Mustard Gas or Sulfur Mustard: An Old Chemical Agent as a New Terrorist Threat

Monica Wattana, MD, BSc; Tareg Bey, MD, FACEP

Department of Emergency Medicine, University of California, Irvine, Orange, California USA

Correspondence:
Tareg Bey, MD, FACEP
Department of Emergency Medicine
University of California, Irvine
101 The City Drive, Rte 128
Orange, CA 92868 USA
E-mail: tbey@uci.edu

Keywords: chemical agents; mustard gas; *sulfur mustard*; *terrorist threat*

Abbreviations:
AEGL = Acute Emergency Guideline Level
CWA = chemical warfare agent
FE = Fuller's Earth
LMA = laryngeal mask airway
PPE = personal protective equipment
RSDL = Reactive Skin Decontamination Lotion

Received: 17 December 2007
Accepted: 02 May 2008
Revised: 30 May 2008

Web publication: 23 January 2009

Abstract

Sulfur mustard is a member of the vesicant class of chemical warfare agents that causes blistering to the skin and mucous membranes. There is no specific antidote, and treatment consists of systematically alleviating symptoms. Historically, sulfur mustard was used extensively in inter-governmental conflicts within the trenches of Belgium and France during World War I and during the Iran-Iraq conflict. Longitudinal studies of exposed victims show that sulfur mustard causes long-term effects leading to high morbidity. Given that only a small amount of sulfur mustard is necessary to potentially cause an enormous number of casualties, disaster-planning protocol necessitates the education and training of first-line healthcare responders in the recognition, decontamination, triage, and treatment of sulfur mustard-exposed victims in a large-scale scenario.

Wattana M, Bey T: Mustard gas or sulfur mustard: An old chemical agent as a new terrorist threat. ***Prehospital Disast Med*** **2009;24(1):19–29.**

Introduction

The North Atlantic Treaty Organization (NATO) defines a chemical agent as: a chemical substance that is intended for use in military operations to kill, seriously injure or incapacitate people.[1] Chemical agents are thought of as weapons of mass effect because a relatively small amount of agent can cause enormous numbers of casualties. Despite the signing of treaties, such as the Geneva Protocol of 1925 and the Chemical Weapons Convention of 1993, usage of chemical agents in warfare and the potential for their usage in acts of terrorism still pose a huge global threat.[1-4]

Since its introduction as a chemical warfare agent during World War I, sulfur mustard has become one of the most well-known and utilized chemical agents.[5] Sulfur mustard has been used during >10 military conflicts, and the current number of chemical casualties caused by sulfur mustard outnumbers the total sum due to all other chemical agents.[4,6] Although sulfur mustard has not been used in a documented act of terrorism, the disaster preparedness mentality following 11 September 2001, encourages education for healthcare providers in the recognition, treatment, and decontamination of sulfur mustard.

The aim of this article is to promote disaster preparedness education by providing a general overview of the physical properties, physiologic manifestations, acute management strategies, and current methods of treatment after exposure to sulfur mustard. Even though sulfur mustard has not been used as a chemical agent by terrorists, its use still should be considered as a major potential threat.

History of Sulfur Mustard

Sulfur mustard belongs to the vesicant class of chemical agents. Vesicants are used to impede rather than kill opposing forces. Opposing forces are hindered because bulky protective equipment must be worn and other precautionary measures also must be utilized. Sulfur mustard was the first vesicant to be synthesized and utilized in military warfare. Destructive properties and the

1822	Belgian scientist Cesar-Mansuete Despretz synthesized an impure uncategorized form of sulfur mustard.
1886	German chemist Victor Meyer created the Levinstein process to purify sulfur mustard. This distilled pure form is known as HD.
July 1917	The Germans utilized sulfur mustard for the first time as a chemical warfare (CWA) agent at Ypres, Belgium. The type of sulfur mustard used during World War I was called Hun Stoffe abbreviated HS or H and contained 20%–30% impurity. During this period soldiers were equipped only with respiratory protection devices. Inadequate skin protection resulted in over 1.3 million people receiving sulfur mustard-related injuries during World War I with >90,000 dying.
1935–1936	Italy conquests Ethiopia using aircraft delivery of sulfur mustard.
1937–1945	Japan conquests China using chemical warfare agents that include sulfur mustard.
1963–1967	Egypt intervenes in the Yemen civil war by using sulfur mustard aerial bombs against royalist forces.
1983–1988	Iraq uses sulfur mustard and nerve agents in the Iran-Iraq conflict.
1987–1988	Iraq uses sulfur mustard against Kurdish fighters.

Table 1—Timeline and history of sulfur mustard from development to the most current tactical usage[6,12,64]

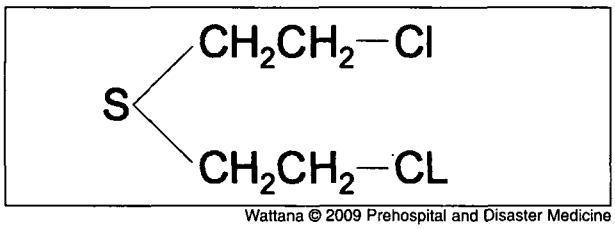


Figure 1—Chemical formula of sulfur mustard

absence of an antidote make sulfur mustard the most significant chemical warfare agent.[7] Currently, an estimated 100,000 military and civilian casualties have been attributed to sulfur mustard and approximately 45,000 victims still suffer from late effects. Sulfur mustard gas has been implicated as a chemical warfare agent for >70 years, especially in conflicts occurring in warmer climates. The timeline and history of the use of sulfur mustard is in Table 1.[8,9]

Physical and Chemical Properties

Sulfur mustard (Figure 1) possesses key physical and chemical properties making it an effective tactical agent. Sulfur mustard has an odor akin to garlic or mustard, exists as a straw-colored oily liquid, and is hazardous to humans in both liquid and vapor form.[10–12] Sulfur mustard may be hydrolyzed in water but its poor solubility (0.07% at 10°C) requires thorough mixing.[10,13] Sulfur mustard is absorbed better by organic solvents and is especially soluble in rubber, porous materials, and food products. Alkalinity and higher temperatures will increase the rate of hydrolysis.[10,14]

During WWI, sulfur mustard was deposited at night because decreased nocturnal temperatures increased persistence, which led to vapor exposure with a rise in temperature during the mid-morning hours. Therefore, despite possessing low volatility, evaporation of the sulfur mustard deposited at night caused more than 80% of the WWI sulfur mustard casualties.[15]

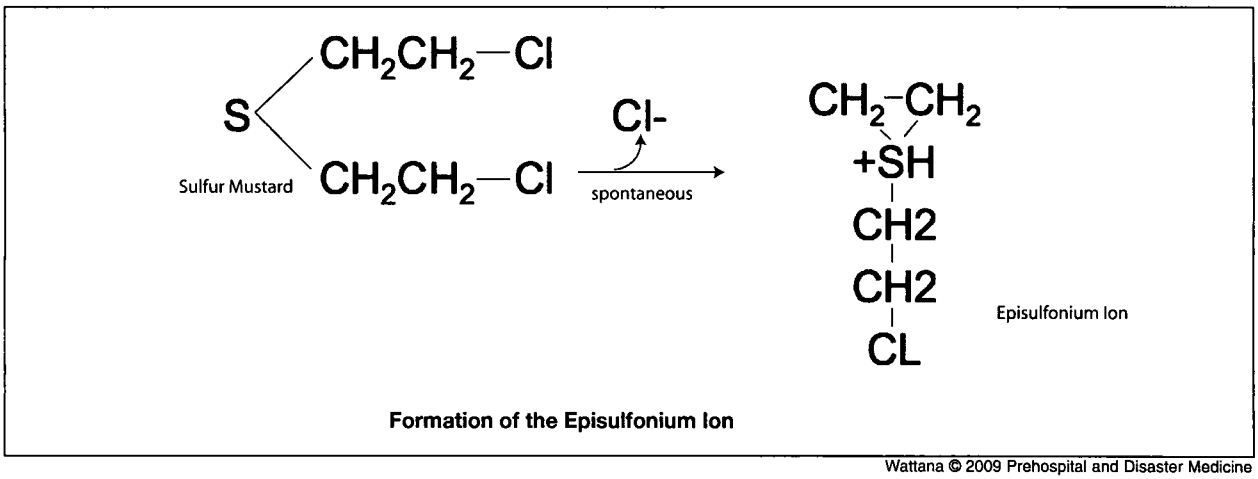
Tactically, sulfur mustard was able to persist around the trenches and gullies of the WWI battlefields. A concentration of 1–25 mg/m^3 can be detected 6–12 inches from the ground. The vapor sinks because the density is greater than air by a factor of 5.4. In temperate climates with little wind, sulfur mustard may persist for more than a week.[16] The persistency of sulfur mustard also can be increased using finely powdered material that also makes the agent difficult to remove during the decontamination process.

