minutes. Severe cases may need repeated doses of methylene blue, and very severe cases may require exchange transfusion. Candidates for exchange transfusion include patients with G6PD deficiency with significant toxicity from methemoglobinemia and patients who fail to respond to methylene blue.

### Hydrocarbons

Hydrocarbons are a heterogeneous group of organic compounds that are derived from carbon and hydrogen molecules. They have become an integral part of modern society and are found in fuels, solvents, paints, paint and spot removers, dry cleaning solutions, lamp oil, rubber cement, and lubricants.

Hydrocarbons are classified as aromatic, in which the carbon moieties are arranged in a ring, or aliphatic, in which the carbon moieties are arranged in a linear or branched chain. Halogenated hydrocarbons are a subgroup of aromatic hydrocarbons in which one of the hydrogen molecules is substituted with a halogen.

The toxicity from hydrocarbons can affect many different organs, but the lungs are the most commonly affected. The toxicity of hydrocarbons is directly related to their volatility and inversely related to the viscosity and surface tension. The primary toxicity from hydrocarbons occurs from aspiration. Thus substances with high volatility, low viscosity, and low surface tension are most likely to be aspirated.

Systemic toxicity from dermal exposure to a hydrocarbon is relatively rare. Significant dermal exposures can occasionally cause local tissue irritation. Treatment involves removal of the patient from the source and removal of any contaminated clothing. Copious irrigation with warm water should be performed, and burns managed as are other burns.

Chronic dermal exposure can result in a perioral or perinasal dermatitis with pyoderma. This so-called “huffer’s rash” is primarily seen with recreational abuse. The hydrocarbon inhalant can dry the skin, thereby causing microscopic cracks and allowing bacteria to enter, causing a bacterial superinfection.

Significant toxicity from inhaled (nonaspiration) exposure to hydrocarbons is also unlikely to produce serious effects. Some patients may develop mild headache, dizziness, nausea, or wheezing. These symptoms resolve after removal of the patient from the source of exposure.

Ingestion of hydrocarbons can result in aspiration and systemic toxicity. After ingestion of hydrocarbons, it is recommended that patients be monitored for 6 hours. Many clinicians advocate obtaining a chest radiograph 6 hours after ingestion, although no randomized study has demonstrated this approach to be superior.
to simply observing for clinical manifestations of aspiration (e.g., coughing, gagging, vomiting, wheezing, tachypnea, or hypoxia). There is no role for gastric decontamination. A patient can be discharged home after a 6-hour observation period, assuming no symptoms develop during the observation period and a chest radiograph (if obtained) is negative. All other patients warrant admission to observe for progression of symptoms and treatment of hydrocarbon-induced pneumonitis. Beta-agonists should be administered for bronchospasm, and supplemental oxygen administered as needed. Endotracheal intubation is occasionally required for severe hypoxia. Neither corticosteroids nor empirical antibiotic administration is indicated. Antibiotics may be warranted, however, if a superimposed bacterial infection develops, which will typically occur several days after the pneumonitis develops.

**Tar**

Burns from hot tar present a treatment challenge. When hot, liquefied tar comes in contact with skin, heat is transferred, and thermal injury results. The tar cools and solidifies on the skin, making removal difficult. There are two types of hot tar: coal tar pitches and petroleum-derived asphalts. Both products are heated to maintain a liquid form. Roofing tar needs to be heated to temperatures of at least 232° C in order to achieve desirable viscosities. Deeper burn injuries are associated with burns from roofing asphalt.

When hot tar touches skin, it rapidly cools, solidifies, and becomes enmeshed in the hair. It is important to facilitate this cooling process by adding cold water to the tar at the scene of the accident. Cooling tar with cold water limits the amount of tissue damage and prevents the spread. The tar is continually washed with water until it has cooled and hardened. After cooling, the skin is dried with towels to prevent systemic hypothermia.

Adherent tar should not be removed at the scene of the accident. In the emergency department, definitive care of tar burn injury involves early removal of tar because it occludes injured skin and encourages bacterial growth. Tar adheres to skin because it is enmeshed in the hair, not because of a direct bond between epidermis and tar.

