



Lewisite September 2003

Lewisite: Introduction

Lewisite is the representative chemical of a group of vesicant, or blistering, agents known as dichloroarsines. Lewisite is dangerous because of its vesicant nature and the arsenic it contains.

Overview: Lewisite

The chemical composition of lewisite is 2-chlorovinyl-dichloroarsine. Although first synthesized late in WWI, its use in battle has never been verified. In pure form, lewisite is a colorless, odorless, oily liquid that is heavier than the more common vesicant, sulfur mustard. It is poorly soluble in water but very soluble in organic solvents and it usually contains impurities that give it a brown to blue-black color and the odor of geraniums. It hydrolyzes rapidly so maintaining biologically active concentrations in high humidity is difficult and rainy conditions will neutralize it quickly. It does, however, remain fluid at low temperatures, making it better than the mustards for winter dispersal. Because it is inherently unstable and is more difficult to manufacture than sulfur mustard, it is less likely than mustard to be used by terrorists.

Overview: Toxicity

Acute toxicity levels for humans are not well defined, but a dermal exposure of 0.05 to 0.1 mg/cm² produces erythema and 0.2 mg/cm² produces vesication. About 30 drops, 2.6 mg, applied to the skin and not decontaminated, would kill an average man through systemic toxicity. In terms of the eyes, a 15-minute ocular exposure to a vapor concentration of 10 mg/m³ produces conjunctivitis, while a single droplet of 0.001 ml can perforate and destroy the eye. With inhalation, it is estimated that LC_{t50}, or lethal concentration of 1500 mg-min/m³ in the air will kill 50% of those exposed.

Protective Equipment

Since ordinary clothing and surgical protective gear offer no protection against lewisite, special equipment including a respirator, NBC suit, gloves and overboots is required.

Detection

The detection of lewisite has not been automated for chemical agent detection systems. Detection is made easier since the arsenic within Lewisite forms colored products with many reagents. Draeger™ tubes which react with organic arsenicals are available. Gas-chromatographic techniques can be used to identify the agent in the lab.

Decontamination

Decontamination of lewisite must be efficient and quick since this agent can cause serious damage within minutes. Skin decontamination is based on physical adsorption of the agent, or on the combination of physical adsorption and chemical inactivation. Physical adsorption is achieved by adsorbing powders such as flour, talcum powder, or Fullers earth; while chemical inactivation is achieved by incorporating chlorinating compounds, such as chloramines or household bleach, into adsorbing powders, ointments, solutions or organic solvents. There is some question as to the efficacy of using water to decontaminate lewisite. Although the CDC and U.S. military do not agree, some worldwide agencies believe lewisite, since it is poorly soluble in water, can be spread by water and, thus, potentially worsen the exposure. Adsorbing powders and chlorinating agents are preferred, but if water is the only thing available, we would recommend its use in liberal amounts.

For decontamination of the mucous membranes and eyes, the substances used for skin decontamination are too caustic. In this case, the affected mucous membranes should be flushed immediately with water. The eyes can be flushed with copious amounts of water, isotonic sodium bicarbonate (1.26%), or saline (0.9%).

Signs and Symptoms

Like mustard agents, lewisite can burn and blister any part of the body it contacts, typically acting on the eyes, mucous membranes, lungs, and skin. The initial signs and symptoms of exposure will depend upon the affected areas. Lewisite can be distinguished from the mustards by its immediate pain upon contact, since, unlike mustards, lewisite has no latency period. Injuries from lewisite should be less severe than those of the mustards, because the immediate burning and lung irritation leads to the prompt use of protective gear and decontamination.

In animal tests, exposure of to the eyes to lewisite caused an immediate edema of the lids, conjunctivae, and cornea, with an early meiosis. There is also early, severe involvement of the iris and ciliary body, followed by depigmentation and atrophy of the iris stroma with severe exposures. Eye injuries with lewisite tend to be less severe than with mustard

agents, because the immediate blepharospasm and edema helps prevent prolonged exposure. However, eye injuries can be serious, with pannus formation, massive necrosis, and ultimately blindness. As stated earlier, a droplet of 0.001 ml can perforate and destroy the eye.

Signs and Symptoms (2)

Dermal exposure to lewisite, either by vapor or liquid agent, produces a burning pain upon contact. Erythema is evident within 15 to 30 minutes, followed by painful vesication within a few hours. Unlike mustards that produce groups of small blisters over erythematous areas, lewisite blisters start small and expand to cover the entire erythematous area. Maximum blistering can take up to 4 days to occur. Unlike the mustard agents, pigment changes do not occur and minor lesions heal more readily. Also, the blister roof contains the entire epidermal layer and is less fragile than mustard blisters.

