Chapter 3

VESICANTS

Overview

Sulfur mustard (HD, H), the main focus of this chapter, has posed a military threat since its introduction on the battlefield in World War I. Unless otherwise noted, the term *mustard* refers here to sulfur mustard.

The nitrogen mustards (HN1, HN2, and HN3) were synthesized in the 1930s but were never produced in large amounts for warfare. Mechlorethamine (HN2, Mustargen [Recordati Rare Diseases, Lebanon, NJ]) became the prototypical cancer chemotherapeutic compound and remained the standard compound for this purpose for many years. Lewisite (L) was synthesized during the late stages of WWI but has probably not been used on a battlefield. The lewisite antidote, British anti-Lewisite (BAL; dimercaprol), finds medicinal use today as a heavy metal chelator. Although classified as a vesicant, phosgene oxime (CX) is a corrosive urticant that also has not seen battlefield use. Lewisite and phosgene oxime pose only minor potential military threats and will be discussed briefly at the end of this chapter.

MUSTARD

Summary

NATO Codes: H, HD

Signs and Symptoms: Asymptomatic latent period (hours). Erythema and blisters on the *skin*; irritation, conjunctivitis, corneal opacity, and damage in the *eyes*; mild upper respiratory signs to marked *airway* damage; also gastrointestinal effects and bone marrow stem cell suppression.

Field Detection: Joint Chemical Agent Detector (JCAD), M256A1 Chemical Agent Detector Kit, M18A2 Chemical Agent Detector Kit, Improved Chemical Agent Monitor (ICAM), M90 Chemical Warfare Agent Detector, M8 and M9 Chemical Agent Detector Paper, M21 Remote Sensing Chemical Agent Alarm (RSCAAL), M93 series Fox Reconnaissance System, M272 Chemical Agent Water Testing Kit, M22 Automatic Chemical Agent Detection Alarm (ACADA).

Decontamination: Reactive Skin Decontamination Lotion, 0.5% bleach solution, soap, and water in large amounts.

Management: Decontamination immediately after exposure is the only way to prevent damage. Supportive care of patients; there is no specific therapy.

Nomenclature

Sulfur mustard manufactured by the Levinstein process contains up to 30% impurities (mostly sulfur) and is known as H. Mustard made by a distillation procedure is almost pure and is known as HD (distilled mustard). An early term for the German agent was HS (probably derived from the World War I slang term *Hun Stoffe*).

Overview

Vesicant agents, specifically sulfur mustard (HD and H), constitute both a vapor and a liquid threat to all exposed skin and mucous membranes. Mustard's effects are delayed, appearing hours after exposure. The organs most commonly affected are the skin (with erythema and vesicles), eyes (with mild conjunctivitis to severe eye damage), and airways (with mild irritation of the upper respiratory tract to severe bronchiolar damage leading to necrosis and hemorrhage of the airway mucosa and musculature). Following exposure to large quantities of mustard, precursor cells of the bone marrow are damaged, leading to pancytopenia and increased susceptibility to infection. The gastrointestinal (GI) tract may be damaged, and there are sometimes central nervous system (CNS) signs. There is no specific antidote, and management is symptomatic therapy. Immediate decontamination is the only established way to reduce damage.

History and Military Relevance

Sulfur mustard was first synthesized in the early 1800s and was first used on the battlefield by Germany in July 1917. Despite its introduction late in World War I, mustard produced the most chemical casualties, although fewer than 5% of the casualties who reached medical treatment facilities died. Italy allegedly used mustard in the 1930s against Abyssinia. Egypt apparently employed mustard in the 1960s against Yemen, and Iraq used mustard in the 1980s against Iran and the Kurds. Most recently, in 2005, the Burmese military allegedly used a substance against the Karenni people of Burma causing many of the clinical symptoms seen in mustard victims. Accidental exposure from old ordinance also occurs frequently, with recent events in China in 2003 and Delaware in 2004. Mustard is still considered a major threat agent. The United States manufactured mustard during World War I and World War II. Most of its stockpile has been or is being destroyed.

Physiochemical Characteristics

Mustard is an oily liquid with a color ranging from light yellow to brown. Its odor is similar to garlic, onion, or mustard (hence its name), but because of accommodation of the sense of smell, odor should not be relied on for detection. Under temperate conditions, mustard evaporates slowly and is primarily a liquid hazard, but its vapor hazard increases with increasing temperature. At 100° F (37.7° C) or above, it is a definite vapor hazard. Mustard freezes at 57°F (13.9°C), and since a solid is difficult to disperse, mustard is often mixed with substances with a lower freezing point such as lewisite (the mixture is called HL), so that the mixture will remain liquid at lower temperatures. The mixture HT refers to mustard that has been thickened with small quantities of newer thickening agents to make it even more persistent.

Detection and Protection

The immediately dangerous to life and health (IDLH) concentration of sulfur mustard (H) is 0.003 mg/m^3. Liquid mustard turns M8 paper a ketchup red, and M9 paper will turn pink, red, reddish-brown, or purple when exposed to liquid nerve agents or vesicants, but does not specifically identify either the class of agent or the specific agent. Because the odor of sulfur mustard may be faint or lost after accommodation, olfactory detection of the odor of mustard, garlic, onions, or horseradish is not a reliable indicator of mustard exposure. The detectors in the Table 3-1 have the capacity to detect sulfur mustard at the threshold limits given.

The activated charcoal in the canister of the US Army chemical protective mask adsorbs mustard, as does the charcoal in the chemical protective overgarment. The butyl rubber in the chemical protective gloves and boots is impermeable to mustard. Proper wear of the chemical protective mask and the chemical protective ensemble affords full protection against sulfur mustard.

Table 3-1. Concentration Thresholds for Sulfur Mustard Detection*

Detector	Concentration Threshold
JCAD	2.0 mg/min^3
M256A1	3.0 mg/min^3
M272 (in water)	2.0 mg/min^3
M18A2	0.5 mg/min^3
M21	150 mg/min^3
M90	0.2 mg/min^3
M93A1 Fox	0.01–1.00 μg/L
ICAM	0.1 mg/min^3

*Values change with updated versions; please refer to the manufacturer for the most up to date thresholds.
JCAD: Joint Chemical Agent Detector
ICAM: Improved Chemical Agent Monitor

Mechanism of Toxicity

Mustard vapor and liquid readily penetrate thin layers of most fabrics (but not the chemical protective ensemble) to reach underlying skin. Although mustard dissolves relatively slowly in aqueous solutions such as sweat, the lipophilicity of mustard guarantees effective absorption through even intact skin. Penetration is rapid (1 to 4 μg/cm^2/min) and is enhanced by moisture, heat, and thin skin. This explains the otherwise baffling observation that World War I mustard burns involved the scrotum in 42% of cases, but the presumably more readily exposed hands in only 4% of cases. Ocular and respiratory routes of entry are also important, as is parenteral absorption in casualties with conventional wounds. Ingestion (enteral absorption) was an important route of entry in the sailors who jumped into mustard floating on the sea from an exploding ship that carried the agent, the SS *John Harvey*, docked at Bari Harbor, Italy, during World War II.