Solvents used to remove tar ideally should have a close structural affinity to tar. Both petroleum-based aromatic hydrocarbon solvents and surface-active agents, such as polyoxyethylene sorbitan (Tween 80) and polysorbate (De-Solv-it), have been used to facilitate tar removal. The last two agents are more water soluble and may remove tar more easily than the petroleum-based products. Use of these surface-active agents is an effective, safe, and inexpensive means of removing tar from skin. Sunflower oil, NISA baby oil, mayonnaise, and butter have also been used to remove adherent tar from skin, requiring 30 to 90 minutes for complete removal. Sunflower oil has proved effective and safe in removing tar without causing further skin damage.

Asphalts are susceptible to both aromatic (e.g., naphthalene) and aliphatic (e.g., hexade) hydrocarbon solvents, whereas coal tars are susceptible only to aromatic hydrocarbons. Broad-spectrum antibiotic ointments can be used both to help with removal and to help prevent infection. If used, they should be removed and a new coating applied every hour until all the tar has been removed. This process typically takes 12 to 48 hours. Commonly used antibiotic ointments include bacitracin (400 µg/g), polymyxin B (5000 U/ kg), and neomycin (5 mg/g). Antibiotic ointment can be used to remove tar layered over the cornea and conjunctiva.

**Elemental Metals**

The elemental metals, such as lithium, sodium, and potassium, are harmless unless they come in contact with water. When this happens, a violent exothermic reaction occurs that produces heat, hydrogen gas, and hydroxide. The evolved heat is sufficient to ignite the hydrogen gas, which results in further heat production and thermal burns. The formation of the hydroxide compound may also result in significant chemical injury to tissue. The reaction occurs more rapidly with elemental potassium than with sodium. These deleterious effects of potassium have been attributed to trace amounts of potassium superoxide released on exposure to room air. Water lavage is therefore contraindicated in these circumstances.

**Miscellaneous Gases**

Chlorine and phosgene (COCl₂) were both used during World War I as part of chemical warfare. However, today, exposure to chlorine most commonly results from accidental industrial exposure. Phosgene is still used in the production of polyurethanes.

Chlorine is a heavy greenish-yellow gas or liquid with a characteristic odor. The combination of bleach (sodium hypochlorite) with an acid produces chlorine gas, and the combination of bleach and ammonia produces chloramine gas. Both chlorine and chloramine gas produce similar toxicities. The clinical effects observed after chlorine or chloramine exposure are directly related to the time and concentration of the gas. Mild exposure may simply cause mucosal membrane irritation, whereas more severe exposure will induce edema of both the upper airway and the lung parenchyma. With large doses, this edema results in cellular exudates, pulmonary congestion, hemorrhage, and ultimately acute lung injury or acute respiratory distress syndrome. In addition, increased secretions, coughing, dyspnea, wheezing, and chest tightness can be observed. Because these gases are primarily reactive only at a local level, absorbed systemic effects are not commonly observed.

In contrast to chlorine or chloramine, phosgene is much less water soluble. As a result, injury to the lower airways is common, resulting in more severe noncardiogenic pulmonary edema.

The first step in treating an exposure to chlorine, chloramine, or phosgene gas is removal of the individual from the environment. After significant exposure to these agents, the patient’s cardiopulmonary status should be assessed. Endotracheal intubation may be required. Bronchospasm is treated with beta-agonists such as albuterol. Irritation of the eyes is managed with copious irrigation with water or saline, followed by an assessment for corneal abrasions if persistent eye irritation is noted. Nebulized 4% sodium bicarbonate can be used for treatment of chlorine or chloramine gas exposure. The role of systemic corticosteroids, if any, has not been established.

Nitrogen oxides include nitrogen dioxide (NO₂), nitric oxide (NO), and nitrous oxide (N₂O). Nitrogen dioxide toxicity can occur from the burning of nitrocellulose, from use of Zamboni machines in poorly ventilated areas, and from silo filler’s disease, in which the gas accumulates within a silo of decomposing grain. Nitrogen dioxide fumes can often be easily recognized because of their reddish-brown color. The nitrogen oxides can cause respiratory tract irritation. Toxicity varies somewhat depending on the oxide, but severe toxicity can result in delayed pulmonary edema, hypotension, hemoptysis, and methemoglobinemia.