In warmer climates, the persistence of mustards is reduced, but vapor production increases. In the Middle East and in Africa, where temperatures of 38°C to 49°C (100°F to 120°F) are common, the warmer temperatures facilitate enhanced vaporization.[7] Conversely, rapid evaporation in warm climates also allows for decreased decontamination efforts. Usage of sulfur mustard by the Japanese against China provides an example of how the volatility of sulfur mustard may be increased in colder temperatures by combination with other vesicants such as Lewisite.[16] Sulfur mustard can be aerosolized by spraying and also can be released via an artillery shell or bomb. Detonation may result in the explosion of sulfur mustard due to a flash point at 105°C (221°F).[17] This agent also has a high freezing point of 14°C (57°F), making delivery by aircraft spraying

Boiling Point	227ºC
Vapor Pressure	0.072 mmHg at 20ºC
Vapor Density	5.4
Liquid Density	1.27 g/mL at 20ºC
Solid Density	Crystal: 1.37g/mL at 20ºC
Volatility	610 mg/m^3 at 20ºC
Appearance	Pale yellow to dark brown liquid
Odor	Garlic or mustard
Water Solubility	0.092 g/100g water at 22ºC
Solvent Solubility	Complete in CCl_4, acetone, other organic solvents

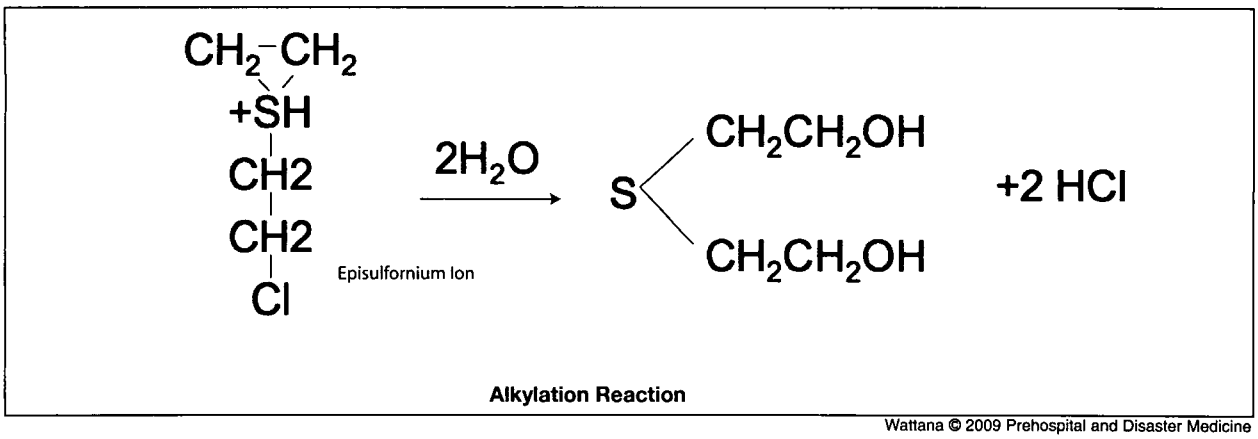
Wattana © 2009 Prehospital and Disaster Medicine

Table 2—Major chemical and physical properties of sulfur mustard[17]



Wattana © 2009 Prehospital and Disaster Medicine

Figure 2a—Biological mechanism of sulfur mustard



Wattana © 2009 Prehospital and Disaster Medicine

Figure 2b—Biological mechanism of sulfur mustard injury

or dispersal during winter extremely difficult. Therefore, agents such as chlorobenzene were used during WWI to lower the freezing point of sulfur mustard allowing for dispersal in colder temperatures (Table 2).

No concrete theory exists to describe the biological effects of sulfur mustard. Although many mechanisms have been postulated based on documented reaction chemistries, these theories fail to explain the time lag between the rapid chemical reactions and resultant tissue damage that occurs after a delay.[16,18] The most popular explanation is based on the ability of sulfur mustard to rapidly undergo two first-order kinetic reactions.[10] The first reaction creates a highly reactive carbonium ion, and the second causes alkylation of target cellular molecules. Carbonium ion formation occurs

https://doi.org/10.1017/S1049023X0000649X Published online by Cambridge University Press

when two chloroethyl groups undergo a cyclic first order (SN1) reaction to produce the episulfonium cation intermediate (Figure 2a). The episulfoniom cation then opens to form the carbonium ion. This second reaction occurs rapidly, resulting in the rapid alkylation of intracellular nucleophilic sulfhydryl and amino group-containing molecules such as the purine bases of DNA, RNA, and other proteins (Figure 2b). The depurinatated areas serve as sites for DNA breakage causing improper template formation during DNA incorporation that ultimately leads to the formation of non-functional proteins. Further complications arise from exhaustion of intracellular repair mechanisms.[5,19–21]

Besides causing errors in DNA replication and the synthesis of non-functional proteins, others postulate that over-activation of the polymerase enzyme results in depletion of intracellular nicotinamide adenine dinucleotide (NAD+) stores. Depletion of NAD+ begins within an hour and reaches a maximal amount after four hours.[16] Depletion of NAD+ ultimately results in cell necrosis via activation of cellular proteases and proinflammatory cytokines that parallel tissue injury development.[10,15,16]

These two hypotheses provide a possible explanation for the observation that sulfur mustard preferentially affects organs with high cell turnover such as the skin, digestive tract, and bone marrow. For skin manifestations, studies have shown that sub-lethally damaged epidermal cells proliferate at a slower rate leading to delayed wound healing and chronic skin manifestations. In addition, the coagulated appearance of the skin can be explained by abnormal bonding between collagen bundles in the papillary dermis due to the formation of non-functional proteins.[22]

Toxicity

Four major features contribute to the toxicity of sulfur mustard: (1) latency period between exposure and consequences; (2) effect of temperature and humidity; (3) different sensitivities of biological tissues; and (4) sensitization potential.[23]

1. *Latency Period*—The high degree of morbidity from sulfur mustard results from the long latency period between exposure and acute symptom presentation.[10,24] Victims initially are unaware of being contaminated, which leads to decreased decontamination efforts and continued absorption from clothing. The latency period ranges from 30 minutes to eight hours and depends on the amount, modality of exposure, and environmental factors.[22,24]
2. *Effect of Temperature and Humidity*—Only small concentrations of sulfur mustard are required to generate debilitating effects at higher temperatures and humidity.
3. *Different Sensitivities of Biological Tissues*—Tissues with a higher rate of metabolism also are affected preferentially due to sulfur mustard's mechanism of action. Victims of sulfur mustard exposure are more likely to die from chronic pulmonary conditions or hematopoietic causes than from the acute effects that may occur immediately after exposure.[24]
4. *Sensitization Potential*—The National Advisory Council established Acute Emergency Guideline Levels (AEGLs) for sulfur mustard to facilitate emergency response planning by state and local government agencies.[23,25,26] Toxicity limits for sulfur mustard are measured in mg/m^3, are expressed as LD_{50} values, and are of an organ-specific route of administration and species specific.[27]

AEGL-1 is the level above which non-disabling, reversible discomfort may begin to be experienced by some of the exposed victims. The symptoms for sulfur mustard are manifested primarily in the eye as conjunctivitis. The onset of symptoms will be delayed following exposure. At a level of AEGL-1, exposed persons may not experience symptoms because calculation of AEGL-1 for sulfur mustard includes a margin of safety. Levels below AEGL-1 do not cause observed adverse effects.[23]