Approximately 10% of the amount of mustard that begins penetrating the skin will bind to the skin as "fixed" (reacted) mustard; the remaining 90% of the dose reaches the circulation and is systemically distributed as "free" (unreacted and hydrolyzed) mustard. Mustard is distributed to almost all the organs and tissues, including kidneys, liver, intestines, and lungs, although, because of dilutional effects and reactions of mustard in the bloodstream, clinical effects from systemic distribution are seen only at high doses. After intravenous (IV) administration, mustard disappears from the blood within seconds to minutes. Because of the rapid fixation of mustard to tissue, the fluid inside the blisters that eventually develop at the sites of skin contact contains no free mustard and does not pose a contamination hazard to healthcare providers.

Mustard participates in a variety of biotransformative (metabolic) reactions in the body. Some of these reactions are catalyzed by enzymes, but most absorbed mustard reacts directly by forming covalent bonds (via alkylation) with DNA, RNA, proteins, components of cell membranes, and other macromolecules in the body. Mustard is eliminated primarily in the urine as a byproduct of alkylation.

Toxicity

The median lethal concentration (LCt_{50}) of sulfur mustard dispersed as a vapor in an unprotected group is approximately six times more lethal than in a group with respiratory protection. This demonstrates not only the importance of respiratory protection, but also the fact that sufficient concentrations of vapor and sufficient exposure times render mustard vapor lethal, even in masked individuals. The median lethal dose (LD_{50}) of liquid mustard on the skin is about the amount of a teaspoon or a single condiment yellow mustard packet. Although a teaspoon of a liquid applied evenly to the surface of the skin may cover approximately 20% to 25% of the total body surface area (BSA), the correlation between BSA involvement and deaths from mustard in the field is poor. One plausible reason for this discrepancy is that using BSA figures alone ignores the inhalational component of mustard exposure.

Another conceivable explanation is that measurement solely of affected BSA neglects factors such as the thickness of coverage, subsequent spread, contact time, and continued exposure. A 10 μg droplet of sulfur mustard can produce a small vesicle on exposed skin.

Toxicodynamics (Mechanism of Action)

Absorbed mustard must first dissolve in an aqueous solution such as sweat or extracellular fluid. Although mustard molecules dissolve slowly in such solutions, once dissolved they rapidly (within seconds to a minute or two) rearrange to form extremely reactive cyclic ethylene sulfonium ions that immediately bind to intracellular and extracellular enzymes, proteins, and other cellular components. Mustard has many biological actions, but the exact mechanism by which it produces tissue injury is not certain. According to one prominent hypothesis, biological damage from mustard results from DNA alkylation and crosslinking in rapidly dividing cells, such as basal keratinocytes, mucosal epithelium, and bone marrow precursor cells. This leads to cellular death and inflammatory reaction, and in the skin, protease digestion of anchoring filaments at the epidermal-dermal junction and the formation of blisters. Mustard also possesses mild cholinergic activity, which may be responsible for effects such as early GI symptoms and miosis.

It should be reemphasized that mustard reacts with tissue within minutes of entering the body and that blood, tissue, and blister fluid do not contain free mustard, nor do they represent a contamination risk for medical personnel.

Clinical Effects

Topical effects of mustard occur in the eye, airway, and skin (Table 3-2). Systemically absorbed mustard may produce effects in the bone marrow, GI tract, and CNS. Direct injury to the GI tract may also occur following ingestion of the compound. Combined data from US forces in World War I and Iranians in the Iran-Iraq conflict suggest equal incidence of eye, airway, and skin involvement (between 80% and 90% for each). However,

Table 3-2. Effects of Mustard Vapor

Organ	Severity	Effects	Onset
Eye	Mild	Tearing, itchy, burning, gritty feeling	4–12 hours
	Moderate	Above, plus reddening, swelling of lids, moderate pain	3–6 hours
	Severe	Marked swelling of lids, possible cornea damage, severe pain	1–2 hours
Airways	Mild	Runny nose, sneezing, nosebleed, hoarseness, hacking cough	12–24 hours
	Severe	Above, plus severe productive cough, shortness of breath	2–4 hours
Skin	Mild to severe	Erythema (redness), blisters	2–24 hours

incidences of eye and lung damage were higher in Iranian casualties than in World War I casualties, probably because of the agent's increased evaporation in the hot climate.

Skin

Erythema is the mildest and earliest form of skin injury after exposure to mustard. It resembles sunburn and is associated with pruritus or burning, stinging pain. Erythema begins to appear in 2 to 48 hours after vapor exposure with time of onset dependent on concentration-time product (Ct), ambient temperature and humidity, and skin site exposed. The skin sites most sensitive are the warm, moist locations with thinner skin such as the perineum, external genitalia, axillae, antecubital fossae, and neck.

Within the erythematous areas, small vesicles can develop that may later coalesce to form bullae. The typical bulla, or blister, is large, dome-shaped, thin-walled, translucent, yellowish, and surrounded by erythema. The blister fluid is clear, at first thin and straw-colored but later yellowish and tending to coagulate. The fluid does not contain mustard and is not a vesicant.

At extremely high doses such as those from liquid exposure, lesions may develop a central zone of coagulation necrosis with

blister formation at the periphery. These lesions take longer to heal and are more prone to secondary infection than the uncomplicated lesions seen at lower exposure levels.

Pulmonary

The primary airway lesion from mustard is necrosis of the mucosa, with later damage to the airway musculature if the amount of agent is large. The damage begins in the upper airways and descends to the lower airways in a dose-dependent manner. Usually the terminal airways and alveoli are affected only as a terminal event. Pulmonary edema is not usually present unless the damage is very severe, and then it is usually hemorrhagic.

The earliest effects from mustard, perhaps the only effects from a low Ct, involve the nose, sinuses, and pharynx. There may be irritation or burning of the nares, epistaxis, sinus pain or irritation, and irritation or soreness of the pharynx. As the Ct increases, other effects occur, such as laryngitis with voice changes and a nonproductive cough, and damage to the trachea and upper bronchi leading to a cough productive of sputum. Lower airway involvement causes dyspnea and an increasingly severe cough with increased quantities of sputum. Terminally, there may be necrosis of the smaller airways with hemorrhagic edema into surrounding alveoli (although this hemorrhagic pulmonary edema is rare).

