# Chapter 7

# CHEMICAL INJURIES OF THE EYE

EDWARD W. TRUDO, JR, MD*; AND WILLIAM RIMM, MD†



*Lieutenant Colonel, Medical Corps, US Army Reserve; Azar Eye Institute, 31519 Winter Place Parkway, Suite 1, Salisbury, Maryland 21804, and Assistant Professor of Surgery (Ophthalmology), Uniformed Services University of the Health Sciences, 4301 Jones Bridge Road, Bethesda, Maryland 20814-4799; formerly, Director, Corneal and External Disease, Walter Reed Army Medical Center, Washington, DC 20307-5001

†Colonel, Medical Corps, US Army; Ophthalmology Service, Walter Reed Army Medical Center, Washington, DC 20307-5001

## INTRODUCTION

Military forces face possible chemical injury caused not only by hazards of the battlefield but also by occupational hazards in the military's industrial base. Therefore, an understanding of the physiological damage and the treatment of chemical eye injuries is required for both the battlefield and the peacetime environment.[1] Occupational hazards come in the form of common chemicals that can injure the eye, including acids (eg, automobile battery acid, refrigerants, vinegar) and alkalis (eg, drain cleaners, fertilizers, building supplies). Military forces run the risk of being exposed to offensive chemical weapons that pose specific ocular risks. The principles of treatment are similar, however, whether the injury occurred as the result of chemical weaponry or of occupational hazards.

Chemical injuries of the eye are true emergencies requiring prompt recognition and treatment. Rapid dilution of the chemical agent is the immediate treatment necessary to reduce tissue damage and preserve vision. The extent of ocular injury is proportional to the departure of the corrosive substance from the neutrality of pH 7.4, the time that it remains in contact with the eye, and the quantity requiring neutralization.

Other factors must be considered when treating patients with injuries caused by chemical warfare agents. Ocular chemical injuries can cause immediate loss of vision, combat ineffectiveness, and even permanent blindness. Some effects are more subtle: the mere *threat* of chemical agents on the battlefield reduces unit morale and efficiency. Medical personnel who discern that injuries might be the result of chemical agents may be in a position to alert field command to the possible use of chemical warfare on the battlefield. In addition, medical personnel must be aware of specific antidotes for treating systemic and ocular effects stemming from exposure to chemical warfare agents.

Three other volumes in the *Textbooks of Military Medicine* series contain additional information on chemical injuries to the eye, which interested readers can peruse: *Occupational Health: The Soldier and the Industrial Base*[2]; *Military Dermatology,* particularly Chapter 5, Cutaneous Reactions to Nuclear, Biological, and Chemical Warfare[3]; and *Medical Aspects of Chemical and Biological Warfare*.[4]

## INJURIES OF THE EYE CAUSED BY COMMON CHEMICALS

### Chemical Agents

Chemical agents with the potential to cause ocular injury are often found in the home, at work within the military's industrial base, on the training field, and on the battlefield. Industrial and household cleaners often contain acidic or alkaline products in sufficient concentrations to cause eye and skin injury. Building materials, such as mortar and plaster, and automobile batteries are the most common sources of household chemical eye injuries today. Any of these agents can significantly damage human tissue after contact (Table 7-1).

Some common examples of acid-containing products are automobile batteries (sulfuric acid), refrigerants, and vinegar (acetic acid). Common alkali products include drain cleaners, fertilizers, refrigerants, and building supplies. Another household chemical injury can occur when an individual mixes cleaning agents and unknowingly liberates chlorine gas. This event can precipitate acute respiratory distress syndrome from chlorine gas inhalation and also cause ocular surface damage.

Peacetime training exposes military personnel to additional chemical hazards. Tear gas is often an element of training scenarios. The term *tear gas* refers to several different agents that can cause lacrimation. Ordinary tear gas (2-chloro-1-phenylethanone, also called CN and Mace) is used in riot control and civilian police activity. The most common military tear gas is 2-chlorobenzalmalonitrile (CS). In addition to its lacrimatory effect, tear gas produces a mild chemical keratitis, which is usually self-limited.[5] In its most concentrated form, tear gas has the potential to rapidly cause significant damage to the ocular surface.