AEGL-2 is the level above which more serious effects may occur for exposed individuals. For sulfur mustard, AEGL-2 produces ocular symptoms, such as severe conjunctivitis, photophobia, and involvement of the eyelid. Other organ systems also become involved such as vesicant burns and respiratory symptoms. These effects will still develop several hours after exposure but will not cause any long-term or permanent effects.[23]

AEGL-3 for sulfur mustard is the level above which exposures may become acutely life-threatening or result in long-term complications. These symptoms include delayed cutaneous and more severe respiratory symptoms. AEGL-3 values still protect against severely incapacitating effects because designation of these values still are expected to result in reversibility of symptoms (Table 3).[23]

The AEGL guidelines are useful in acute emergency situations because the three zones of health effect endpoints are devised in a time-dependent manner applicable for the duration of 10 minutes to 8 hours post-exposure.[28] The AEGLs in conjunction with site-specific knowledge and known population characteristics within each delineated zone, allows disaster planners to estimate toxic effects for victims and responders.[20] These new guidelines with incorporated CWA-AEGL values provide a useful estimate of the geographic area of highest risks in relation to exposure time.

These four major features: (1) latency period between exposure and consequences; (2) effect of temperature and humidity; (3) different sensitivities of biological tissues; and (4) sensitization potential contribute to the toxicity of sulfur mustard. A tentative prediction of the effects that this agent may have on affected individuals can be assessed based on these variables. Although lethal dosages of sulfur mustard have been recorded, exposure results in substantial morbidity but rarely does exposure result in mortality.[22]

The Material Data Safety Sheet (MSDS) of the US Army Soldier and Biological Chemical Command (SBCCOM) list median LD50 doses of sulfur mustard by skin absorption of 100 mg/kg in humans.[27]

Clinical Manifestations

Acute

Injury from sulfur mustard exposure occurs via direct absorption by the skin and the eyes or by inhalation into the respiratory tract. High doses of exposure after absorption may lead to systemic toxicity resulting in bone marrow, gastrointestinal, and renal effects.[10,16,29] The acute effects of sulfur mustard exposure on organ systems follows.

	Category	Characteristics	Single Episode Exposure Duration	Sulfur Mustard Concentration (mg/m^3)
AEGL-1 (Non-Disabling)	Detectable	Symptom manifestation, when present, is mostly ocular in nature with no long-term complications.	10 min	0.40
			30 min	0.13
			1 hr	0.067
			4 hr	0.017
			8 hr	0.0083
AEGL-2 (Disabling)	Discomfort	Exposure does not produce disability, impair escape, or result in permanent or long-term effects. An increased chance of eye irritation and possible delayed vision impairment is possible	10 min	0.60
			30 min	0.20
			1 hr	0.10
			4 hr	0.025
			8 hr	0.013
AEGL-3 (Lethal)	Disability to lethal	Exposure incapacities individuals resulting in need for outside assistance. Exposure may result in permanent or long-lasting ocular, respiratory, cutaneous, and systemic effects	10 min	3.9
			30 min	2.7
			1 hr	2.1
			4 hr	0.53
			8 hr	0.27

Table 3—Characteristics of each Acute Emergency Guideline Level and corresponding concentrations of sulfur mustard in relation to duration[13,28]

Ocular Manifestations

The interface between the aqueous cornea and conjunctival mucosa provides an optimal environment for rapid penetration and extended tissue exposure. The corneal epithelium has a high intrinsic metabolic rate and rapid turnover rate causing these cells to be preferentially affected by sulfur mustard. Ocular endothelial cells exposed to sulfur mustard undergo apoptosis resulting in dosage-dependent effects after a time lag of 30 minutes to eight hours.[11,24,29]

The relatively low dosage threshold for symptom onset makes the eye the most sensitive organ to sulfur mustard exposure. Ocular manifestations have been documented in up to 90% of the individuals exposed to mustard gas during World War I. A review of Iranian casualties reported that conjunctivitis occurred in 85% of all Iranian casualties with 8% of these casualties sustaining long-term consequences.[11,24] The acute ocular manifestations of sulfur mustard are grouped into three categories of injuries based on severity. These are (1) mild; (2) moderate; and (3) severe injuries.

Mild Injuries—Symptoms are described as a foreign body sensation within the eye and feelings of soreness. The eye may become bloodshot in appearance and physical examination reveals vessel engorgement and edema within the conjunctiva. The cornea is spared and total recovery occurs within a few days.[10,20]

Moderate—Moderate injury affects the cornea, conjunctiva, and eyelid. Physical examination findings include the same findings as in mild injury but to a more severe degree along with blepharospasm and chemosis. Fluorescein examination of the cornea reveals erosions ranging from small pinpoint to larger sized defects.[10,30]

Severe Injury—Severe ocular manifestations with extensive injury occur after exposure to high concentrations or direct droplets of sulfur mustard into the eye. Besides exhibiting symptoms consistent with mild-moderate injury, inflammation of the anterior chamber, with a concomitant, transient rise in intra-ocular pressure can occur. The eyelid also may exhibit signs of first- or second-degree burns. Whitening of the nasal and temporal limbus occurs due to necrosis of the limbal vasculature within the deeper corneal layers. Fluorescein examination reveals large corneal lesions that may lead to the development of symblepharon formation. Although documented, symblepharon formation is a relatively rare phenomenon because conjunctival lesions from sulfur mustard usually are limited to the interpalpebral fissures.[10,24,30]

Respiratory Manifestations

The extent of respiratory symptoms from acute sulfur mustard exposure depends on duration of exposure and the amount of agent that has been inhaled.[10,29] Onset of symptoms usually begins 4–16 hours after initial exposure with edema and erythema extending from the nasal mucosa to the terminal bronchioles. Low inhaled concentrations of sulfur mustard produce pain inside the nose and sinuses accompanied by rhinorrhea, sneezing, and sore throat. Increasing concentrations of vapor cause development of a non-productive hacking cough and aphonia due to irritation and necrosis of laryngeal, tracheal, and bronchial epithelium. Severe exposure can cause airway obstruction, pulmonary hemorrhage, and respiratory failure due to formation of purulent discharge and pseudomembrane formation from necrosis and ulceration of upper airway epithelium. Respiratory infections, particularly with *Pseudomonas* may develop 36–48 hours after exposure causing bronchopneumonia and ultimately death.[10] Recovery from acute expo-

https://doi.org/10.1017/S1049023X0000649X Published online by Cambridge University Press

sure varies depending on presence of secondary infections and may take 1–2 months.[3]

Skin

Areas of the body that possess a high sweat gland concentration, such as the groin and axillae, help facilitate sulfur mustard absorption.[10,12] Acute effects develop after a latency period of up to 24 hours.[3,12] Although symptoms usually do not develop before 12 hours after initial exposure, studies involving the pediatric population or with high concentrations have documented that symptom onset can occur as early as 2–3 hours after the exposure.[11]

Momeni *et al* characterized the cutaneous manifestations of sulfur mustard in a review of 535 patients admitted to the dermatology ward during the Iran-Iraq conflict (1980 to 1988).[31] After the latency period, 67% of patients developed erythematous lesions in the axillae, nape of the neck, chest, face, and genitals accompanied by subjective feelings of itching and burning within these areas. Erythema either progressed to formation of small vesicles and bullae or resolved after 2–3 days. Fifty-five percent of patients developed bullae and blisters on sites previously affected by erythema, but sites without previous lesions also were affected. The bulla varied in size and developed on the periphery of erythematous skin after 2–18 hours of erythema.[31] Bullae fluid is not toxic and poses no threat to the patient or healthcare provider.[11] After the bullae coalesced, epidermal necrosis occurred causing full thickness skin loss and ulceration resulting in areas of raw exposed dermis. An eschar appeared approximately 72 hours after exposure and sloughed off in 4–6 days.[24] Ultimately, healing occurred in 2–3 weeks after moderate exposure or 6–12 weeks after the initial full-thickness erosion. Resulting changes in pigmentation were seen in 20.4% of patients and included hypopigmentation of damaged cells and an area of surrounding hyperpigmentation indicative of an area of sublethally damaged cells. The article by Momeni *et al* also contains several color photographs of sulfur mustard victims depicting the damaging blistering effects to skin and mucosa.[31]