Zinc or aluminum phosphide pellets are often used as rodenticides. When the phosphide pellets come in contact with water, phosphine (PH₃) gas is formed. In addition, phosphine gas can also be formed during the production of methamphetamine from red phosphorus. Inhalation of phosphine gas produces near instantaneous symptoms. Toxicity occurs via several mechanisms, including free radical formation, inhibition of cytochrome oxidase, and increased lipid peroxidation. Both pulmonary toxicity and gastrointestinal toxicity result after exposure to phosphine gas. Common pulmonary symptoms include cough, chest tightness, and dyspnea, followed later by pulmonary edema.
and acute lung injury. Vomiting, diarrhea, and abdominal pain are also commonly encountered. Coma, seizures, hypotension, renal failure, and various dysrhythmias are common.\textsuperscript{26} Treatment is largely supportive. Trimetazidine, an antiarrhythmic, has been reported in the treatment of phosphine-induced dysrhythmias but is not currently available in the United States.\textsuperscript{27}

Phosgene, phosphene, nitrogen dioxide, nickel carbonyl, diborane, and zinc smoke bombs can cause delayed-onset pulmonary edema. Therefore patients exposed to these chemicals are best admitted for observation, even if asymptomatic early on. In addition, chlorine gas, chloramine gas, cadmium, and polymer fume fever can cause delayed pulmonary edema. However, unlike the former group of gases, with which patients can be asymptomatic for hours and then develop pulmonary edema, delayed pulmonary edema is unlikely with chlorine, chloramine, cadmium, and polymer fume fever in the absence of earlier pulmonary symptoms, and asymptomatic individuals who have been exposed to these chemicals therefore do not require prolonged observation.

**CHEMICAL TERRORISM**

After the terrorist attack on September 11, 2001, the public has become increasingly aware of chemical terrorism. Despite being banned by the 1925 Geneva Convention, chemical weapons have been used in both the military and the civilian arenas for many years, including the decades preceding the September 11 attack. In the 1980s, chemical weapons were employed against Iraqi civilians. In 1995, Aum Shinrikyo, a Japanese cult, released VX nerve gas in the Tokyo subway, causing 12 deaths and more than 5000 casualties.\textsuperscript{28}

As terrorist organizations continue to use unconventional weapons such as chemical and biologic agents, the civilian medical community needs to better understand their characteristics and pathophysiology.

**Response**

The U.S. government recognizes the emerging threat of terrorism and the potential for terrorist organizations to use unconventional weapons. Appropriate casualty triage remains a critical component of dealing with unconventional weapons. Triage should be performed by specially trained emergency medical personnel who are familiar with these agents and with the use of PPE. The emergency department could be quickly overwhelmed with masses of noncritically injured survivors. Ideally, triage would be conducted both at the scene of the attack and again at a second point before emergency department arrival. The greatest challenge for emergency departments in caring for these individuals is the sudden increase in patients requiring treatment.\textsuperscript{29}

**Chemical Agents**

Chemical agents are classified as (1) nerve agents, (2) vesicants, (3) choking agents, or (4) cyanide and related toxins (Table 64-1). The first nerve agent documented was tabun, which was synthesized by German chemist Gerhard Schrader in 1937. Schrader developed tabun (military symbol: GA) while researching new insecticides. The following year, sarin (GB) was created. Other popular nerve agents include soman (GD) and VX. Although nerve agents were stockpiled for use during both World Wars, the first documented use in a war was in the 1980s during the Iran-Iraq War. The largest use of nerve agents by terrorists was by the Aum Shinrikyo cult of Japan, which produced both VX and sarin.