In military field-training exercises, weapon and grenade simulators, flares, and other incendiary devices also are ocular hazards. These training devices may cause thermal injury in addition to chemical injury from the magnesium hydroxide contained in them.[6] Also, the projectile and explosive nature of these devices poses a risk of penetrating or perforating foreign bodies in addition to their toxic effects. Open globe injury must always be suspected.

### Acids and Alkalis

The normal pH of the human eye is approximately pH 7.4. Acids (considered here as substances

**TABLE 7-1**

**COMMON SOURCES OF CHEMICAL INJURY**

| Chemical | Example |
|---|---|
| **Acids** | |
| Sulfuric acid | Battery acid<br>Industrial cleaner |
| Acetic acid | Vinegar<br>Glacial acetic acid |
| Hydrochloric acid | Chemistry laboratories<br>Muriatic acid (cleaner) |
| Sulfurous acid | Bleach<br>Refrigerant<br>Fruit and vegetable preservative |
| Hydrofluoric acid | Glass polishing and etching<br>Gasoline alkylation<br>Silicone production |
| **Alkalis** | |
| Ammonia | Fertilizer<br>Refrigerant<br>Cleaning agent |
| Lye | Drain cleaner |
| Lime | Plaster<br>Mortar<br>Cement<br>Whitewash |
| Potassium hydroxide | Caustic potash |
| Magnesium hydroxide | Sparklers<br>Incendiary devices |

with lower-than-normal pH values) precipitate tissue proteins, creating a barrier to further ocular penetration. The corneal epithelium offers some protection against weaker acids. Very weak acids may cause only temporary loss of the corneal epithelium with minimal damage to the deeper structures.

Sulfuric acid is the most common cause of chemical ocular injury, usually the result of the explosion of a car battery.[7,8] Sulfuric acid has a great potential for permanent ocular damage; it reacts with the water present in the preocular tear film, producing heat sufficient to cauterize the corneal and conjunctival epithelium. Hydrochloric acid is commonly found in school and college chemistry laboratories. Fortunately, it has poor ocular penetration in its usual laboratory concentration. Acidic refrigerants contain oils, which make removal and decontamination difficult and prolong contact with the body. Hydrofluoric acid and heavy metal acids are exceptions to the penetration rules of acidic agents. They penetrate quite rapidly and destroy the corneal endothelium. Most of the ocular damage is the direct result of fluoride ion toxicity. Although acids usually do not penetrate the eye to cause the deeper destruction associated with alkali injuries, their injury of the ocular surface tissues results in corneal vascularization, scarring, and reduced vision.

Alkalis (bases) are agents with a pH in the higher-than-normal physiological range. In contrast to acids, alkaline agents rapidly penetrate the cornea, reacting with the cellular lipids to form soaps. Alkaline agents essentially dissolve the cell membranes; they continue destroying tissues much longer than acids do, permanently damaging ocular tissues and entering the anterior chamber in as short a time as 5 seconds. Alkaline substances continue their destruction of tissues within the eye for up to several days. Alkalis also dehydrate cells and destroy enzymatic and structural proteins. The most severe effects occur in the pH range 11.0 to 11.5. Penetration rates differ by the type of base; ammonium hydroxide is one of the fastest penetrating bases, followed by sodium hydroxide, potassium hydroxide, and calcium hydroxide.