With exposure to liquid lewisite, deep necrotic lesions may be expected. Necrosis is coagulative with deeper injury to the connective tissue and muscle, greater vascular damage, and a more severe inflammatory reaction than is seen in mustard burns. In large, deep, lewisite burns, there may be considerable necrosis, gangrene and slough.

Signs and Symptoms (3)

Upon inhalation, lewisite causes irritation and congestion from the nasal cavity to the lower airways. Symptoms start with rhinorrhea, a burning pain in the throat and hoarseness. Airway secretions and fragments of necrotic epithelium may cause obstruction, with resultant rales and marked dyspnea. Pseudomembrane formation and pulmonary edema are seen with severe cases, and bronchopneumonia is a major complication to be avoided. If the inhaled dose is sufficiently high, the victim dies in a few days from pulmonary edema, mechanical asphyxia due to obstruction, and/or sepsis.

Signs and Symptoms (4)

Systemically absorbed by any route, lewisite may cause liver toxicity and systemic arsenic toxicity with diarrhea, neuropathy, nephritis, hemolysis, a true hemolytic shock, and encephalopathy. "Lewisite shock" has also been described, and is caused by protein and plasma leakage from the capillaries, with subsequent hemoconcentration and hypotension. Other systemic findings, such as subnormal body temperature, restlessness, hypotension, and T-wave elevations, are occasionally seen, while generalized weakness, muscle cramping, and red or green colored urine have also been reported. Gastrointestinal symptoms include nausea, vomiting, diarrhea, anorexia, and abdominal pain.

Treatment

There is no specific treatment for lewisite toxicity, although specific measures are available to address its arsenic toxicity. The aim of therapy is to relieve symptoms, prevent infection and promote healing. The indications for systemic treatment following exposure by any route are: (1) cough with dyspnea and frothy sputum, which may be blood tinged, or any other signs of pulmonary edema; (2) a skin burn the size of the palm of the hand or larger, which was not decontaminated within the first 15 minutes, and (3) skin contamination covering 5% or more of the body surface, with evidence of immediate damage, such as grey or dead-white blanching of the skin, or where erythema develops over the area within 30 minutes.

Treatment (2)

Since lewisite is an arsenical compound, systemic arsenic poisoning is treated with dimercaprol, also known as British Anti-Lewisite or BAL, which acts as a chelator by binding arsenic. It is available for deep, intramuscular injection, which itself may be painful, and has significant systemic toxicity. The standard dosing regimen is 3 to 5 mg/kg IM every 4 hours for four doses. Dosing depends on body weight and the severity of the symptoms. Recently, two water-soluble analogues of dimercaprol have become available, meso-2,3-dimercaptosuccinic acid (DMSA) and 2,3-dimercapto-1-propanesulfonic acid (DMPS). They are less toxic, water soluble, and can be given orally. Dimercaprol treatment is generally reserved for severe exposures exhibiting pulmonary edema or shock.

When treating lewisite exposure it is important to remember several things. With eye injury, do not use topical anesthetics for pain relief, as they may increase corneal damage. Instead, use systemic, narcotic analgesics when needed. Similarly, do not bandage the eyes; use dark, protective goggles. Dermal exposure with involvement of greater than 20% of the skin, or the presence of deep, severe burns, require hospitalization. Finally, if the agent has been ingested, do not induce vomiting or attempt to neutralize. Activated charcoal is of no use. Administer several ounces of milk, which, as an alkali, will help hydrolyze the agent.

Long-term Medical Sequelae

There is no real data from which to predict the long-term medical consequences of lewisite exposure. It is believed that chronic pulmonary disease and the persistence of acute, severe injuries to the eye are the main long-term effects. Lewisite does not appear to be mutagenic, teratogenic, or carcinogenic.

Environmental Sequelae

Lewisite is seven times less persistent in the environment than the mustard agents. It hydrolyzes rapidly and is not found in soil. However, lewisite oxide, when found in the soil, demonstrates legacy contamination.

Summary

Lewisite is less likely than mustards to be used by terrorists because it is inherently unstable and relatively difficult to manufacture. Ordinary clothing and surgical garb offer no protection, and only military-grade protective gear can prevent exposure. Immediate decontamination is critical since injury can occur within minutes of exposure. The signs and symptoms of exposure will be dependent upon affected areas and, with no latency period, pain and physical signs are immediate. With no specific antidote or treatment, the aim of therapy is to relieve symptoms, prevent infection, and promote healing. Finally, systemic arsenic toxicity is treated with dimercaprol (BAL) chelation.