Systemic Complications

Systemic symptoms caused by sulfur mustard mimic those induced by radio- or chemotherapy. General symptoms such as nausea, headache, vomiting, and loss of appetite are reported from low-dose exposure. Systemic complications due to high dose exposure affect the gastrointestinal tract with symptoms, such as diarrhea.[32] High dosage exposure also affects the bone marrow.[33]

Tabarestani *et al* examined the effects of sulfur mustard on bone marrow in a study that demonstrated dose-dependent manifestations consistent with decreased cellularity and nuclear atypia of erythrocyte precursors. These findings support the predisposition of sulfur mustard to alkylate rapidly dividing cells.[34] Polymorphic leukocytosis can be seen in the first three days after acute exposure, but decreases dramatically afterwards reaching a minimal level around the ninth day.[34–37] During this period, bone marrow biopsies show hypo-cellular marrow and pancytopenia.[34] Severe leukopenia was reported in half of the most severely exposed patients during the Iran-Iraq conflict.[33,35,36] Leukopenia causes an increased susceptibility to secondary infections leading to higher mortality rates. In a retrospective chart review of 65 patients evacuated to Europeans hospitals during Iran-Iraq war, Willems found that sulfur mustard victims with a white cell count of <200 cells/mm^3 had a higher probability of mortality during initial hospital admission.[37]

Chronic Effects

Ocular Manifestations—The long-term ocular effects of sulfur mustard exposure are categorized into one of three types: (1) complete resolution without further inflammation; (2) persistent symptoms consistent with a chronic course; and (3) late-onset lesions appearing many years after an asymptomatic initial exposure. Chronic and delayed mustard gas effects are characterized by involvement of the conjunctiva, limbus, and cornea.[25,29]

1. *Complete Resolution*—Several hours after exposure, the corneal epithelium vesicates and sloughs leading to decreased visual acuity. If untreated, recovery still begins within 48–72 hours and full regeneration of corneal epithelium occurs within 4–5 days. Complete symptomatic recovery may take up to six weeks. The patient still may complain of photophobia after the six-week period, but eventually, all symptoms disappear.[5,29]
2. *Persistent Chronic Course*—Ongoing inflammation produces symptoms, such as photophobia, foreign body sensation, and dry eye that are consistent with a chronic course. Conversely, ongoing inflammation may be asymptomatic, leading to a false sense of resolution. Physical examination findings, such as limbal ischemia, corneal erosions, and corneal neovascularization also may be observed. Persistent inflammation ultimately results in corneal irregularity and thinning that may lead to perforation.[5,29]
3. *Late Onset*—Delayed manifestations can present with an abrupt onset within a timeframe of anywhere from 1 to 40 years after initial exposure. Characteristics attributed to delayed manifestations include limbal ischemia, corneal neovascularization, thinning, and irregularity, chronic blepharitis, Meibomian gland dysfunction, and dry eye. Patients with delayed symptom onset also subjectively report experiencing the same complaints that recur following acute exposure such as photophobia, tearing, and decreased visual acuity. Late onset symptoms also exacerbate and remit in an unpredictable manner. Both eyes usually are affected, although the extent of involvement may be asymmetrical.[29]

Respiratory Manifestations

Various studies indicate that late onset symptoms can occur 15 years after exposure in initially asymptomatic individuals. These respiratory complaints consist of dyspnea, chronic cough, and increased phlegm production. Among these individuals, the pulmonary physical examination showed clubbing, wheezing, rales, and decreased breath sounds. Airway hyper-responsiveness and chronic bronchitis are other common late respiratory effects. Recurrent respiratory infections also cause development of bronchiectasis.[8]

Sulfur mustard is a known chemical carcinogen, but confounding factors make it difficult to determine if exposure to sulfur mustard alone leads to cancer in exposed persons.[8,33,38] Epidemiological studies have shown that American soldiers exposed to sulfur mustard during WWI had a higher incidence of lung cancer.[38] These studies also suggest that Japanese factory workers filling mustard ammunition during WWII had a higher incidence of cancer of the upper respiratory tract.[39]

Skin

A study of 40 male subjects exposed to sulfur mustard 16–20 years earlier shows that the most common chronic cutaneous complications are hyperpigmentation (55%), dry skin (40%), multiple cherry angiomas (37.5%), atrophy (27.5%), and hypopigmentation (25%). Although mustard scar formation is the characteristic long-term sulfur mustard skin lesion, it is reported in only 2–13% of chronic complications.[40] Shohrati *et al* found the most common chronic complaint to be pruritis followed by burning, pain, and redness. The same authors also found the genitalia, face, and axilla to be the most affected areas.[5] Mustard scars vary in shape and can have an atrophic, hypertrophic, or keloid appearance. Persistent skin conditions such as eczema, seborrheic dermatitis, cherry angioma, and urticaria also have been shown to be associated with sulfur mustard exposure. Although sulfur mustard possesses carcinogenic effects, data do not support an increased risk of skin cancer in victims of a short-term sulfur mustard exposure.[24]

Specific Treatment

Eyes

Initial management consists of rapid and copious irrigation of the eye after exposure to sulfur mustard. Solutions such as 0.5% hypochlorite that work well for the skin cannot be utilized to irrigate the eye. A solution of 0.9% buffered saline or plain water is recommended. Once irrigation is performed, treatment is focused on symptomatic management. Soothing eye solutions are helpful to treat pain associated from eye injuries. Petroleum can also be used on the lid margins to minimize adherence and to help drain the excessive fluid that results from conjunctivitis and blepharospam. Topical antibiotics, corticosteroids, and cycloplegics also may be used for more severe lesions. Chronic delayed effects such as dry eye are treated symptomatically, and more serious effects, such as keratopathy are treated with corneal transplantation.[8,19,24]

Skin

The treatment of cutaneous complications due to sulfur mustard is based on symptomatic management as well. Chemical burns from sulfur mustard are treated in the same manner as second-degree thermal burns. Analgesics, opioids, and cooling of affected areas are ways to treat associated pain while antihistamines are used to control itching. A solution consisting of 1% phenol and 1% menthol mixture also can be used to control sulfur mustard induced pruritis.[41]

Although the initial cutaneous injury caused by sulfur mustard is superficial, subsequent bulla formation results in histopathological changes reflective of dermal injury that ultimately results in delayed healing times. Momeni *et al* showed that large bullae that are opened and drained during the first 24 hours of onset resulted in more rapid healing of 1–2 weeks rather than 4–6 weeks.[31] Sterile dressings with topical antibiotics or silver sulfadiazine cream also can be used to treat cutaneous injuries caused by sulfur mustard.

Current research into post-exposure therapy is divided into: (1) therapy prior to the advent of lesions; and (2) therapy that will expedite healing of skin lesions after formation occurs. Extensive ongoing research is being conducted into post-exposure agents that may lessen the amount of sulfur mustard damage. These agents act in a variety of mechanism such as electrophilic scavenging of oxidative species and DNA-repair enzymes.[41] The use of carbon-dioxide laser debridement to shorten wound healing currently is being used and studied.[42–44] Studies show that laser debridement promotes wound healing at the cellular level by eliminating cytologically atypical cells, removing alkylated laminas that play a major role in delayed healing, as well as other mechanisms. The use of lasers also allows for debridement to occur in a relatively bloodless field and a reduction of infection risk because instruments are not directly introduced into the wound.[44] Research also focuses on treatment for chronic wounds via inhibition of protease deregulation. The control of proteases plays a major role in remodeling and re-epithelization of the dermis.[42]

Respiratory

Acute management of respiratory complications involves symptomatic management with the use of supplemental oxygen, cough suppressants, moistening the air for upper respiratory symptom relief, and assisted ventilation.[19] The risk for development of pneumonia and other bacterial infections is highest approximately one week after initial exposure. Victims exposed to high doses of sulfur mustard also may experience laryngospasm. If these victims present with or develop stridor and hoarseness, early tracheostomy is recommended. Bronchoscopy through the stoma also may be necessary to remove pseudomembranes and debris.[16] For patients with chronic bronchitis from sulfur mustard exposure, inhaled corticosteroids and long-acting beta-2-agonists have been found to be effective.[45]