Vesicants, also known as blistering agents, are a class of drugs that produce blisters at the site of contact. Despite their discovery in the 1800s, their introduction to warfare did not occur until the 20th century. Since World War I, however, sulfur mustard (also known as mustard gas, mustard, or CAS No. 505-60-2) has remained a constant threat in modern warfare. Other vesicants include lewisite (dichloro-2-chlorovinylarsine), which is an organic arsenical, and phosgene (dichloroformoxime), which is a halogenated oxime. Although phosgene is often considered a vesicant, it technically is not, as the urticarial lesions that develop after contact are not fluid-filled.

Choking agents have been used in both military and civilian settings. Although there are many different agents and uses, the collective term *choking agent* refers to a chemical that can potentially induce pulmonary edema. Phosgene and chlorine are two agents that were used in World War I. Although chlorine is no longer used as a warfare agent, it is still used widely in the industrial setting. Zinc-containing smoke is another choking agent that is used in conventional warfare. Other agents are used for riot control. These agents were discussed earlier in the section on miscellaneous gases.

Cyanide agents, such as hydrogen cyanide or sodium azide, are cellular toxins. Cyanide was discovered in the 18th century by the Swedish chemist Carl Wilhelm Scheele. Today, hydrogen cyanide is one of the most toxic chemicals known, with potential deadly consequences if used by a terrorist organization.

**Nerve Agents**

The nerve agents are classified as either “G” agents or “V” agents. The nerve agents are all derived from phosphoric acid and are volatile liquids at room temperature. As such, they must be aerosolized or evaporated in order to be used as an inhalational weapon. Because the vapors are heavier than air, they tend to remain close to the ground and will travel downwind and downhill.

The nerve agents work by affecting acetylcholine (ACh). ACh receptors are found on the postsynaptic receptor of cholinergic synapses. These receptors can be either nicotinic or muscarinic. Activation of the nicotinic receptors results in depolarization of the postsynaptic neuron or skeletal muscle cell, whereas

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Table 64-1 Common Gases That Can Be Encountered as Weapons of Mass Destruction

<table>
<thead>
<tr>
<th>CLASS</th>
<th>EXAMPLE*</th>
<th>TREATMENT</th>
</tr>
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<tbody>
<tr>
<td>Nerve agents</td>
<td>Tabun (GA)</td>
<td>Atropine and pralidoxime</td>
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<tr>
<td></td>
<td>Sarin (GB)</td>
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<tr>
<td></td>
<td>Soman (GD)</td>
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<tr>
<td></td>
<td>Cyclosarin (GF)</td>
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<tr>
<td></td>
<td>VX</td>
<td></td>
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<tr>
<td>Vesicants</td>
<td>Mustard agents</td>
<td>Hydrotherapy</td>
</tr>
<tr>
<td></td>
<td>Mustard, sulfur mustard (H)</td>
<td>Moist dressing on blisters</td>
</tr>
<tr>
<td></td>
<td>Distilled mustard, sulfur mustard (HD)</td>
<td>Supportive care</td>
</tr>
<tr>
<td></td>
<td>Nitrogen mustard (HN1, HN2, HN3)</td>
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<tr>
<td></td>
<td>Organic arsenical agents (e.g., lewisite; L)</td>
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<tr>
<td></td>
<td>Halogenated oxime agents (e.g., phosgene oxime; CX)</td>
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</tr>
<tr>
<td>Choking agents</td>
<td>Phosgene (CG)</td>
<td>Supportive care</td>
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<tr>
<td></td>
<td>Chlorine (CL)</td>
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<td></td>
<td>Military smoke (HC)</td>
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<td></td>
<td>Chloropicrin (PS)</td>
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<tr>
<td>Cyanide agents</td>
<td>Hydrogen cyanide</td>
<td>Cyanide kit</td>
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<td></td>
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<td>Amyl nitrite</td>
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<td></td>
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<td>Sodium nitrite</td>
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<td></td>
<td></td>
<td>Sodium thiosulfate</td>
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<tr>
<td></td>
<td></td>
<td>Hydroxocobalamin</td>
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</tbody>
</table>

