

BLISTER AGENTS OR VESICANTS

Vesicants cause blistering. They may be plant, animal, chemical, or sunlight. Those discussed are the chemical warfare vesicants, namely sulfur mustard and Lewisite. A close relative of sulfur mustard, nitrogen mustard was the first cancer chemotherapeutic agent.

Sulfur Mustard

Sulfur mustard is a vapor inhalation and liquid contact hazard. Mustard causes injury to the eyes, skin, airways, and some internal organs. This chemical warfare agent has a delayed action, and exposure to it may result in blisters on the skin, temporary blindness, and respiratory distress. More extensive injury can result in death due to respiratory failure from airways injury, sepsis as a result of bone marrow damage, decrease in white blood cells, and impairment of the immune system. There is no specific therapy.

Characteristics

Mustard is an oily liquid yellow to brown in color. Its name comes from its odor of garlic or mustard, but odor should not be relied upon for detection. Mustard is a persistent agent and not volatile at temperate conditions; however at temperatures above 100 °F it is a definite vapor hazard. Mustard has a relatively high freezing point and is often mixed with similar agents such as Lewisite to lower the freezing point. Because of its oily and persistent nature, mustard poses a definite concern for cross contamination.

Mechanism of action

Mustard is absorbed and causes chemical cellular damage within 1 to 2 minutes, but clinical effects do not begin for hours. There is no immediate pain, there is no immediate skin discoloration, and there is no immediate eye irritation. However, hours later, the casualty realizes that he or she has been exposed and presents to the ED for evaluation and treatment. The onset time for clinical effects ranges from 2 to 24 hours, but the most common interval is 4 to 8 hours.

Despite years of research, the exact mechanism by which mustard damages cells is unknown. It alkylates DNA and clings to proteins and other cellular components. The end result is DNA damage and cellular death. The injury is very similar to that produced by radiation, and mustard is a radiomimetic agent. Topically, three organ systems directly affected by mustard are the eyes, skin, and respiratory tract.

Clinical Effects

Ophthalmic

There is a spectrum of eye involvement. The eye lesion, after a small exposure to mustard, may consist only of mild conjunctivitis. A larger exposure will produce a more severe conjunctivitis, lid inflammation and edema, blepharospasm, and corneal roughening. These casualties will be unable to open their eyes and will be temporarily without sight. A larger exposure, particularly if by liquid, may produce corneal opacification, corneal ulceration, or corneal perforation. Miosis is sometimes observed after mustard exposure and is thought to be due to cholinergic effects.

Integumentary

Skin effects begin hours after exposure with erythema accompanied by burning and itching. This is followed by the development of small vesicles, which later coalesce to form blisters. The size and depth of the lesion depends on the amount of exposure and whether exposure was by vapor or liquid. Coagulation necrosis extending into the dermis may develop under blisters caused by liquid.

Pulmonary

Mustard damages the mucosa or lining of the airways. This damage begins in the upper airways and descends in a dose-dependent manner to the smallest bronchiole. After a small exposure or initially after a large exposure, there may be epistaxis, sinus discomfort, and a mild to moderate pharyngitis with a hacking cough. After a moderate to large exposure, there may be laryngitis with voice loss and a productive cough. If the exposure is large, the agent reaches the smallest airways to cause dyspnea and productive cough, as the mustard will damage not only the mucosa, but the underlying musculature as well. At this stage, there may be hemorrhagic pulmonary edema around the bronchioles, but otherwise, pulmonary edema is rare.

Gastrointestinal

Gastrointestinal effects within the first 24 hours following exposure include nausea and vomiting. These effects are thought to be in part due to cholinergic stimulation. There may be some added effects of mustard on the GI tract from the swallowed tracheal secretions. Gastrointestinal effects seen after 3 to 5 days are thought to be due to tissue destruction in the abdomen.

Hematopoietic or Blood Forming System

Absorption of significant amounts of mustard produces damage to and death of the stem or precursor cells of the bone marrow. If this occurs, the white blood cell count, after an initial increase because of the toxic exposure, starts decreasing on about the third or fourth day after exposure and continues downward until recovery begins. If the amount of mustard absorbed is quite large, there is no recovery and the cell count will reach zero. Survival usually does not occur when this happens. The absence of these cells increases susceptibility to infection and contributes to death. The red blood cells and platelets also decline following the white blood cells.