### Thermal Injury

In addition to the damage created by the pH of chemical agents, associated thermal injury is also encountered. When the face and eyes are exposed to pure water at its boiling point, the normal cells

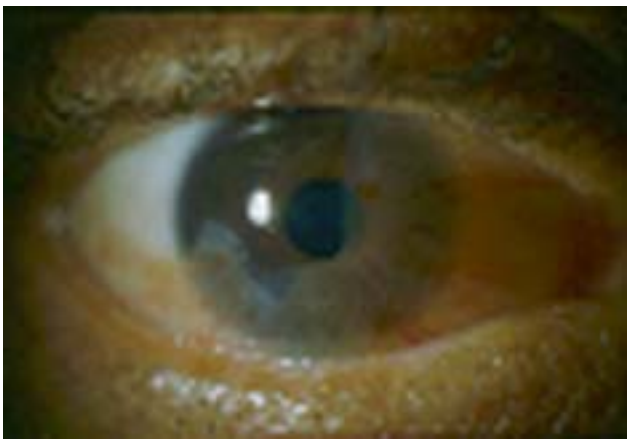

**Fig. 7-1.** Localized corneal scarring as a response to limbal stem cell thermal damage from pure water at the boiling point.

that populate the cornea (limbal stem cells) are destroyed, resulting in altered corneal surface healing. Scarring and opacification ensue (Figure 7-1). Chemical munitions are often delivered at a high temperature generated by explosions, or they may generate heat due to exothermic chemical reactions. For these reasons, the extent of injury from a chemical agent may have additional thermal damage not evident when the casualty presents to medical personnel.[8]

## OCULAR RESPONSE TO CHEMICAL INJURY

Each ocular structure responds uniquely to a chemical insult. The conjunctival tissues are cauterized. The corneal epithelium sloughs; the corneal stroma swells and opacifies; endothelial cells die and are replaced by neighboring cells that stretch to cover the resultant empty space. The angle structures scar, resulting in increased intraocular pressure (IOP). Cataracts form as a result of insult to the lens.[9–12]

Weak acids and alkalis in the eye cause similar injurious effects, including injection, chemosis, mild corneal clouding, and edema with minimal visible inflammation. In severe acid burns, however, the cornea and conjunctiva rapidly turn white and opaque. Nitric and chromic acids turn tissue yellow-brown. An initially deepithelialized cornea with clear stroma may belie the severity of the burn. The most severe acid burns produce corneal anesthesia, limbal pallor, and uveitis. Severe alkali burns can result in corneal melting and perforation within 2 to 4 weeks.[13]

The extent of injury to the limbal area is critical in determining the severity and prognosis of chemical burns. The ocular reparative response to chemical injuries involves reepithelialization and vascularization. If the perilimbal blood supply is damaged, sterile necrosis of the peripheral cornea can ensue. Injury to deep structures at the limbus can destroy the normal source (stem cells) for reepithelialization.

## CLINICAL COURSE OF CHEMICAL OCULAR INJURY

According to McCulley,[14] the clinical course of ocular chemical injury can be divided into the following four phases: immediate, acute, early reparative, and late reparative.

### Immediate Phase

The immediate phase begins the moment a chemical agent comes in contact with the ocular surface. The major determinants of prognosis are based on the initial clinical examination, although predictors of ocular recovery after chemical injury have proven to be more accurate if the evaluation is made 24 to 48 hours after the injury. Animal models demonstrate that the pH of the involved substance, its concentration, and the length of time the substance is in contact with the tissue are the major determinants of the depth of penetration and damage to deeper ocular structures.[15]

Because these factors are often unknown to the presenting physician and may not be recoverable from the patient's history, classification schemes and prognostic data have been based on examination findings. The clinical utility of classification schemes is to better predict which patients will respond to conventional medical therapy and which will require extensive treatment or are at risk for loss of the eye. In a military scenario, this classification of chemical injury is useful during triage for assigning patients for therapy on-site versus immediate evacuation. The most common classification schemes of ocular chemical injury are those by Ralph (Exhibit 7-1),[16] Hughes (Table 7-2),[17,18] and Thoft (Table 7-3).[19] The key elements for determining the extent of chemical ocular injury and prognosis are

- the total area of the corneal epithelial defect;
- the area of the conjunctival epithelial defect;
- the number of clock hours or degrees of limbal blanching (ischemia);
- the area and degree of density of corneal opacification;
- evidence of increased IOP on presentation, especially if resistant to treatment; and
- any loss of lens clarity.