*Chemical or common name (military chemical symbol).
muscarnic activation affects exocrine glands and smooth muscle, primarily in the CNS. Under normal conditions, the enzyme acetylcholinesterase hydrolyzes ACh in the synapse, thereby inactivating ACh. The primary mechanism of action of the nerve agents is to prevent acetylcholinesterase from hydrolyzing ACh. As a result, excess ACh accumulates in the synapse. The effects at the muscarinic receptors include excess secretions and smooth muscle contractions. The mnemonics DUMBELS (diarrhea, urination, miosis, bronchoconstriction or bronchorrhrea, emesis, lacrimation, and salivation) and SLUDGE (salivation, lacrimation, urination, defecation, and gastrointestinal emesis) are often used to describe these effects. The nicotinic manifestations include muscle fasciculations and weakness. The primary clinical toxic effects are respiratory, however, and treatment should be aimed at correcting these effects.

Victims of dermal exposure are undressed and thoroughly decontaminated with large-volume, low-pressure irrigation with water. After decontamination, the initial treatment is aimed at maintaining an airway and restoring adequate oxygenation and ventilation. If rapid sequence intubation is desired for airway management, the paralytic succinylcholine is used with caution for stopping atropine administration is not improvement in heart rate but, rather, drying of bronchial secretions. Pralidoxime is also administered to patients with suspected or known ingestion with significant symptoms. The traditional dose of pralidoxime is 30 mg/kg (2 g maximum) intravenously over 30 minutes, followed by a maintenance infusion of 8 to 10 mg/kg/hr (650 mg maximum). Pawar and colleagues examined a high-dose strategy of pralidoxime for organophosphate poisoning. In their study, all patients received 2 g of pralidoxime intravenously as a loading dose. Patients were then randomized to receive either 1 g (over 1 hour) every 4 hours for a total of 48 hours or a continual infusion of 1 g/hr for 48 hours. The continual infusion strategy resulted in lower morbidity and mortality compared with the intermittent bolus group. Lastly, benzodiazepines are recommended to prevent and to treat seizure activity. Exact dosage and treatment strategies are not well defined.

For pediatric patients, if accurate weight-based dosage cannot be achieved, children younger than 1 year can receive 0.5 mg atropine, whereas children older than 1 year can receive the standard adult dose of 2 mg atropine as a starting dose.

**Vesicants**

At temperatures below 14°C, mustard exists in the solid form. Once in the liquid or gaseous form, mustard gas can be recognized by its unique garlic or fishlike odor. Mustard vapor is also much heavier than air and, as a result, tends to remain close to the ground. When stored as an oil-based liquid, it can be readily aerosolized and attached to a bomb or shell. Because vaporization occurs slowly, the risk of injury is much greater in cold environments and closed spaces. Several minutes of exposure can result in skin and eye injury, and exposure for more than 30 minutes can lead to respiratory injury and death.

Mustard gas can enter the body after inhalational, dermal, or oral exposures. After entering the body, it functions as an alkylating agent. The altered molecules then interact with proteins and nucleic acids, forming covalent bonds. Mustard is the only vesicant that does not cause immediate pain. Several hours after exposure, manifestations of exposure occur. After exposure to aerosolized mustard gas, cutaneous manifestations appear after a latent period of up to 24 hours. Initial dermal symptoms include burning, itching, and erythema, followed by hyperpigmentation, vesicle formation, and, later, bullae. Electrolyte depletion and secondary bacterial infection can occur if the affected body surface area is large. In addition, inhaled mustard gas can lead to vomiting and diarrhea. Myelosuppression can occur within 3 to 5 days of exposure, resulting in leukopenia and thrombocytopenia. Direct mucosal damage in the respiratory tract can occur, resulting in bronchiolar damage and hemorrhage. The systemic manifestations can occur with any route of exposure.

Treatment consists first and foremost of removing the patient from the environment and decontaminating the vesicant. Water can be used for decontamination if that is all that is available, but it might not be the preferred agent. Currently, the U.S. military recommends using an alkaline hypochlorite solution (pH 10 or 11) as the decontamination method of choice, a 0.5% hypochlorite solution (diluted household bleach [1:9]) is another alternative. However, these solutions should not be used on open abdominal or chest wounds. No specific antidote exists. British antilewisite (BAL; 2,3-dimercapto-1-propanol; dimercaprol) was originally developed as an antidote for lewisite. Although BAL is currently available as a chelator for several heavy-metal poisonings, it should be used cautiously, if at all, for mustard poisonings.