Necrosis of the airway mucosa with resulting inflammation can cause pseudomembrane formation. Pseudomembranes may occur from the most proximal parts of the airways to the most distal portions. These membranes may cause local airway restriction at the sites of formation, and detachment may lead to obstruction of lower airways.

The cause of death in mustard poisoning is commonly respiratory failure. Mechanical obstruction by pseudomembranes and agent-induced laryngospasm are important causes of death in the first 24 hours after exposure. Deaths occurring from the third to the sixth day after exposure result from secondary bacterial pneumonia caused by bacterial invasion of denuded respiratory mucosa and necrotic debris. Agent-induced bone

marrow suppression is a contributory factor in later, septic deaths from pneumonia.

Eyes

The eyes are the organs most sensitive to mustard vapor injury. The latent period is shorter for eye injury than for skin injury and is also Ct dependent. After low-dose vapor exposure, irritation evidenced by reddening of the eyes may be the only effect. As the dose increases, the spectrum of injury includes progressively more severe conjunctivitis, photophobia, blepharospasm, pain, and corneal damage.

Blisters do not normally form in the eyes. Instead, swelling and loosening of corneal epithelial cells lead to corneal edema and clouding with leukocytes (which affects vision). Corneal vascularization with secondary edema may last for weeks. Scarring between the iris and lens may follow severe effects; this scarring may restrict pupillary movements and may predispose victims to glaucoma.

The most severe damage is caused by liquid mustard from airborne droplets or by self-contamination. After extensive eye exposure, severe corneal damage with possible perforation of the cornea and loss of the eye can occur. Eye loss also results from panophthalmitis if appropriate therapy is not instituted. Miosis noted after mustard exposure in both humans and experimental animals is probably from the cholinomimetic activity of mustard.

During World War I, mild conjunctivitis accounted for 75% of eye injuries, with recovery in 1 to 2 weeks. Moderate conjunctivitis with minimal corneal involvement, blepharospasm, edema of the lids and conjunctivae, and orange-peel roughening of the cornea accounted for 15% of the cases, with recovery in 4 to 6 weeks. Severe corneal involvement accounted for 10% of the cases. Those with permanent corneal damage accounted for less than 1% of cases. About 0.1% of these severe casualties would meet the criteria for legal blindness today.

Gastrointestinal Tract

The mucosa of the GI tract is very susceptible to mustard damage, from either systemic absorption or ingestion of the

agent. However, reports of severe GI effects from mustard poisoning are relatively infrequent. Mustard exposure, even exposure to a small amount, will often cause nausea, with or without vomiting, lasting 24 hours or less. However, the nausea and vomiting appear to result not from the agent's effects on the GI tract, but rather from a stress reaction, a nonspecific reaction to the odor, or cholinergic stimulation by mustard. Further GI symptoms are usually minimal unless the exposure was severe (even then, GI signs are not common) or resulted from ingestion of contaminated food or drink. Diarrhea has been reported; constipation is equally common. Diarrhea (rarely bloody) and vomiting beginning days after a high-dose exposure imply a poor prognosis.

Central Nervous System

The CNS effects of mustard remain poorly defined. Animal research has demonstrated that mustards (particularly the nitrogen mustards) are convulsants, and several human case reports describe victims exposed to very large amounts who had neurological effects within several hours after exposure, just prior to death. Reports from World War I, and again from Iran, described people exposed to small amounts of mustard who appeared sluggish, apathetic, and lethargic. These reports suggest that minor psychological problems could linger for a year or longer.

Time Course of Effects

Mustard binds irreversibly to tissue and causes tissue damage within several minutes of contact without causing any concomitant clinical effects such as burning or erythema. To prevent injury, *decontamination must be carried out immediately after contact*. If decontamination is not carried out immediately after exposure, there is no way to prevent injury. Because of the lack of immediate effects, the contaminated person is often unaware of the exposure and does not decontaminate. Later decontamination may prevent further damage, absorption, or spread of the agent.

After a high-dose exposure, signs and symptoms may appear

as early as 2 hours after contact. Following a low-dose vapor exposure, the latent or asymptomatic period may extend to 48 hours. There are several reports of individuals exposed to very large amounts who died within hours; this type of occurrence is extremely rare. The typical onset time is between 4 and 8 hours. The concentration of the mustard vapor, time of exposure, ambient weather, and body site exposed are factors in onset time.

Differential Diagnosis

Of the three vesicant agents, mustard is the only one that does not cause immediate pain. The casualty is asymptomatic until the lesion becomes apparent hours later. Lewisite and phosgene oxime, in contrast, cause immediate pain or irritation to the eye, skin, or respiratory tract, which is sufficient stimulus to decontaminate immediately or to mask.

Isolated small blisters or a small group of blisters suggest possible exposure to mustard as well as to plants such as poison ivy or poison oak, drugs, or other substances. The physical characteristics of the lesion are not distinctive; therefore, the history of exposure is invaluable. Although the blisters of mustard and lewisite are slightly different (there is less erythema around the lewisite blister), this distinction is of little value in individual cases.

Laboratory Findings

Leukocytosis occurs during the first day, and the magnitude of increase in leukocytes during subsequent days correlates roughly with the amount of tissue injury, primarily to skin or pulmonary tissue. If systemic absorption is large, leukocytes in the peripheral blood will decrease beginning on day 3 to day 5; this decrease indicates damage to precursor cells in the blood-forming organs. The decrease may be precipitate, for example, a decrease of 5,000 to 10,000 cells per day. If the marrow damage is severe, erythrocytes and thrombocytes may decrease later, but the casualty usually recovers or dies before this is apparent. A leukocyte count of 500 or fewer is a sign of an unfavorable prognosis.

Signs of a chemical pneumonitis may appear within the first 2 to 3 days after inhalation exposure. Leukocytosis, fever, and sputum production suggest a bacterial process, but within this time period sputum cultures are usually negative for pathogens. Organisms commonly invade the damaged airway tissue at days 3 to 5. A change in the fever pattern, an increase in leukocytosis, and a change in the character of the sputum in this time period suggest a bacterial process. Sputum Gram stain and culture should be done for identification of the specific organism. Damaged skin should be cultured routinely, particularly if there is an increase in the exudate or in the inflammatory reaction.