The last two elements imply deeper effects of the chemical agent and damage to the inner ocular structures.

### Acute Phase

The first 7 days after chemical eye injury constitute the acute phase of recovery. During this time, the tissues rid themselves of contaminants while reestablishing the superficial protective layer of the corneal epithelium. *Reepithelialization is the most crucial factor in ultimate visual recovery; therefore, the first*

**EXHIBIT 7-1**

**RALPH'S CLASSIFICATION OF OCULAR CHEMICAL INJURY**

| Clinical Finding | Prognosis Code (Total score determines prognosis) |
|---|---|
| Perilimbal hyperemia | 0 |
| Chemosis | 1 |
| Spotty perilimbal ischemia | 1 |
| Clouded epithelium | 1 |
| Spotty denudation of epithelium | 1 |
| Up to 50% loss of epithelium | 2 |
| Mild stromal haze (iris detail visible) | 2 |
| Vertically oval fixed pupil (long posterior ciliaries) | 2 |
| Iridocyclitis | 2 |
| Perilimbal ischemia < $\frac{1}{3}$ of circumference | 2 |
| Complete epithelial loss | 3 |
| Moderate stromal haze (iris details barely visible) | 3 |
| Perilimbal ischemia $\frac{1}{3}$ to $\frac{1}{2}$ of circumference | 3 |
| Sustained intraocular pressure during the first 23 h | 3 |
| Severe stromal haze (no iris details visible) | 4 |
| Perilimbal ischemia > $\frac{1}{2}$ of circumference | 4 |

| Total Score (from above) | Category of Injury | Prognosis |
|---|---|---|
| 0–3 | Insignificant injury | Rapid recovery expected without permanent sequelae |
| 4–6 | Mild injury | Rapid reepithelialization and clearing of stromal haze<br>Return to baseline acuity in 1–2 wk |
| 7–9 | Moderately severe burn | Complete reepithelialization takes 1–3 wk<br>Persistent haze may reduce visual acuity<br>Stable pannus of 1–2 mm is common<br>Perforation not expected |
| 10–12 | Severe burn | Slow reepithelialization and frequent pannus<br>Furrow from collagenolytic activity in advance of pannus is common<br>Perforation very possible<br>Final visual acuity is low because of pannus and stromal haze |
| ≥ 13 | Worse cases | Inflammation quiets only after months<br>Dense pannus<br>Perforation is common<br>Vascularized corneal scar, cataract, and secondary glaucoma often ensue in those who retain the globe |

Adapted with permission from Ralph RA. Chemical burns of the eye. In: Duane TD, Jaeger EA, eds. *Clinical Ophthalmology*. Vol 4. Philadelphia, Pa: Harper & Row; 1987: 4, 6.

**TABLE 7-2**

**HUGHES'S CLASSIFICATION OF OCULAR CHEMICAL INJURY**

| Category of Injury | Clinical Finding |
|---|---|
| Mild | Erosion of corneal epithelium |
| | Faint haziness of cornea |
| | No ischemic necrosis of conjunctiva or sclera |
| Moderately severe | Corneal opacity blurs iris detail |
| | Mild ischemic necrosis of conjunctiva or sclera |
| Very severe | Blurring of pupillary outline |
| | Significant ischemic necrosis of conjunctiva or sclera |

Source: Ralph RA. Chemical burns of the eye. In: Duane TD, Jaeger EA, eds. *Clinical Ophthalmology*. Vol 4. Philadelphia, Pa: Harper & Row; 1987: 4.