Systemic

Oral antibiotics should be considered to sterilize the gastro intestinal tract and protect damaged intestinal mucosa in patients with cell counts <200 cells/mm^3. Granulocyte-macrophage colony-stimulating factor (GM-CSF) and granulocyte colony-stimulating factor (G-CSF) should be also considered to counteract severe sulfur mustard-induced leucopenia.[19]

Sulfur Mustard as a Terrorist Threat: Preparedness

After 11 September 2001, an enhanced desire for community preparedness prompted more research and planning for a mass-casualty incident triggered by sulfur mustard, even though this agent never has been used in this type of setting.[46,47] To date, sarin, a nerve agent, is the only documented chemical that has been used in a terrorist setting.[7] A disaster plan should include interdisciplinary collabora-

tion between physicians, paramedics, firefighters, toxicologists, and law enforcement.[48] An all-hazard approach is critical to improving public health preparedness.[49] The goal of any emergency medical response plan is to create a rapid and efficient approach with the following five goals: (1) rapid recognition and identification of contaminant; (2) prevention of further contamination; (3) stabilization of medical conditions; (4) decontamination of victims; and (5) triage of victims. (Personal Communication, Kahn CA, May 2008).[50]

1. *Rapid Recognition and Identification of the Contaminant*—This is the first step for efficient mass-casualty decontamination. Any device used to detect CWA vapors must meet five essential requirements: (1) law detection limit; (2) high selectivity; (3) law response time; (4) capacity of compound identification; and (5) portability.[51] Although time-consuming, gas chromatography/mass spectrometry (GC-MS) is the gold standard for chemical agent detection. Gas chromatography/mass spectrometry can be used to identify chemical agents at low concentrations.[52–54]

   Modification advancements of the traditional GC-MS method have yielded enhanced detection speed. Bowerbank *et al* report that rapid and correct identification can be achieved by solvating gas chromatography (SGC) coupled to an aerosol chamber and time-of-flight mass spectrometer.[55] The Thermodesorber-Gas Chromatograph-Mass Spectrometer System (TD-GC-MS) is another sophisticated and accurate technique for analysis of trace concentrations of airborne chemical agents.[56]

   Current research focuses on increasing the sensitivity and lessening the false-positive values for more mobile, versatile, and rapid chemical detection methods. The use of detection tubes provides high specificity for detection of airborne chemical agents and values can be compared to the AEGL-limit values for health risk determination.[52] Other types of chromatography are being explored, such as packed capillary liquid chromatography-electrospray ionization mass spectrometry (LC-ESI-MS). D'Agostino *et al* demonstrated that LC-ESI-MS, when compared to the GC-MS standard, had similar sensitivity, but was better suited for chemical agents that had lower volatility than sulfur mustard.[57] Future advancements for more rapid and specific detection methods will improve the speed with which decontamination efforts occur. This will allow for more correct mapping of decontamination areas, adequate protection for first responders, and appropriate medical care for victims.[52]
2. *Prevention of Further Contamination*—Responder safety is important during victim decontamination. The level of personal protective equipment (PPE) used depends on the zone and function of the healthcare provider. Exposure within highly contaminated areas requires full level-A protective gear. Level-A gear also is utilized if identification of the CWA is unknown. Level-B gear is used by people working in the decontamination zone or other areas away from the main site of contamination. Leakage for a level-B full-faced respirator should be less than 0.001%.[52,58] Sulfur mustard can penetrate through latex; therefore, gloves should have an outer layer made of butyl rubber for chemical protection and an inner globe for the absorption of perspiration and water to provide protection for approximately six hours of work with a contaminated surface.[52] Level-C protection is used in areas excluding the main site of decontamination if the type and air concentrations of the contaminant have been identified. Level-D protection does not afford any protection for healthcare providers working with contaminated victims.

   On-site responders of CWA attacks should wear either a level-A PPE if they are working directly in decontaminated areas or level-B PPE if they are working in decontamination areas (Table 4). There is an increasing need for the creation of standard hospital PPE guidelines.[59] Many hospitals currently use level-C PPE due to the assumption that victims arriving at a hospital are minimally contaminated. Several experts in PPE urge for higher PPE levels in hospitals because enhanced protection might become necessary since the hospital could serve as a target and it is likely that hospitals will receive contaminated victims that have circumvented initial decontamination efforts.[58,59]
3. *Stabilization of Medical Conditions*—Medical stabilization within contaminated areas consists of a basic assessment for hemodynamic, respiratory, and neurological status.[47] Since sulfur mustard has a latency period, most victims develop early ocular and respiratory symptoms only after a high-dose-exposure. Although high-level PPE gear hinders dexterity and the performance speed for life-saving medical procedures, Garner *et al* showed that workers in PPE level-A gear are able to perform airway maintenance in a clinically acceptable timeframe.[58] In this study, researchers used the laryngeal mask airway (LMA) and demonstrated that establishment of an airway using a LMA could be performed in the highest level of PPE under appropriate timing. Although this study suggests the use of an LMA as a possible initial airway management method, sulfur mustard can cause supraglottic swelling and edema, which are classic contraindications for the use of LMAs. Therefore, it is emphasized that this recommendation should be viewed with caution and that more research is needed to determine the efficacy and feasibility of LMA usage in this setting. If a LMA or an Intubating LMA were to be used, after victims are decontaminated and moved to a stable area, the LMA insertion should be followed by endotracheal tube intubation, especially since exposure to high sulfur mustard concentrations may results in upper airway mucosal swelling, necrosis, or obstruction.
4. *Decontamination of Victims*—Since fixation of sulfur mustard occurs rapidly, decontamination efforts must focus on preventing continued exposure.[60]

   Removal of sulfur mustard from the skin to prevent further contamination is the primary focus, but decontamination efforts also may be needed for eyes

Level	Description
A	Fully encapsulated and chemically resistant suit with integral gloves and boots with a self contained breathing apparatus
B	Chemically resistant suit, gloves, and boots, with full-faced respirator using positive pressure
C1	Chemically resistant splash suit, boots, and gloves with positive pressure respirator
C2	Chemically resistant splash suit, boots, and gloves with negative pressure respirator
D	Work uniform with minimal protection, no breathing apparatus required

Table 4—Different levels of personal protective equipment[58,59]

and skin wounds. The first step for sulfur mustard decontamination is removing clothing. Removal of clothing eliminates 80–90% of the contaminate and should occur within the first two minutes to minimize penetration into the skin and mucosa.[60] Under realistic conditions, this is a difficult task. Clothing acts as an occlusive dressing that increases absorption and prevents evaporation. Patients exposed to sulfur mustard may be asymptomatic leading to a false sense of safety. In public situations, hesitant victims must be encouraged to remove their clothing. Removed clothing should be placed in an airtight container or double-bagged and left at the hazard scene to prevent further contamination.[52,61]

Other alternative forms of decontamination include absorbent powders such as Fuller's earth (FE), a clay-like, earthy material. Fuller's earth has been shown to be an effective broad-spectrum adsorbent for chemical agents such as sulfur mustard. Fuller's earth does have drawbacks such as dust creation and inability to detoxify chemical agents. Therefore, more research into broad-spectrum, liquid chemical decontaminating and detoxifying agents is being conducted. An example of a liquid decontamination and detoxification agent is the Canadian Reactive Skin Decontamination Lotion (RSDL). This lotion was designed as a combination barrier cream and skin decontaminant.[63] Reactive Skin Decontamination Lotion has been shown to dissolve liquids from the skin surface and has detoxifying properties due to the possession of a nucleophilic compound.