Medical Management

Decontamination

Decontamination should consist of physical removal of any residual agent by whatever means available. The casualties should remove all clothing, rings, and jewelry. Skin and hair decontamination should be performed with soap and water. Decontamination must be done as quickly as possible since cellular damage occurs in as little as two minutes. Decontamination of the casualty at the ED 30 minutes or more after contact with mustard will not change the clinical course of the patient's illness, but is effective in preventing cross-contamination of providers.

Treatment

Treatment is largely supportive since there is no antidote for the effects of sulfur mustard.

Skin

Soothing creams or lotions might be effective for irritation and itching. Large blisters should be unroofed and denuded areas irrigated several times a day followed by a topical antibiotic (Silvadene, etc.) to prevent skin bacterial superinfection. Oral pain medications will likely be necessary. Fluid requirements should be assessed, less fluid replacement is necessary than with thermal burns. Care must be taken not to over hydrate the patient (burn formula resuscitation is not recommended). Rarely will burns be full thickness requiring skin grafting.

Eyes

Again, mustard fixes to tissues within the first several minutes after exposure. Gentle irrigation with saline or water during this time period will be helpful. Aggressive attempts to pry apart severely painful, blepharospastic eyelids to accomplish an irrigation 30 minutes or more after exposure is of dubious value, since the damage has been done and the agent has evaporated or has been absorbed. With severe eye injuries, homatropine or other mydriatics should be applied topically to prevent synechiae formation. Topical antibiotics should be applied several times a day and petroleum jelly should be applied to lid edges to prevent them from adhering. Topical ophthalmic analgesics may be used to facilitate initial examination. However, oral pain medication

is preferred to topical analgesics, since topical agents may damage the cornea and delay healing. Many ophthalmologists feel that the application of topical steroids within the first 24 hours, but not after, might be of benefit. Early involvement of an ophthalmologist is advised, and visual acuity should be obtained before treatment measures are instituted.

Pulmonary

Upper or minor airway symptoms (sore throat, non-productive cough, hoarseness) may be relieved by steam inhalation and cough suppressants. The initial chemical pneumonitis should be treated in the usual manner; however, antibiotics should not be used until an organism is demonstrated, which usually occurs between the third and fifth day post-exposure. A patient with severe airway effects will benefit from oxygen and assisted ventilation, particularly positive end expiratory pressure (PEEP) or continuous positive airway pressure (CPAP). Intubation should be performed if there are signs of severe upper airway involvement, and should be done early, before laryngeal spasm or edema makes it difficult. Bronchodilators may be needed; if they fail to relieve bronchospasm, steroids may be tried. Otherwise, steroids are of questionable benefit.

Lewisite

Characteristics

Lewisite is a vesicant that has been stockpiled militarily, but there have been few human exposures to the chemical.

Clinical Effects

Lewisite is rapidly absorbed by the eyes, skin, and lungs and produces blisters similar to sulfur mustard. In contrast to sulfur mustard, however, lewisite is highly irritating on initial exposure. It also produces visible lesions more quickly. Unlike mustard, it does not damage the bone marrow. Lewisite is an arsenical compound, thus a heavy metal poison.

Integumentary

Lewisite causes greater skin damage than sulfur mustard. A gray area of dead skin can progress to blisters and severe tissue necrosis and sloughing.

Pulmonary

Since lewisite causes immediate irritation to the nose and sinuses, an effort by the victim to evacuate the area of contamination may prevent more severe lung damage. Pseudomembrane formation is common.

Cardiovascular

Lewisite causes increased capillary permeability, leading to volume depletion, hypotension, hepatic and renal injury.

Medical Management

Decontamination

Casualties should remove all clothing and jewelry. Decontamination of skin and hair with soap and water will remove most of the chemical, if performed quickly after contamination.

Treatment

The antidote available is dimercaprol which is called British Anti-Lewisite (BAL**). BAL can be administered IM to reduce the systemic effects of the vesicant. Since it is administered parenterally, BAL has no effect on Lewisite damage to the skin and eyes.

***BAL is also used for some other heavy metal poisonings.*