*important therapeutic consideration is prompt, unhindered reepithelialization.* In severe eye injury, reepithelialization may determine whether the globe is retained. The epithelium serves as a protective barrier against the enzymes in tears that lead to corneal thinning and progression to perforation. It also modulates stromal regeneration and repair. Exposed stromal surfaces are a target for tear-borne enzymes of destruction and modulators that promote the release of stromal collagenases.[13,20]

Significant inflammatory mechanisms begin to evolve on the ocular surface and inside the eye. *Control of ocular inflammation is the second important therapeutic consideration during this period.* If severe, ocular inflammation can impair reepithelialization. Corticosteroid drops are the standard therapy during this period. In addition to promoting rapid reepithelialization and controlling inflammation, medical officers should also pay special attention to corneal clarity, IOP, degree of intraocular inflammation, and development of lens opacification. An acute rise in IOP may be due to the shrinkage of ocular collagen. After the acute rise abates, a more sustained increased IOP is the result of the elaboration of prostaglandins.[12]

### Early Reparative Phase

The healing period from 8 to 20 days after the injury constitutes the early reparative phase. This is the transition period of ocular healing, in which the immediate regeneration of ocular surface epithelium and acute inflammatory events give way to chronic inflammation, stromal repair, and scarring. The most important treatment goal remains the establishment of an intact epithelium. If the corneal epithelium did not fully heal during the acute phase, then the physician must aggressively treat the patient to minimize the risk of corneal thinning and perforation.

**TABLE 7-3**

**THOFT'S CLASSIFICATION OF OCULAR CHEMICAL INJURY**

| Category of Injury | Clinical Findings | Prognosis |
|---|---|---|
| Grade I | Corneal epithelial damage<br>No ischemia | Good |
| Grade II | Cornea hazy, but iris detail seen<br>Ischemia less than ⅓ of limbus | Good |
| Grade III | Total loss of corneal epithelium<br>Stromal haze blurs iris detail<br>Ischemia of ⅓ to ½ of limbus | Guarded |
| Grade IV | Cornea opaque, obscuring view of iris or pupil<br>Ischemia more than ½ of limbus | Poor |

Sources: (1) Roper-Hall MJ. Thermal and chemical burns. *Trans Ophthalmol Soc UK.* 1965;85:631. (2) Thoft RA. Chemical and thermal injury. *Int Ophthalmol Clin*. 1979;19(2):243–256. (3) Parrish CM, Chandler JW. Corneal trauma. In: Kaufman HE, Barron BA, McDonald MB, eds. *The Cornea*. 2nd ed. Boston, Mass: Butterworth-Heinemann; 1998: 642.

Ocular inflammation must also be controlled during this stage because inflammation can continue to inhibit epithelial migration over the corneal defects.[21] High-dose corticosteroids are usually required for the first 10 days of treatment, tapering at 14 days if an epithelial defect persists. The use of corticosteroids for more than 21 days in an eye without an intact epithelium risks collagenolysis and perforation.[22]

**Late Reparative Phase**

Three weeks after a chemical injury occurs, the healing process begins the late reparative phase. Application of ocular lubricants and tear substitutes must be continued to ensure a healthy epithelium. Chemical agents can cause loss of corneal sensation, decreasing the blink reflex and reducing the production of tears. Destruction of the associated mucin and lipid-producing cells also leads to an inadequate corneal tear film. Severe injury can lead to pannus formation during this time. Persistent corneal epithelial defects or recurring epithelial breakdown can be surgically managed by tarsorrhaphy.

## PATIENT TREATMENT AND EVALUATION

**Immediate Action**

At first glance, this section appears to be erroneously titled. However, in any known or even *suspected* chemical injury of the eye, immediate treatment with irrigation precedes patient evaluation. Prompt recognition and immediate treatment of a chemical injury are the most important aspects in the preservation of vision because only then can reepithelialization be optimized. In a wartime scenario, maintaining a high degree of suspicion that a chemical attack is imminent or has occurred is also important to ensure that proper protective measures are taken and that medical resources are preserved. Observing isolation and decontamination regimens and recognizing the type of agent involved may support intelligence gathering in the combat zone and preserve the lives of the evacuation and medical teams.