Although GI bleeding is unusual, declining hematocrit values should prompt serial analyses of stool for occult blood. Thiodiglycol, a urinary metabolite of sulfur mustard, can be measured in a deployed Army medical laboratory. There is no clinical laboratory test for mustard in blood or tissue, nor is one expected since mustard is biotransformed and bound to tissues within minutes after absorption. However, ways to measure blood and tissue adducts produced in the body after reaction with sulfur mustard are being studied.

Medical Management

The management of a patient exposed to mustard may be simple, as in providing symptomatic care for a sunburn-like erythema, or extremely complex, as in providing total management for a severely ill patient with burns, immunosuppression, and multisystem involvement. Suggested therapeutic measures for each organ system are provided below. Guidelines for general patient care are not intended to take the place of sound clinical judgment, especially in the management of complicated cases.

Skin

Erythema should be treated with calamine or another soothing lotion or cream (eg, 0.25% camphor and menthol) to reduce burning and itching. Small blisters (under 1–2 cm) should be left intact, but because larger ones will eventually break (the

blister fluid does not contain mustard), they should be carefully unroofed, or the fluid can be aspirated. Denuded areas should be irrigated three to four times daily with saline, another sterile solution, or soapy water and then liberally covered with a topical antibiotic such as silver sulfadiazine or mafenide acetate to a thickness of 1 to 2 mm. If an antibiotic cream is not available, sterile petrolatum may be useful. Modified Dakin solution (sodium hypochlorite) was used in World War I and in Iranian casualties for irrigation and as an antiseptic. Multiple or large areas of vesication suggest the need for hospitalization and whirlpool bath irrigation.

Systemic analgesics should be used liberally, particularly before manipulation of the patient or irrigation of the burn areas. Systemic antipruritics such as trimeprazine should be tried if needed. Monitoring of fluids and electrolytes is important in any sick patient, but it must be recognized that fluid loss is not of the magnitude seen with thermal burns. Clinicians accustomed to treating patients with thermal burns must resist the temptation to overhydrate a mustard casualty with a similar amount of burned body surface.

Eyes

Conjunctival irritation from a low Ct will respond to any of a number of available ophthalmic solutions after the eyes are thoroughly irrigated. Regular application of homatropine (or other anticholinergic drug) ophthalmic ointment will reduce or prevent future synechiae formation. A topical antibiotic applied several times a day will reduce the incidence and severity of infection. Vaseline or a similar substance should be applied to the edges of the lids regularly to keep them from sticking together. This prevents adhesions and later scarring during healing and also permits drainage of any underlying infection or pus. Topical analgesics may be useful initially if blepharospasm is too severe to permit an adequate examination, but topical analgesics should otherwise be avoided, and systemic analgesics should be given for eye pain. Topical steroids are not of proven value, but their use during the first day or two might reduce inflammation. Further use should be left to an ophthalmologist. Sunglasses may reduce discomfort from photophobia. The patient should

be constantly reassured that complete healing and restoration of vision will be the outcome.

Pulmonary

Upper airway symptoms (sore throat, nonproductive cough, and hoarseness) may respond to steam inhalation and cough suppressants. Although a productive cough and dyspnea accompanied by fever and leukocytosis occurring 12 to 24 hours after exposure may suggest a bacterial process, clinicians must resist the urge to use antibiotics to treat these symptoms, which result from sterile bronchitis or pneumonitis. Infection often occurs on about the third day. Its presence is signaled by an increased fever, an increase in the pulmonary infiltrate by x-ray, and an increase in sputum production and change in sputum character to purulent. Appropriate antibiotic therapy should await confirmation of the clinical impression by positive sputum studies (Gram stain and culture).

Intubation should be performed early, before laryngeal spasm or edema makes it difficult or impossible. Intubation permits better ventilation and facilitates suction of the necrotic and inflammatory debris. Oxygen may be needed, and early use of positive end-expiratory pressure or continuous positive airway pressure may be of benefit. If there is a suggestion of pseudomembrane formation, bronchoscopy should be performed to permit suctioning of the necrotic debris by direct vision.

Bronchodilators may be of benefit for bronchospasm. If they fail, steroids may be tried. There is little evidence that the routine use of steroids is beneficial. The need for continuous use of assisted or controlled ventilation suggests a poor prognosis.

Death often occurs between the 5th and 10th day after exposure because of pulmonary insufficiency and infection complicated by a compromised immune response from agent-induced bone marrow damage.

Gastrointestinal

Atropine (0.4–0.6 mg, intramuscular or IV), another anticholinergic drug, or an antiemetic should control the early nausea and vomiting. Prolonged vomiting or voluminous diarrhea beginning

days after exposure suggests direct involvement of the GI tract by severe systemic poisoning, a poor prognostic sign.

Bone Marrow

Alteration of gut flora by nonabsorbable antibiotics should be considered to reduce the possibility of sepsis from enteric organisms. Cellular replacement (bone marrow transplants or transfusions) may be successful, because intact mustard does not persist beyond the few minutes following absorption and would not damage the new cells.

General

A patient severely ill from mustard poisoning requires the general supportive care provided for any severely ill patient, as well as the specific care given to a burn patient. Liberal use of systemic analgesics and antipruritics, as needed, maintenance of fluid and electrolyte balance, and other supportive measures are necessary. Parenteral nutrition and supplements, including vitamins, may also be helpful.

In studies, sulfur donors such as sodium thiosulfate decreased systemic effects and elevated the LD_{50} when given before exposure or within 20 minutes after exposure in experimental tests. Activated charcoal given orally to casualties was of no value. Hemodialysis was not only ineffective, but actually harmful in several casualties. The rapid biotransformation of the mustard molecule suggests that none of these measures would be beneficial hours or days after exposure.

Triage

Most mustard casualties will be triaged as *delayed*. Those with skin lesions covering a small percentage to half of the BSA require further medical care but do not need immediate lifesaving assistance. (In contrast, patients with thermal burns covering 20% to 70% of BSA are considered immediate because of their fluid requirements.) Those with mild to moderate pulmonary effects will also eventually require further care but are not in the immediate category for triage. Eye injuries from other causes

require immediate care, but by the time the mustard eye lesion develops, there is no possibility of reducing the injury. These casualties are also in the delayed category.

Patients with skin lesions covering a small percentage of BSA (under 5%) when the lesions are not in vital areas (eg, a burn on the face might prevent mask donning) are triaged as *minimal*. Clinical judgment should dictate whether these patients should be evacuated for care or whether they can return to duty. The tactical situation will also be a factor in the decision. Patients with minor eye injuries including irritation and reddening can be treated and returned to duty. Those with slight upper respiratory complaints such as a hacking cough and irritated throat that developed 12 hours or longer after exposure might be given symptomatic therapy and returned to duty.