Taysee *et al* demonstrated that FE and RSDL both were able to decontaminate sulfur mustard from pigskin, but RSDL had slightly better efficacy if used five minutes after contamination, due to its ability to counteract the progression of the early inflammatory process that leads to dermal changes. In this study, efficacy was measured by the degree of histopathologic dermal changes. Once sulfur mustard is fixed into the skin, the study showed no difference between FE and RSDL. Previous studies noted that FE was found to be less effective than RSDL when applied at four minutes on skins of guinea pigs.[63]

If possible, victims should wash with soap and water after the removal of clothing. Water with or without soap produces equivalent or better results than FE if used in a timely manner.[60] The eyes also should be irrigated copiously for 5–10 minutes. Studies during the Iran-Iraq war showed efficacy using copious soap and water lavage. During decontamination of larger communities, the use of Hazmat tents and trailers for soap and water decontamination should be available, but setup may be time-consuming and logistically difficult. The use of spray tunnels, pre-soaked towels, and other methods have not been examined in detail. If water is not available, an alternative solution consists of fresh 0.5% hypochlorite solution at pH of 10–11 for the skin.[60]

Currently, none of the available topical decontaminants have been useful once sulfur mustard has penetrated deeper into the skin. Therefore, regardless of additional decontamination strategies, it is important to remember that physical removal of sulfur mustard via clothing removal and rapid removal of victims from contaminated areas is the most important measure.[60]

5. *Triage of Victims*—Levitin *et al* classified victims into one of three categories: (1) deceased; (2) non-ambulatory injured; and (3) ambulatory injured and ambulatory worried well, in order to allow for more rapid identification, evacuation, and treatment of exposed civilians. The classification into the category "worried well" in the context of a sulfur mustard exposure may be misleading for healthcare professionals since pain, skin lesions, and respiratory toxicity may be delayed for several hours, and patients potentially may be triaged as "healthy" or have a false sense of security, thus avoiding medical attention. Deceased victims should be bagged or decontaminated on-scene to prevent exposure of healthcare providers and other victims. The non-ambulatory injured group must undergo decontamination prior to transport, and this group comprises a small percentage of survivors. The ambulatory injured and worried well comprise 80–90% of survivors. According to Levitin *et al* these individuals will transport, themselves to the hospital, evacuate themselves from the area of chemical release, or will not seek care. After initial triage, all victims exposed to sulfur mustard should undergo a secondary medical evaluation and monitoring for signs and symptoms of a vesicant toxicity. These Levitin categories only should be considered for the initial triage of sulfur mustard-exposed victims.[61]

https://doi.org/10.1017/S1049023X0000649X Published online by Cambridge University Press

This triage protocol has not been tested in a real situation. It may over- or under-triage individuals exposed to sulfur mustard in terms of severity of illness and outcome.

The hospital disaster plan must consider the possibility of the contaminated ambulatory injured and working well victims arriving at the hospital so that proper precautions for healthcare workers and other patients are used.[62]

Conclusions

Sulfur mustard is a chemical agent that is cheap and easy to manufacture, has the potential to cause long-term medical complications, and has the capacity to impact large groups of people simultaneously. Until now, sulfur mustard only has been used by governments as a military weapon. Sulfur mustard is a chemical warfare agent, which, in case of a civil attack, has the potential to overwhelm existing public health resources. Disaster planners should consider creating protocols to prepare for a large-scale, civilian, chemical threat like sulfur mustard and for surge capacity in disasters in general. Disaster plans should include and focus on the collaboration of different local and regional organizations and the educator, and training of first-line, and healthcare professionals in the rapid recognition and prevention of secondary contamination. Triage, evacuation, treatment protocols, and preparation of adequate surge capacity are further important components in a successful disaster plan. Disaster plans should take an all-hazard approach and should be integrated into a local and national framework in order to be efficient, flexible, and practical.

References

1. North Atlantic Treaty Organization (NATO): NATO handbook on the medical aspects of NBC defensive operations AMedP-6(B). Available at http://www.fas.ord/nuke/guide/usa/doctrine/dod/fm8-9/3ch1.htm#s1. Accessed 11 December 2008.
2. International Humanitarian Law—Geneva Protocol 1925. Available at http://www.icrc.org/ihl.nsf/intro/280?OpenDocument. Assessed 11 December 2008.
3. The Chemical Weapons Convention (CWC). Available at http://www.un.org/depts/dda/wmd/cwc. Accessed 11 December 2008.
4. Saladi R, Smith E, Persaud A: Mustard: A potential agent of chemical warfare and terrorism. *Clin Exp Dermatol* 2006;31:1–5.
5. Shohrati M, Peyman M, Peyman A, *et al*: Cutaneous and ocular late complications of sulfur mustard in Iranian veterans. *Cutan Ocul Toxicol* 2007;26:73–81.
6. Szinicz L: History of chemical and biological warfare agents. *Toxicology* 2005;214:167–181.
7. Bey T, Walter FG: Senfgas, Stickstofflost, Lewisit und Phosgenoxim. Hautschädigende Militärkampfstoffe und deren Bedeutung für die Rettungsdienste, Feuerwehren, Polizei und das Militär. (Mustard gas, nitrogen mustards, lewisite and phosgene oxime. Vesicant-type chemical warfare agents and their significance to the emergency medical services, fire departments, law enforcement agencies and the military [in German with English abstract]. *Notfall Rettungsmed* 2003;6:327–336.
8. Ghanei M, Harandi A: Long term consequences from exposure to sulfur mustard: A review. *Inhal Toxicol* 2007:19;451–456.
9. Khateri S, Ghanei M, Keshavarz S, *et al*: Incidence of lung, eye, and skin lesions as late complications in 34,000 Iranians with wartime exposure to mustard agent. *J Occup Environ Med* 2003;45:1136–1143.
10. Papirmeister B, Feister AJ, Robinson SL, *et al*: *Medical Defense Against Mustard Gas: Toxic Mechanisms and Pharmacological Implications*. Boca Raton: CRC Press, 1991, p 359.
11. Davis K, Aspera G: Exposure to liquid sulfur mustard. *Ann Emerg Med* 2001;37:653–653.
12. Evison D, Hinsley D, Rice P: Chemical weapons. *BMJ* 2002;324:332–335.
13. Williams KE: Physical properties of sulfur mustard HD. Available at http://chppm-www.apgea.army.mil/dts/docs/dethhd.pdf. Accessed 29 May 2008
14. Anonymous: Chemical casualties: Vesicants (blister agents). *J R Army Med* Corps 2002;148:358–370.
15. Sidell FR, Urbanetti JS, Smith WJ, *et al*: Vesicants. In: Sidell FR, Takafuji ER, Franz DR (eds) *Textbook of Military Medicine. Part I, Warfare, Weaponry, and the Casualty. Medical Aspects of Chemical and Biological Warfare*. Washington, DC: Office of the Surgeon General, Department of the Army, Walter Reed Army Medical Center, 1997, pp 197–228.
16. Borak J, Sidell F: Agents of chemical warfare: sulfur mustard. *Ann Emerg Med* 1992;21:303–308.
17. Compton JAG (ed): Blister Agents. In: *Military Chemical and Biological Agents Chemical and Toxicological Properties*. Caldwell, NJ: Telford Press, 1988, pp 6–86.
18. Peters RA, Sinclair H, Thompson R: An analysis of the inhibition of pyruvate oxidation by arsenicals in relation to the enzyme theory of vesication. *Biochem J* 1946;40:516–524.
19. Kehe K, Szinicz L: Medical aspects of sulphur mustard poisoning. *Toxicology* 2005;214:198–209.
20. Papirmeister B, Gross, CL, Meier, HL, *et al*: Molecular basis for mustard-induced vesication. *Fundam Appl Toxicol* 1985;5:s134–s149.
21. Korkmaz A, Yaren H, Topal T, Oter S: Molecular targets against mustard toxicity: Implication of cell surface receptors, peroxynitrite production, and PARP activation. *Arch Toxicol* 2006;80:662–670.
22. Mellor SG, Rice P, Cooper GJ: Vesicant burns. *Br J Plast Surg* 1991;44:434–437.
23. Watson A, Opresko D, Young R, Hauschild V: Development and application of acute exposure guideline levels (AEGLs) for chemical warfare, nerve, and sulfur mustard agents. *J Toxicol Environ Health B Crit Rev* 2006;9:163–263.
24. Balali-Mood M, Hefazi M: Comparison of early and late toxic effects of sulfur mustard in Iranian veterans. *Basic Clin Pharmacol Toxicol* 2006;99:273–282.
25. National Research Council (NRC) Subcommittee on Acute Exposure Guideline Levels, Committee on Toxicology, Board on Enviornmental Studies, Commission on Life Sciences, National Research Council: *Standing Operating Procedures for Developing Acute Exposure Guideline Levels for Hazardous Chemicals*. Washington, DC: National Academy Press, 2001, pp 1–202.
26. Hartmann HM: Evaluation of risk assessment guideline levels for the chemical warfare agents mustard, GB, and VX. *Regul Toxicol Pharmacol* 2002:35:347–356.
27. US Army Soldier and Biological Chemical Command: Material Safety Data Sheet. Mustard Gas. Available at http://www.castleviewuk.com/Frameless/Safe/msds/ex/MSDS_mustard.htm. Accessed 29 May 2008.
28. Rusch G, Garrett R, Tobin P, *et al*: The development of acute exposure guideline levels for hazardous substances. *Drug Chem Toxicol* 2002;25:339–348.
29. Javadi MA, Yazdani S, Sajjadi H, *et al*: Chronic and delayed-onset mustard gas keratitis: Report of 48 patients and review of literature. *Ophthalmology* 2005;112:617–625.
30. Vidan A, Luria S, Eisenkraft A, Hourvitz A: Ocular injuries following sulfur mustard exposure: Clinical characteristics and treatment. *IMAJ* 2002;4:577–578.
31. Momeni AZ, Enshaeih S, Meghadadi M, Amindjavaheri M: Skin manifestations of mustard gas: A clinical study of 535 patients exposed to mustard gas. *Arch Dermatol* 1992;128:775–780.
32. Dacre JC, Goldman M: Toxicology and pharmacology of the chemical warfare agent sulfur mustard. *Pharmacol Rev* 1996;48:289–326.
33. Ghanei M, Vosoghi AA: An epidemiologic study to screen for chronic myelocytic leukemia in war victims exposed to mustard gas. *Environ Health Perspect* 2002;110:519–521.
34. Tabarestani M, Farhoudi M, Balali M: Stem Cell and Erythroid Precursors Disorders in Three Patients with Sulfur Mustard Poisoning. In: Proceedings of the First International Medical Congress on Chemical Warfare Agents in Iran, June 1988, Mashhad University of Medical Sciences, Mashhad, Iran. Mashhad, Mashhad University Press, 1988;F10.
35. Tabarestani M, Balali M, Farhoudi M: Hematologic findings of sulfur mustard poisoning in Iranian combatants. *Med J Islamic Rep of Iran* 1990;3:185–189.
36. Newman-Taylor AJ, Morris AJR: Experience with mustard gas casualties. *Lancet* 1991;337:242.
37. Willems J: Clinical management of mustard gas casualties. *Ann Med Militaris Belgicae* 1989;3:s1–s61.
38. Beebe GW: Lung cancer in WWI veterans: Possible relation to mustard gas injury and the 1918 influenza epidemic. *J Natl Cancer Inst* 1960;25:1231–1252.