Immediately on suspecting a chemical injury, medical personnel should begin treatment. The most readily available nontoxic liquid is used to flush the area of the face, eyes, and any other areas of contact. Tap water is usually the most readily available, but using iced tea, milk, or any neutral liquid is better than delaying treatment. Research indicates that attempts to chemically neutralize the original agent (eg, using a dilute acidic solution such as vinegar to neutralize an alkali injury) are contraindicated because they may cause even more damage. The exception is the use of prepared neutralization kits, specific for the known chemical agent encountered.

Medical treatment begins by irrigating with 2 L of normal saline or lactated Ringer's solution over 20 to 30 minutes. Because of its flexibility, an intravenous line attached to the bottle is a useful means of delivering the irrigation fluid. These injuries are painful and result in blepharospasm and squeezing of the eyelids. These responses to pain often oblige medical personnel to hold the patient's eyelids open with a speculum or bent paperclips while the diluting solution is delivered to the globe (Figure 7-2). Because the pain is severe, topical anesthetics are helpful in maintaining patient cooperation. (It is essential that irrigating fluid be kept from running into the patient's ears to preclude any chemical agent from contacting the tympanic membrane; eg, the eardrums of casualties of a blast may be perforated). After irrigation is completed, the pH of the eye is measured with pH paper or a urine dipstick (for ease of use, the strip is cut to expose the pH plate at the edge of the strip).

After sufficient irrigation, the eyes and ocular adnexa are inspected for particulate matter. Evert-

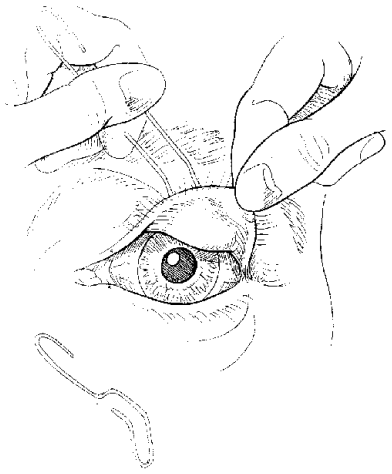

**Fig. 7-2.** Eyelid eversion using a bent paper clip. Drawing prepared for this textbook by Gary Wind, MD, Uniformed Services University of the Health Sciences, Bethesda, Md.

ing both the upper and lower eyelids is mandatory to search for retained particles trapped in the conjunctival fornix or embedded in the tissues themselves. Five minutes after the end of irrigation, the pH is again measured. If the pH is nearly normal, irrigation is temporarily suspended, particulate matter removed, and the examination portion begun. If the pH is not normal, irrigation is again performed with an additional 2 L of fluid. If the observed pH does not match the initial incident history, the patient and others should be questioned again.

**Patient Examination**

Once a normal pH level is attained and the patient's eye remains neutralized, a full ophthalmological examination is performed. Visual acuity measurements are taken for each eye independently. If a Snellen chart is not available, recording the ability of the patient to read newspaper headlines of "x" inches in height at a distance of "y" feet away is helpful.

Pupil examination is performed, noting any irregular shape or sluggish response to light. An irregular response may indicate iris ischemia due to chemical coagulation of the blood vessels in the iris or in the ciliary vessels. The external examination consists of the facial skin, eyelids, lashes, and lacrimal apparatus. Look for areas of lid burn, which can cause incomplete globe coverage, and for residual chemical particulate matter.

Ask the patient to look at an object straight in the line of view as the examiner looks at the eyelid position. Then the examiner should talk to the patient about other subjects while observing for a more relaxed lid position as well as blink reflex excursion and frequency. The patient is then asked to look up and down while the examiner observes the upper and lower eyelid position over the globe during the motion. Finally, the patient is asked to squeeze his or her eyelids tightly and then relax. It is also important for the physician and the assisting staff to observe the eyelid position and exposure of the globe while the patient is sleeping. Corneal or conjunctival exposure can lead to epithelial breakdown, infection, and corneal melting, and is a risk factor for loss of the eye.