The only mustard casualties who might be triaged as *immediate* are those with moderately severe to severe pulmonary signs and symptoms. Two factors should temper this decision. First, casualties who develop severe pulmonary effects within 4 to 6 hours of exposure will probably not survive despite maximal medical care, and it might be better to expend limited medical resources elsewhere. Second, if evacuation to a higher role of care is required, some casualties may survive the lengthy trip, but their lesions may progress to an irreversible stage during the delay.

A mustard casualty who has severe pulmonary effects that developed within 4 to 6 hours of exposure should be triaged as *expectant*. A casualty who has over 50% BSA burns from mustard liquid might also be categorized as expectant, but this decision depends on available medical resources at the far rear roles of medical care. (The LD_{50} for liquid mustard is about a teaspoon of liquid. This amount will cover about 25% BSA, so an individual with a 50% BSA burn could possibly have two LD_{50} lesions on his or her skin. This person might be saved, but at great expenditure of medical resources.)

Long-Term Effects

Repeated symptomatic exposures to mustard over a period of years (such as manufacturing workers might experience) seem to be well established as a causal factor in an increased incidence of

upper-airway cancer. However, the association between a single exposure to mustard and airway cancer is not well established. A single, severe exposure to mustard may have contributed to other airway problems, such as chronic bronchitis, in World War I casualties. A new complication seen in Iranian casualties from the Iran-Iraq War in the 1980s was late-onset tracheobronchial stenosis, which presumably would have been seen in World War I casualties had antibiotic therapy been available to save the lives of those who died from secondary bacterial pneumonia.

Several eye diseases, such as chronic conjunctivitis and delayed keratitis, may follow a single severe exposure of the eye to mustard. Skin scarring and pigment changes may follow a severe skin lesion from mustard, and cancer sometimes develops in scarred skin.

Mustard is classed as a mutagen and carcinogen, based on laboratory studies. However, there are no data to implicate mustard as a reproductive toxin in humans, and there is no evidence that mustard is a causative factor in nonairway, non-skin cancer in humans.

Supplemental Considerations for Treatment and Disposition

In addition to the treatment modalities cited above, ongoing research on the management of mustard injuries and observation of sulfur mustard accidents that occurred in the United States and abroad has resulted in the information summarized below. The only major information on human mustard casualties is from World War I and the Iran-Iraq conflict in the 1980s because human mustard injury research is unethical.

Eye

Research at the US Army Medical Research Institute of Chemical Defense (USAMRICD) has shown remarkable results using steroids and antibiotic eye combinations. Eyes that would have been nearly destroyed appeared almost normal when these combinations were applied early and frequently. In the study, the treatments were given both by injection and topically in the form

of solutions and ointments. The results were so remarkable that commercially available ophthalmologic steroid and antibiotic solutions or ointments were recommended for inclusion in the field medical sets. The recommended application is as soon as possible in connection with even the mildest mustard eye injury. The frequency of use is every 1 to 2 hours until the full extent of the developing mustard injury becomes known. The treatment should then be modified accordingly, with consultation and examination by an ophthalmologist as soon as possible. This initial treatment should be applied only in the absence of a penetrating injury to the eye or in the case of obvious, secondary bacterial infection. Narcotic analgesia may be used if eye pain is severe.

Exposure to sulfur mustard can lead to a chronic eye inflammation with associated pain, erosions, and even frank ulceration. This keratitis has been seen to develop as early as 8 months and as late as 20 years after initial exposure. It does not seem to be associated with severity of exposure, although a higher incidence with more severe exposures may be expected. Mustard-induced chronic keratitis was either infrequent or undetected in the years following World War I.

Pulmonary

No specific antidotes for mustard injury to the lung exist; however, standard supportive care should be employed for all pulmonary injuries. Mustard injuries to the trachea and bronchi have a high rate of secondary bacterial infection starting as early as 3 days and developing as late as 2 to 3 weeks after exposure. Late development is especially frequent with doses leading to significant bone marrow depression. Prophylactic administration of antibiotics is contraindicated and will lead to the selection of resistant bacterial infections. Vigilant lookout for the early signs and symptoms of infection, and Gram stain and cultures to aid selection of the most appropriate antibiotic, are key.

The sloughing of necrotic bronchial mucosa, as pseudomembranes or as amorphous debris, can be severe enough to cause mechanical blockage and suffocation. Soldiers in World War I died from these blockages. Treatment is rigorous percussion, postural drainage, and provision of humidified air

with supplemental oxygen. At times, fiberoptic bronchoscopy may be needed to remove the blockage.

A complication not reported from World War I, but seen in casualties from the Iran-Iraq War in the 1980s, is severe tracheobronchial stenosis. Bronchospasm with asthma-like symptoms can be a frequent complication of the mustard lung injury. The medicines used for the bronchospasm are the same as with asthma: β-adrenergic dilators, steroids, and theophylline-type drugs. Steroidal antiinflammatory agents have never been scientifically shown to be beneficial in cases of mustard lung injury. However, if β-adrenergic bronchodilators do not provide complete relief, many clinicians would be quick to add steroids to aid in ending the bronchospasm. Again, caution is warranted because of the likelihood of secondary bacterial infection in cases of exposure to sulfur mustard.

With significant irritation to the larynx, acute closure caused by laryngospasm is possible and may result in death if a patent airway is not maintained. Pulmonary edema is not a normal feature of mustard lung injury except in cases of very large exposures, when hemorrhagic pulmonary edema may be seen. Mounting circumstantial evidence suggests the possibility of chronic bronchial disease developing after significant pulmonary exposure.

Mustard is a proven carcinogen, but no cases of cancer have been documented with acute exposures. However, some factory workers chronically exposed to low doses of sulfur mustard in World War I developed cancers of the respiratory tract (nasopharynx, larynx, and lung). A small amount of laboratory data in rats and mice points to reproductive abnormalities. Anecdotal stories about reproductive abnormalities are now coming out of Iran and Iraq, but these will take years to substantiate with good epidemiological studies. The possibility of a causal link between mustard exposure and late onset or chronic health effects should always be investigated in patients with a documented or suspected history of exposure.

Skin

Vesication may take several days to complete. Mustard blister fluid does *not* contain active sulfur mustard. Once a patient has been adequately decontaminated, medical personnel do not have to fear contamination. Mustard casualties with skin injury may require narcotics for analgesia.

Mustard skin burns are generally more superficial than thermal burns, but the services of an intensive care unit or surgical burn unit may be a necessity. Judicious IV fluid and electrolyte therapy are required with significant mustard skin burns, but fluid requirements are less than with corresponding thermal burns. Fluids and electrolytes should be closely monitored because fluids may be lost to edematous areas, with resultant dehydration. Medical personnel are cautioned not to over-hydrate the patient because hypervolemia and pulmonary edema can be iatrogenically induced in mustard casualties. The exact fluid replacement requirements for cutaneous mustard injuries should be based on patient status and considered on a case-by-case basis.