**Cyanide**

Cyanide salts and hydrocyanic acid are commonly used for metal cleaning, precious metal extraction, photographic processes, electroplating, laboratory assays, and jewelry cleaning. In addition, cyanide gas is often liberated from the combustion of plastic-containing compounds. Iatrogenic cyanide toxicity can result from exposure to cyanogens, including plant or herbal cyanogenic glycosides, nitriles, and nitroprusside. There is concern that cyanide can be used by terrorists as a weapon.

Cyanide is a cellular toxin. It binds to both Fe+3 and cobalt. By binding and inactivating the enzyme cytochrome oxidase, which is part of cytochrome a3 on the electron transport chain, cyanide inhibits oxidative phosphorylation. This inhibition results in profound cellular hypoxia and death.

After ingestion of cyanide, patients experience sudden cardiovascular collapse coma and profound metabolic acidosis. A characteristic odor of bitter almonds is frequently discussed but only rarely clinically noted.

Although cyanide levels are confirmatory, they are rarely immediately available and are fraught with difficulty. However, most patients with significant cyanide exposure will have a profound lactic acidosis. In addition, because the cellular utilization of O2 is blocked, venous blood is highly oxygenated. Therefore an elevated mixed venous O2 saturation, or an elevated peripheral venous partial pressure of oxygen (PO2) may be observed. Cyanide toxicity commonly results in shortening of the QT interval, with subsequent “T-on-R“ phenomena. The pulse oximeter reading may be near normal in cyanide toxicity, despite significant cellular hypoxia.

A diagnosis of cyanide poisoning requires careful consideration. The initial treatment focuses on maintaining airway, breathing, and circulation (the ABCs). Standard antiarrhythmic medications are appropriate for the treatment of cyanide-induced arrhythmias. Vasopressors may be required.

First responders need to wear PPE when rescuing a patient unresponsive after cyanide gas exposure. Patients with cyanide salts on their skin must have the salts brushed off, followed by topical irrigation; decontamination from other routes of exposure is rarely indicated. Currently, two specific types of antidotes can be used to treat known or suspected cyanide intoxication. One
method of treatment involves the administration of amyl nitrite, sodium nitrite, and sodium thiosulfate. With this combination of medications, amyl nitrite pearls are broken open, and the patient is allowed to breathe a pearl for 30 seconds of each minute. A new pearl is needed every 3 or 4 minutes. Once intravenous access has been established, 300 mg of sodium nitrite (one 10-mL ampule of 3% solution for adults and 0.12–0.33 mL/kg for children) can be administered. Because sodium nitrite is a potent vasodilator, hypotension can ensue. Therefore the sodium nitrite is administered over a minimum of 5 minutes. After sodium nitrite administration, sodium thiosulfate is administered at a dose of 12.5 g (one 50-mL ampule of a 25% solution for adults and 1.65 mL/kg for children). The function of the nitrites is to induce methemoglobinemia. Thiosulfate enhances transulfuration of hydrogen cyanide to thiocyanate, which is renally excreted. If coexisting carbon monoxide toxicity is suspected, as can occur with smoke inhalation, nitrites should be avoided.

In December 2006, the Food and Drug Administration approved hydroxocobalamin (Cyanokit) for treatment of cyanide intoxication. Hydroxocobalamin binds to cyanide to form cyanocobalamin, which subsequently undergoes renal excretion. Hydroxocobalamin appears to be safe for use in both the hospital and the out-of-hospital settings, although there may be a reddish discoloration of the skin. Its use is also associated with alteration in laboratory measurements of magnesium, iron, aspartate aminotransferase, total bilirubin, and creatinine. In treating a patient for known or suspected cyanide toxicity, nitrites and sodium thiosulfate, hydroxocobalamin, or both can be used.

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The references for this chapter can be found online by accessing the accompanying Expert Consult website.
References