Attention is then directed to the globe itself. A penlight, or preferably a slitlamp, examination is performed to detect epithelial loss, corneal opacification, and limbal ischemia. First, shine a light onto the corneal surface and observe the luster of the epithelium. Injured epithelial cells lack their typical reflective luster, resulting in an irregular corneal light reflex from the ocular surface. Note any gray or white areas of stromal opacification by observing whether iris detail or pupillary border is apparent when looking through the cornea. Limbal ischemia is measured by the number of clock hours of blood vessel loss of the conjunctival tissues where it nears the peripheral edge of the cornea.

Once the previous examination details are noted, a fluorescein strip may be wetted and placed on the ocular surface to delineate the extent of corneal epithelial loss (see also Chapter 3, Ocular Trauma: History and Examination). IOP is measured with one of the many instruments for this purpose or simply by comparing the tactile IOP of an intact globe by gently placing the fingertips on the closed eyelids. To facilitate evaluation of the posterior segment of the eye, eye drops (tropicamide or cyclopentolate) are instilled to achieve pupillary dilation. Cycloplegic eye drops also help control pain by effectively "splinting" pupillary reaction and reducing the pain associated with pupil constriction in bright light. Pupil dilatory drops also enhance the outflow of aqueous from the eye, helping to control IOP. The use of phenylephrine is not recommended, because its vasoconstrictive properties may lead to an increased risk of ocular ischemia.

A summary of evaluation and treatment is provided for rapid reference (Exhibit 7-2).

**Acute Phase Treatment**

Once the emergency treatment and evaluation are completed, the challenging task of healing the chemically injured eye begins. The major treatment goals that are important throughout the healing phases are (*a*) the reestablishment and maintenance of an intact and healthy corneal epithelium, (*b*) control of the balance between collagen synthesis and collagenolysis, and (*c*) minimizing the adverse sequelae that often follow a chemical injury. This triad of care for casualties with ocular chemical injuries takes place in the acute (urgent) phase of treatment.

The top priority in the acute phase is the reestablishment of an intact corneal epithelium. Without an intact epithelium, the risks of corneal thinning and perforation (melt), infection, and other complications that follow a chemical injury are significantly higher. The source for healthy epithelial cells is the rim of corneal epithelial stem cells that lie near the limbus.[23] A severe ocular chemical injury may permanently damage all stem cells. The corneal surface is therefore lacking in progenitor epithelial cells, and the surface is replaced with

**EXHIBIT 7-2**

**CHEMICAL INJURY: EVALUATION AND TREATMENT SUMMARY**

A. History

1. Suspected or known chemical contact
2. Possible wartime/lethal chemical agent
   a. Observe mission-oriented protective posture (MOPP) gear or self-protection
   b. Sound chemical alarm

B. Initiate Treatment

1. Irrigation
   a. 1–2 L normal saline or lactated Ringer's solution (30 min)
   b. Intravenous tubing
   c. Speculum
   d. Topical anesthetic
2. Inspection
   a. Remove particulate matter
   b. Pull down lower eyelid, inspect fornix
   c. Evert upper eyelid, inspect fornix
3. Indicator test: test pH at end of irrigation and 5 min after completion of irrigation
   a. If pH = 7: Stop irrigation
      Begin examination (see below)
      Recheck pH after 20 more min elapse
      Debride devitalized tissue
      Initiate medical therapy
   b. If pH < 7 or > 7: Restart irrigation with another 2 L
   c. If pH matches history (eg, low pH for acid injury), continue therapy
   d. If pH does not match history, obtain more details of injury while continuing treatment
4. Examination
   a. Visual acuity
      DISTANCE: Right Left
      NEAR: Right Left
   b. Pupils
      SHAPE: Round/Irregular
      REACTION: Fast/Sluggish
   c. External examination
      (1) Facial skin
      (2) Eyelid skin
      (3) Lashes
         (a) Loss
         (b) Eversion
         (c) Inversion
   d. Slitlamp or pen light examination
      (1) Conjunctiva
         (a) Number of clock hours of limbal ischemia
         (b) Areas of fluorescein staining

(**Exhibit 7-2** *continues*)

**Exhibit 7-2** *continued*

(2) