# Ocular Injuries Following Sulfur Mustard Exposure: Clinical Characteristics and Treatment

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## Abstract

The chemical warfare agent sulfur mustard affects primarily the eyes, skin and respiratory tract. Of these, ocular injury is the most immediate and distressing. Learning to recognize ocular injury enables the treating physician to provide early and suitable treatment, which will reduce complications and allow the victim a rapid recovery.

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Sulfur mustard, Bis [2-chlorethyl] sulfide or HD, was one of the first chemical warfare agents to be used on a large scale [1]. Owing to its simple and inexpensive synthesis, as well as its physical and chemical properties, it has the potential of being one of the leading threats from both terrorist and military sources. During World War I sulfur mustard was used widely, leading to estimates of hundreds of thousands of casualties [2]. Since then, its use has been reported in several conflicts, mainly the Iran-Iraq war of the 1980s [3,4].

Sulfur mustard is a potent alkylating agent, readily penetrating the skin, mucus membranes and the eyes, which are the most sensitive [5,6]. Most victims sustain non-fatal but disabling injuries, mostly to the eyes, respiratory tract and skin [7]. Ocular injuries appear in 75–90% of all mustard gas casualties, with reports of delayed ocular morbidity appearing years later [8,9]. The severity of ocular lesions depends on the dose and duration of exposure, and ranges from mild ocular discomfort to corneal perforation with anterior chamber scarring, neovascularization and blindness. Recovery may take weeks to years, and long-term morbidity, even in the mildly injured, has been documented [9,10].

## Physical and chemical properties

Despite the existence of more highly effective chemical warfare agents that are more toxic, mustard gas has not lost its military usefulness because of its special characteristics. It is very toxic and difficult to treat, versatile, persistent, cheap, easy to produce, and difficult to protect against. Moreover, sulfur mustard is toxic as droplets, liquid and vapor.

### Physical properties

Pure sulfur mustard is a transparent liquid with a slight odor of castor oil, whereas technical sulfur mustard is a dark liquid with an odor typically described as that of mustard or garlic [1]. It is barely soluble in water (0.07% at 10°C) and very soluble in organic solvents, fuels and lubricants. It is easily absorbed by many food products, porous materials, paint and varnish coatings, and rubber articles, all of which remain contaminated for long periods [6].

### Chemical properties

Sulfur mustard degrades rapidly during the aqueous phase in two first-order kinetic steps: cyclic sulfonium intermediate, and a hydrolytic reaction with water or the alkylation of target molecules [1]. The second chlorine of sulfur mustard reacts subsequently to that of the first reaction and alkylates target molecules.

## Pathophysiology

A few mechanisms are responsible for the damage caused by sulfur mustard. It readily are penetrates cells, alkylating proteins, nucleic acids (DNA) and other small molecules such as glutathione. It also alkylates extracellular components such as basement membranes. It is a cytotoxic and vesication agent that also exerts dose-dependent mutagenic and carcinogenic effects [7,10]. During the last decade it became clear that this agent can also directly initiate inflammation and apoptosis by activating genes [11].

### Clinical appearance and course of injury

During exposure, the victim feels nothing. A latent period of 0.5–8 hours, depending on dosage, precedes the onset of noticeable symptoms [8,12].

### Mild to moderate injury

Ocular discomfort, tearing and photophobia are the first symptoms. As injury progresses, patients report severe ocular pain, dryness of the eyes and, occasionally, difficulties to see. Upon examination, blepharospasm, conjunctival hyperemia, and edema with secretions are prominent. Fluorescein staining reveals corneal erosions, varying from central punctata to large epithelial defects [4,9]. This acute phase usually dissipates, even if untreated, within 48–72 hours and appears fully healed within 2 weeks [13].

### Severe injury

When exposed to sulfur mustard vapor in high doses, or when droplets come in contact with the eye, the injury is extensive and the prognosis grave. These victims exhibit, in addition to the signs and symptoms described above, full-thickness corneal injury with chemical anterior uveitis, accompanied by posterior synechiae and cataract [9]. Intra-ocular pressure may rise transiently [14]. The skin and eyelid may present first- or even second-degree burns. These injuries eventually heal, leaving corneal opacifications, with new blood vessels growing from the limbal area towards the center of the cornea. Corneal perforation and phthisis bulbi might occur in extreme cases [9].

### Late complications

Over 90% of the casualties followed for a period of 10–14 years still exhibit ocular symptoms [15]. Conjunctiva may remain very sensitive to irritants, and attacks of blepharoconjunctivitis often occur [8,9]. In some cases, symblepharon may develop. There may be abnormal conjunctival vascularization and occasionally true varices. The cornea usually heals clinically, although animal histologic studies have shown that the seemingly healthy epithelium is irregular, exhibiting areas of hyperplasia with edematous collagen fibers [13,16]. Similar findings were described in corneas removed from patients who received a corneal transplant [17].

Follow-up of mustard gas casualties that was begun soon after World War I revealed delayed keratopathy [17], characterized by recurrent corneal erosions, stromal keratitis, corneal opacity and neovascularization. The use of sulfur mustard in the Iran-Iraq conflict elicited additional reports [3,15,18,19] of this unusual and interesting phenomenon of an injury occurring years after the initial exposure.

## Management

There is no known antidote for this agent. The main goal of treatment is to minimize damage and prevent complications and delayed illness. The first step after removing the victim from the affected area is decontamination. Clothing should be removed, skin dusted with Fuller's earth, and the victim's body scrubbed with detergent and rinsed with water. Fuller's earth must be kept from the eyes as it causes irritation. Eyes should be irrigated with copious amounts of a sterile solution – water or saline. If no sterile solution is at hand, tap water may be used.

The timing of decontamination is critical and it should be initiated as soon as possible following exposure. Victims should be reassured that their injury is transient and treatable and that their sight will return. Since pain is the first prominent symptom and makes examination difficult, a local anesthetic (such as benoxinate) should be used when examining the patient or when transport is required. Systemic analgesics should be used generously, if there is no significant respiratory injury, starting immediately after initial examination. New data from animal studies [20] have established the beneficial effect of topical anti-inflammatory drugs, especially corticosteroids (dexamethasone), on sulfur mustard ocular lesions. When given, starting 1 hour after exposure, it decreases inflammation but has no effect on the corneal erosions. An immediate course of topical dexamethasone given 4 times a day for one week is recommended for every patient exposed to sulfur mustard. This treatment will alleviate symptoms related to the inflammation accompanying the acute injury, such as conjunctival and eyelid edema, hyperemia and secretions, and will not cause a significant delay in corneal healing. Furthermore, reducing inflammation will improve the patient's sense of well-being. In addition, topical antibiotics should be administered to prevent secondary bacterial infection, as corneal erosion is usually present.

In general, all sulfur mustard casualties suffering any degree of ocular involvement should be under ophthalmologic supervision. The ophthalmologist can add additional treatments, such as ocular anti-hypertensive drugs and mydriatics to relieve ciliary spasm and pain and prevent posterior iridolenticular adhesions.

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