39. Yamada A: On the late injuries following occupational inhalation of mustard gas with special relationship to carcinoma of the respiratory tract. *Acta Pathol Jpn* 1963:13;131–155.
40. Hefazi M, Maleki M, Mahamoudi M, *et al*: Delayed complications of sulfur mustard poisoning in the skin and the immune system of Iranian veterans 16–20 years after exposure. *Int J Dermatol* 2006;45:1025–1031.
41. Panahi Y, Davoodi S M, Khalili H, *et al*: Phenol and menthol in the treatment of chronic skin lesions following mustard gas exposure. *Singapore Med J* 2007;48:392–395.
42. Smith KJ: The prevention and treatment of cutaneous injury secondary to chemical warfare agents. Application of these findings to other dermatologic conditions and wound healing. *Dermatol Clin* 1999;17:41–60.
43. Rice P, Brown R, Lam D, *et al*: Dermabrasion—A novel concept in the surgical management of sulphur mustard injuries. *Burns* 2000;26:34–40.
44. Evison D, Brown RF, Rice P: The treatment of sulphur mustard burns with laser debridement. *J Plast Reconstr Aesthet Surg* 2006;59:1087–1093.
45. Ghanei M, Shohrati M, Harandi A, *et al*: Inhaled corticosteroids and long-acting beta2-agonists in treatment of patients with chronic bronchiolitis following exposure to sulfur mustard. *Inhal Toxicol* 2007;19:889–894.
46. Macintyre AG, Christopher GW, Eltzen E Jr, *et al*: Weapons of mass destruction events with contaminated casualties. *JAMA* 2000;283:242–249.
47. Karayilanoglu T, Kenar L, Gulec M: Evaluations over the medical emergency responding to chemical terrorist attack. *Mil Med* 2003;168:591–594.
48. Kenar L, Karayilanoglu T, Eryilmaz M, *et al*: Chemical release at the airport and lessons learned from the medical perspective. *J Hazard Mater* 2007;144: 396–399.
49. Carmona RH: The science of surge: An all-hazard approach is critical to improving public health preparedness. *Acad Emerg Med* 2006;13:1097–1097.
50. Kahn CA: Personnel communication, May 2008.
51. Buryakov IA: Express analysis of explosives, chemical warfare agents and drugs with multicapillary column gas chromatography and ion mobility increment spectrometry. *J Chromatogr B Analyt Technol Biomet Life Sc* 2004;800:75–82.
52. Schwenk M, Kluge S, Jaroni H: Toxicological aspects of preparedness and aftercare for chemical-incidents. *Toxicology* 2005;214:232–248.
53. Capacio BR, Smith JR, DeLion MT, *et al*: Monitoring sulfur mustard exposure by gas chromatography-mass spectrometry analysis of thiodiglycol cleaved from blood proteins. *J Anal Toxicol* 2004;28:306–310.
54. Makas AL, Troshkov, ML: Field gas chromatography-mass spectrometry for fast analysis. *J Chromatogr B Anal Technol Biomed Life Sci* 2004;800:55–61.
55. Bowerbank CR, Smith PA, Drown DB, *et al*: Chemical detection in deployment toxicology using high speed gas chromatography with a solvating mobile phase and time-of-flight mass spectrometry. *Drug Chem Toxicol* 1999;22:57–71.
56. Muir B, Quick S, Slater BJ, *et al*: Analysis of chemical warfare agents. II. Use of thiols and statistical experimental design for the trace level determination of vesicant compounds in air samples. *J Chromatogr A* 2005;1068:315–326.
57. D'Agostino PA, Hancock JR, Chenier CL: Mass spectrometric analysis of chemical warfare agents and their degradation products in soil and synthetic samples. *Eur J Mass Spectrom* 2003;9:609–701.
58. Garner A, Laurence H, Lee A: Practicality of performing medical procedures in chemical protective ensembles. *Emerg Med Australas* 2004;16:108–113.
59. Koenig KL, Boatright CJ, Hancock JA, *et al*: Health care facilities' "war on terrorism": A deliberate process for recommending personal protective equipment. *Am J Emerg Med* 2007;25:185–195.
60. Hurts G: Decontamination. In: Sidell FR, Takafuji ER, Franz DR (eds) *Textbook of Military Medicine. TMM Publications Borden Institute, Part I, Warfare, Weaponry, and the Casualty. Medical Aspects of Chemical and Biological Warfare*. Washington, DC: Office of the Surgeon General, Department of the Army, Walter Reed Army Medical Center, 1997, pp 351–359.
61. Levitin H, Siegelson H, Dickinson S, *et al*: Decontamination of mass casualties—Re-evaluating existing dogma. *Prehospital Disast Med* 2003;18:200–207.
62. Kollek D: Canadian emergency department preparedness for a nuclear, biological or chemical event. *CJEM* 2003;5:18–26.
63. Taysee L, Daulon S, Delamanche S, *et al*: Skin decontamination of mustards and organophosphates: Comparative efficiency of RSDL and Fuller's earth in domestic swine. *Hum Exp Toxicol* 2007;26:135–141.
64. Robinson J, Leitenberg M (eds): *The Rise in CB Weapons. The Problem of Chemical and Biological Warfare. Volume 1: The Use of CB Weapons*. Stockholm: Alquist and Wiksell Humanities Press, 1971.

Editorial Comments: Mustard Gas or Sulfur Mustard: An Old Chemical Agent as a New Terrorist Threat

Samuel J. Stratton, MD, MPH

Medical Director, Health Disaster Management/Emergency Medical Services Orange County California Health Care Agency; Professor, University of California-Los Angeles School of Public Health, Center for Public Health and Disasters, Los Angeles, California USA

Correspondence:
E-mail: strattos@ucla.edu

Web publication: 23 January 2009

Drs. Wattana and Bey are to be congratulated for an excellent paper on the chemical agent sulfur mustard. The paper is a detailed analysis of the literature and serves as a definitive reference paper on sulfur mustard.

As described in the paper, sulfur mustard was used extensively during World War I and in the 1980s Iran-Iraq conflicts. Further, reserves of sulfur mustard developed for use in World War II still are in the process of being destroyed.[1,2] It is important to realize that, as stated by the authors, sulfur mustard is cheap and easy to make. Study of mustard vapors and liquids allows for review of all the characteristics of toxic irritant chemicals including poisonous industrial gases. In the classic 1921 novel, *Three Soldiers*, written by John Dos Passos that describes his ambulance attendant experiences during World War I, there are clear descriptions of the effects of mustard and other gases used as weapons. He describes the frequent use of chemical weapons with the insidiousness of symptoms of initial exposure, delayed symptoms causing horrid death, and the devastating psychological impact of the use of these weapons. Considering these characteristics and effects of sulfur mustard, it is important to realize that this inexpensive and easily formulated chemical agent always will be a threat as a device for use in human conflict and terrorism.

These comments address some of the less technical aspects of mustard and similar air-borne toxins, focusing rather on the triage of multiple casualties that result from toxic vapor exposures, education of emergency responders for response to such hazards, and expectations for decontamination of persons exposed to hazardous vapors. While sulfur mustard is classified as a chemical that has no uses outside that of being a chemical weapon by the international Chemical Weapons Convention, it serves as the ideal hazardous chemical threat with which to model emergency medical mitigation and response planning.[3]

Recently, there has been great interest in improving mass-causality triage and rapidly transporting victims of mass-casualty incidents from the field to more definitive care. Mass triage traditionally focuses on large traumatic incidents such as bombings and train accidents. In these settings, it is traditional for rescuers to rapidly move into the event area to initiate triage. An aspect of response to these multi-victim incidents is that there is high risk for ignoring scene safety before rescuers enter the event zone. The issue of scene safety is a considerable problem when considering mass-victim poisonous vapor and gas events.[4]

Sulfur mustard is an excellent example of a hazard for which rescuers could unknowingly enter a danger zone to attempt rescue and triage, and become victims themselves. Sulfur mustard, hydrogen sulfide, and various hazardous industrial vapors have high potential for being poorly recognized by someone with significant exposure to the poisons. Without proper training in the awareness of risk for potential exposure to such chemicals in unsecured rescue settings, field responders are at high risk for sustaining chemical injury. The risk for exposure to airborne and liquid poisons, such as sulfur mustard, must be recognized by field responders so that they understand the need for proper equipment and securing the safety of a scene before entering. Ensuring

scene safety particularly is important when approaching potential terrorist attack sites because sulfur mustard or other chemical agents can be deployed jointly with a bomb or other device and may initially be unrecognized.

In their paper, Drs. Wattana and Bey describe the classic symptoms that occur with initial contact to irritant chemical vapors and gases. The importance of educating emergency responders to be aware of the initial symptoms of potential toxic vapors and gases must be emphasized continually. Mucous membranes and the conjunctiva often are most sensitive to a toxic vapor or gas exposure, and, in a emergency medical response situation, eye irritation, nasal and throat irritation, and respiratory distress must be considered a strong sign of potential aerosolized hazardous material exposure and the need to immediately evacuate the scene or isolate the potential source. As with scene safety, recognition of the subtle symptoms that may indicate exposure to air-borne hazardous materials is important not only in the field, but in the accident and emergency department that may be receiving a contaminated patient.

Discussion of sulfur mustard allows for the exploration of the proper tactic for decontamination of individuals exposed to potentially hazardous liquids, vapors, and gases. While techniques for decontamination have been well-explored, decontamination strategies have not been established. Decontamination in the field is considered the foundation for maintaining safety for healthcare workers and limiting secondary contamination. While decontamination is a well-defined field practice, it may be of a limited nature or ignored.[4] Failures to properly decontaminate in the field when indicated is an error that leads to secondary contamination of ambulances and receiving hospital accident and emergency departments. This secondary contamination leads to loss of resources for response to large scale events as ambulances and emergency-accident wards then must be taken out of service for decontamination. A conservative approach to potential secondary decontamination by receiving hospital facilities is to proceed with decontamination procedures for all victims arriving from the field regardless of reported decontamination attempts in the field. Experience by this author has been that when there is one to two hazardous exposure victims in the field, those victims are thoroughly decontaminated before transport and pose little risk to the receiving medical facility. When more than a few victims are involved, there is a tendency to decrease the thoroughness of decontamination and focus more on efforts to move victims away from the scene as quickly as possible. Realizing that allowing one contaminated individual into the treatment area of an accident and emergency department will result in multiple secondary exposures and the need to close that medical unit to incoming traffic allows for support of an aggressive approach toward secondary decontamination of all victims of hazardous exposures upon arrival to a receiving facility. Accident and emergency department medical care providers should be well-versed in decontamination procedures and have the appropriate equipment and physical locations to effect proper decontamination.[5] It also is important that those in authority positions in an accident and emergency department take an aggressive early leadership role to provide secondary decontamination procedures and limit unrestricted entry into the treatment areas.[6]

In summary, Drs. Wattana and Bey have presented an authoritative paper on sulfur mustard that will serve as a detailed medical reference resource. The risk of sulfur mustard as a chemical weapon cannot be ignored because it is inexpensive, easy to produce, and has proven to be a formidable agent. Study of the chemical and physical aspects of sulfur mustard strongly supports training emergency responders in the need to always be aware of scene safety and their own subtle physical symptoms of potential hazardous exposure when performing rescues. Finally, a conservative approach to decontamination is rational when considering the risk of secondary contamination and loss of medical care resources if a contaminated victim is inadvertently allowed to enter an accident and emergency department.

References

1. American Chemical Society, Chemical weapons disposal is critical to national security, Chemical and Engineering News, Jan 18, 2007. Available at http://pubs.acs.org/cen/news/85/i04/8504disposal.html.
2. [US] Federal Emergency Management Agency: CSEPP Background Information (description of US Congress directive to destroy specific chemical weapons). Available at http://www.fema.gov/gpvernment/grant/cse[[1.shtm. Accessed 03 October 2008.
3. Chemical Weapons Convention Treaty: Annex on chemicals. Available at http://opcw.org/html/db/cwc/eng/cwc_annex_on_chemicals.html. Accessed 06 October 2008.
4. Lehavi O, Leiba A, Dahan Y, Schwartz D, Benin-Goren O, Schwartz R, Augarten A, Ben-Ari J, Ben-Yehuda Y, Weiss G, Levi Y, Bar-Dayan Y: Lessons learned from chlorine intoxications in swimming pools: The challenge of pediatric mass toxicological events. *Prehospital Disast Med* 2008;23:90–95.
5. Daugherty EL: Health care worker protection in mass casualty respiratory failure: infection control, decontamination, and personal protective equipment. *Respir Care* 2008;53:201–212.
6. Pinkert M, Bloch Y, Schwartz D, Ashkenazi I, Nakhleh B, Massad B, Peres M, Ben-Davan Y: Leadership as a component of crowd control in a hospital dealing with a mass-casualty incident: Lessons learned form the October 2000 riots in Nazareth. *Prehospital Disast Med* 2007;22:522–526.