Multiple techniques exist for caring for mustard skin burns/blisters/wounds: (*a*) leaving the blisters intact; (*b*) removing or debriding the roof of large blisters; (*c*) leaving the blister roof intact and aspiring the fluid with a sterile needle; or (*d*) removing the blister roof and temporarily covering it with artificial or pig skin. A universal measure is the use of a topical antibiotic cream or ointment whether the blister is intact or not. The topical antibiotic depends on individual experience and preference, starting with traditional surgical preparations and working down to whatever is available. A moist wound-healing environment should be maintained during the reepithelialization process for optimal outcome. Initially, the attachment of the neoepidermis to the underlying dermis may be weak, and protective dressings may be needed to avoid or minimize damage as a result of friction with clothing or bedding.

The tremendous inflammation caused by sulfur mustard in human skin can easily be confused with bacterial cellulitis; however, mustard skin wounds can easily develop a secondary bacterial cellulitis, requiring the use of appropriate systemic

antibiotics. Infection surveillance and specialty consultation may be necessary.

It has long been recognized that mustard skin wounds are slow to heal, taking sometimes twice the time that would be expected with a conventional wound or a thermal burn. The hypothesis explaining these observations is that abnormal compounds of DNA (DNA adducts) are produced, delaying the healing time. Also, the skin histologically very often looks more like scar tissue than normal skin. Recent studies in the United States (USAMRICD) and England (Porton Down) have shown that appropriate debridement of the deeper mustard burns leads to more normal healing times and return to regular skin architecture. Good results were obtained with both laser debridement and traditional mechanical techniques. Accurate depth assessment is important, because it dictates how aggressive treatment must be to minimize or prevent cosmetic and functional deficits (eg, deep injuries will need to be excised and grafted). Microcutaneous blood flow is a good prognostic indicator and should be monitored using laser Doppler perfusion imaging or indocyanine green fluorescence imaging.

Bone Marrow

Sulfur mustard, like nitrogen mustard and certain chemotherapeutic compounds, is an alkylating agent. Systemic absorption of sulfur mustard above what would be 25% of a lethal dose can lead to significant bone marrow depression. This is why the systemic effects of sulfur mustard have been described as radiomimetic. The earliest indicator that a patient may have received a significant systemic exposure is nausea and vomiting persisting longer than the first hour or 2 after exposure. Nausea and vomiting 24 hours later is definitely a warning sign. The next most sensitive indicator is a fall in the lymphocyte count; this lymphopenia may occur as early as the first 24 hours. The polymorphonuclear cell count may actually rise in the first 24 hours. Other cellular components of blood may show a significant decline as early as 3 days after exposure, and patients can be in profound marrow suppression by 1 to 3 weeks following exposure. The usual life-threatening complication is sepsis and septic pneumonia. Transfusions, isolation techniques,

hormonal stimulation of the marrow, and appropriate antibiotics may all be utilized.

Studies in nonhuman primates conducted by the US Navy using nitrogen mustard and by the US Army with sulfur mustard showed an improved bone marrow recovery time using granulocyte colony stimulating factor (GCSF). GCSF is a commercially available product for use in standard cases of marrow suppression.

Gastrointestinal

Severe hemorrhagic diarrhea may be caused either by direct ingestion of sulfur mustard or by systemic absorption following exposure by other routes. High doses of sulfur mustard can induce necrosis and sloughing of the GI mucosa. The most important aspect of treatment is IV fluids and electrolytes. Anticholinergics to control bowel spasm and possibly narcotic analgesia are indicated if acute surgical abdomen is not a complication. Hemorrhage may be severe enough to require transfusion.

Central Nervous System

In the first few hours after exposure to sulfur mustard, patients may experience mood swings ranging from depression to euphoria. The mechanism for these mood changes is not understood. Supportive care is indicated. A few individuals in World War I who received massive exposures to sulfur mustard experienced seizures and died rapidly. This phenomenon has also been observed in animals.

Return to Duty

Casualties with minor skin, eye, or pulmonary injuries might be returned to duty as soon as they are given symptomatic therapy at a medical facility. The range of return-to-duty times for those with more severe but treatable injuries is from a week to a year or longer. Those with eye injuries should recover in 1 to 3 weeks, except for the low percentage of casualties with severe injuries or complications. Casualties with mild to moderate pulmonary

injuries should return to duty in a week to a month. Healing of mild skin lesions will enable the casualty to return within several weeks, but patients with large skin lesions will require hospitalization for many months. Because of the slow healing of sulfur mustard injuries, casualties with significant injury to the eyes, respiratory tract, skin, GI tract, or CNS will not return to duty for weeks to months.

Eye

Only individuals with the mildest eye irritations to sulfur mustard will be able to return to duty. The mildest form of conjunctivitis causes a functional blindness caused by pain, photophobia, and spasm of the eyelid muscles; this conjunctivitis takes an average of 2 weeks to resolve. As the severity of the injury increases, so does the time for healing. A moderate conjunctivitis may require 2 full months before return to duty is possible. In rare instances, blindness may result from severe exposures.

Lung

Only individuals experiencing an irritation without significant tissue injury will be able to return to duty. Determining whether patients have received only an irritation or the mildest of injuries will require 3 to 7 days of observation. Anyone with documented mustard lung injury producing a bronchial pneumonia or pseudomembrane formation will not be able to return to duty for several months. Those with severe cases may never return to duty.

Skin

Only casualties with lesions on a small percentage of BSA (less than 5%) in noncritical areas will be able to return to duty following treatment with topical antibiotic, dressings, and oral analgesics. Burns to the hands, feet, face, axillae, and groin are all potentially disabling. Return to duty will require weeks to months in all but the mildest of injuries.

Burns by liquid on the skin and in the eye cause the most severe injury. It is possible in some instances to receive a nearly total body burn from mustard vapor with effects no more severe than

those from second-degree sunburn. A vapor burn of this milder level of severity takes 48 hours or more to develop. However, a vapor burn developing in only a few hours could be as severe as a liquid burn. Severity of a mustard burn is dependent upon the total absorbed dose of vapor and liquid.

Guidelines for Medical Evacuation

A casualty who requires hospital care for longer than 2 weeks, specialty care not available in theater, or intensive care or burn center-level treatment should be medically evacuated as soon as feasible to a Role 3 or 4 facility.

Physical Examination, Laboratory, and Procedures at Role 5

These recommendations pertain *only* to patients requiring Role 5 care. There should be a full, appropriate internal medicine, dermatology, ophthalmology, or burn surgical examination on admission. Serial evaluations should focus on any abnormalities until they are resolved with time and appropriate treatment. Patients with injury involving specific organ systems (eyes, respiratory tract, GI tract, blood, or CNS) should receive consultative care by the appropriate specialists.

Return to duty should be delayed until after full recovery. Temporary duties during convalescence should be appropriate to the patient's condition until full return to duty or medical retirement. After full recovery, the patient should have follow-up evaluations every 6 months with appropriate studies for specific injuries. If problems are found, appropriate care should be given, with return visits as frequently as necessary. After two 6-month follow-up visits showing no problems, the patient should be reevaluated annually for 5 years. Any associated medical problems will extend the period of close follow-up until complete resolution or maximal medical improvement.

In the absence of related medical problems at 5 years, the patient may be discharged to an as-needed follow-up status. However, patients with a mustard eye injury should undergo ophthalmology evaluations every 5 years (or more frequently

as needed) for life, and patients with mustard pulmonary injury (larynx, nasopharynx, trachea, and lung) should undergo a pulmonary evaluation as clinically indicated, and at least every 5 years, for life. Also, patients who have recovered from pancytopenia caused by sulfur mustard should be refered to a hematologist as indicated and at a mnimum every 5 years, for life.

LEWISITE

Summary

NATO Code: L

Signs and Symptoms: Lewisite causes immediate pain or irritation of skin and mucous membranes. Erythema and blisters on the skin and eye and airway damage similar to conditions seen after mustard exposures develop later.

Field Detection: Joint Chemical Agent Detector (JCAD), M256A1 Chemical Agent Detector Kit, M18A2 Chemical Agent Detector Kit, Improved Chemical Agent Monitor (ICAM), M90 Chemical Warfare Agent Detector, M8 and M9 Chemical Agent Detector Paper, M21 Remote Sensing Chemical Agents Alarm (RSCAAL), M93 series Fox Reconnaissance System, M272 Chemical Agent Water Testing Kit, M22 Automatic Chemical Agent Detection Alarm (ACADA).

Decontamination: Reactive Skin Decontamination Lotion, soap and water, 0.5% bleach solution.

Management: Immediate decontamination; symptomatic management of lesions is the same as for mustard lesions; a specific antidote (BAL) will decrease systemic effects.

Overview

Lewisite (L) is a vesicant that damages the eyes, skin, and airways by direct contact. After absorption, it causes an increase in capillary permeability that produces hypovolemia, shock, and organ damage. Exposure to lewisite causes immediate pain or irritation, although lesions require hours to become full-blown. Management of a lewisite casualty is similar to management of a mustard casualty, although a specific antidote, BAL, will alleviate some pathophysiological effects.

History and Military Relevance

Dr. Wilford Lee Lewis first synthesized lewisite in 1918, too late for its use in World War I. It has not been used in warfare, although some countries may stockpile it. Lewisite is sometimes mixed with mustard to achieve a lower freezing point of the mixture for ground dispersal and aerial spraying.

Physiochemical Characteristics

Lewisite is an oily, colorless liquid with the odor of geraniums. It is more volatile than mustard.

Detection and Protection

The IDLH concentration of lewisite is 0.003 mg/m^3. The M8A1 Automatic Chemical Agent Detector Alarm cannot detect lewisite. However, liquid lewisite turns M8 paper red, and M9 paper turns pink, red, reddish-brown, or purple when exposed to liquid nerve agents or vesicants, but does not specifically identify either the class of agent or the specific agent. The detectors in Table 3-3 can detect lewisite at the threshold limits given.

Because the odor of lewisite may be faint or lost after accommodation, olfactory detection of the odor of geraniums is not a reliable indicator of exposure. The activated charcoal in the canister of the chemical protective mask adsorbs lewisite, as does the charcoal in the chemical protective overgarment. Lewisite attacks the butyl rubber in the chemical protective gloves and boots, which are expected to protect against field concentrations of lewisite until they can be exchanged for fresh gloves and boots. Proper wear of the chemical protective mask and ensemble affords full protection against lewisite.

Mechanism of Toxicity

Lewisite is readily absorbed through the skin, eyes, and respiratory tract, as well as by ingestion and via wounds. It is systemically distributed to almost all organs and tissues of the

Table 3-3. Concentration Thresholds for Lewisite Detection*

Detector	Concentration Threshold
JCAD	2.0 mg/min^3
M256A1	14.0 mg/min^3
M272 (in water)	2.0 mg/min^3
M18A2	10.0 mg/min^3
M21	150.0 mg/min^3
M90	0.2 mg/min^3
M93 series Fox	10–100 μg/L
ICAM	2.0 mg/min^3

*Values change with updated versions; please refer to the manufacturer for the most up to date thresholds.
JCAD: Joint Chemical Agent Detector
ICAM: Improved Chemical Agent Monitor

body, where it participates in a variety of chemical reactions. It is eventually eliminated primarily as reaction products in the urine.

Toxicity

Lewisite causes nasal irritation at a Ct of about 8 mg•min/m^3, and its odor is noted at a Ct of about 20 mg•min/m^3. Lewisite causes vesication and death from inhalation at the same Ct as mustard. Liquid lewisite causes vesication at about 14 μg, and the LD_{50} of liquid lewisite applied to the skin is about half that of mustard.

Mechanism of Action

Although lewisite contains trivalent arsenic and combines with thiol groups in many enzymes, its exact mechanism of action is unknown.

Clinical Effects

Unlike mustard, lewisite vapor or liquid causes *immediate* pain or

irritation. A person with a droplet of lewisite on the skin will feel burning and immediately try to remove the substance. The vapor is so irritating that those affected will seek to mask or leave the contaminated area if possible. These immediate steps may lessen severity of lewisite lesions as compared to mustard, because exposure to mustard is often undetected and decontamination is often delayed. There are almost no data on humans exposed to lewisite. The following information is based on laboratory investigations.

Skin

Within about 5 minutes after contact, liquid lewisite will produce a grayish area of dead epithelium. Erythema and blister formation follow more rapidly than in a similar lesion from mustard, although the full lesion does not develop for 12 to 18 hours. The lesion develops more tissue necrosis and tissue sloughing than does a mustard lesion.

Eye

Lewisite causes pain and blepharospasm on contact. Edema of the conjunctiva and lids follows, and the eyes may be swollen shut within an hour. Iritis and corneal damage may follow if the dose is high. Liquid lewisite causes severe eye damage within minutes of contact.

Pulmonary

The extreme irritancy of lewisite to the central airway compartment causes the person to mask or exit the area. Lewisite may cause the same airway signs and symptoms as mustard. The airway mucosa is the primary target, and damage progresses down the airways in a dose-dependent manner. Pseudomembrane formation is prominent. Pulmonary edema, which occurs rarely and usually only to a minimal degree after mustard exposure, may complicate exposure to lewisite.

Other Symptoms

Available data suggest that lewisite causes an increase in permeability of systemic capillaries with resulting intravascular fluid loss, hypovolemia, shock, and organ congestion. This may lead to hepatic or renal necrosis with more prominent GI effects (including vomiting and diarrhea) than after mustard. Physical findings are similar to those caused by mustard. Tissue damage at the site of the skin lesion may be more severe.

Time Course of Effects

Pain and irritation from either liquid or vapor lewisite are immediate. Early tissue destruction is more obvious than after mustard, but the lesion is not full-blown for 12 hours or longer.

Differential Diagnosis

Although differences have been reported between the skin lesions from mustard and lewisite (less surrounding erythema and more tissue destruction characterize lewisite blisters), these are of little diagnostic assistance. The history of immediate pain on contact is absent after mustard exposure and present after lewisite or phosgene oxime exposures. Other substances also cause erythema and blisters, and often the history of exposure is the most helpful tool in diagnosis.

Laboratory Findings

There is no specific diagnostic test for lewisite. Leukocytosis, fever, and other signs of tissue destruction will occur.

Medical Management

Early decontamination is the only method of preventing or lessening lewisite damage. This self-aid must be accomplished within minutes after exposure. Medical treatment follows the guidelines for mustard casualty management. Lewisite does not

cause damage to hematopoietic organs as mustard does; however, fluid loss from the capillaries necessitates careful attention to fluid balance.

BAL is an antidote for lewisite and is used as a chelating agent for heavy metals. There is evidence that BAL in oil, given intramuscularly, will reduce the systemic effects of lewisite. However, BAL itself has some toxicity, and the user should read the package insert carefully. BAL skin and ophthalmic ointment decreases the severity of skin and eye lesions when applied immediately after early decontamination; however, neither is currently manufactured.

Triage

Triage using the guidelines for mustard.

Return to Duty

Casualties with minor skin lesions who receive symptomatic therapy can be returned to duty quickly. Because lewisite generally causes more tissue damage than mustard, casualties with eye and larger skin lesions should be triaged as *delayed* and evacuated. Pulmonary injury casualities may be triaged as immediate, delayed, or expectant depending on the severity of the injury and time of onset.

PHOSGENE OXIME

Summary

NATO Code: CX

Signs and Symptoms: Immediate burning and irritation followed by wheal-like skin lesions and eye and airway damage.

Field Detection: Joint Chemical Agent Detector (JCAD), M256A1 Chemical Agent Detector Kit, M18A2 Chemical Agent Detector Kit, M90 Chemical Warfare Agent Detector, M93 series Fox Reconnaissance System.

Decontamination: Reactive Skin Decontamination Lotion, soap and water, 0.5% bleach solution.

Management: Immediate decontamination, symptomatic management of lesions.

Overview

Phosgene oxime (CX) is an urticant or nettle agent that causes a corrosive type of skin and tissue lesion. It is not a true vesicant because it does not cause blisters. The vapor is extremely irritating, and both the vapor and liquid cause almost immediate tissue damage upon contact. There is very scanty information available on CX.

Military Significance

There is no current assessment of the potential of CX as a military threat agent.

Physiochemical Characteristics

Phosgene oxime is a solid at temperatures below 95° F (35° C), but the vapor pressure of the solid is high enough to produce symptoms. Traces of many metals cause it to decompose; however, it corrodes most metals.

Detection and Protection

The IDLH concentration of CX has not been defined. M8 and M9 paper should not be depended upon to detect this agent. The M256A1 detector ticket reacts to the presence of CX, but the detection threshold is not known with certainty. The detectors in Table 3-4 are capable of detecting CX at the threshold limits given. Because the odor of phosgene may be faint or lost after accommodation, olfactory detection of a pepperish or pungent odor is not a reliable indicator of the presence of CX. The activated charcoal in the canister of the chemical protective mask adsorbs CX, as does the charcoal in the chemical protective overgarment. Phosgene oxime may attack the butyl rubber in the chemical protective gloves and boots, which nevertheless are expected to protect against field concentrations of CX until they can be exchanged for fresh gloves and boots. Proper wear of the chemical protective mask and chemical protective ensemble affords full protection against CX.

Table 3-4. Concentration Thresholds for Phosgene Oxime Detection*

Detector	Concentration Threshold
M18A2	0.5 mg/min^3
M90	0.15 mg/min^3
M93A1 Fox	10–100 μg/L

*Values change with updated versions; please refer to the manufacturer for the most up to date thresholds.

Mechanism of Toxicity

The toxicokinetics of CX are not known in detail. Penetration of exposed surfaces is rapid, and systemic distribution to most organs and tissues, including the GI tract, is probably important.

Toxicity

The estimated LCt_{50} by inhalation is approximately the same as mustard. The LD_{50} for skin exposure has been estimated as approximately three to four times as much as mustard, or about 3 to 4 teaspoons.

Toxicodynamics (Mechanism of Action)

The mechanism by which CX causes biological effects is unknown.

Clinical Effects

Skin

Phosgene oxime liquid or vapor causes pain on contact, which is followed in turn by blanching with an erythematous ring in 30 seconds, a wheal in 30 minutes, and necrosis later. Extreme pain may persist for days.

Eye

Phosgene oxime is extremely painful to the eyes. The damage is probably similar to that caused by lewisite.

Pulmonary

Phosgene oxime is very irritating to the upper airways. This agent causes pulmonary edema after inhalation and after skin contact.

Other

Some animal data suggest that CX may cause hemorrhagic inflammatory changes in the GI tract.

Time Course of Effects

Phosgene oxime causes immediate pain and irritation to all exposed skin and mucous membranes. The time course of damage to other tissue probably parallels that of damage to the skin.

Differential Diagnosis

Other causes of urticaria and skin necrosis must be considered. Common urticants do not cause the extreme pain of CX exposure.

Laboratory Findings

There are no distinctive laboratory findings.

Medical Management

Management is supportive. The skin lesion should be managed in the same way that a necrotic ulcerated lesion from another cause would be managed.

Triage

Because of continuing pain, most casualties should be placed in the *delayed* category and evacuated.

Return to Duty

The decision to return a CX casualty to duty should be based on healing of the lesions and resolution of discomfort.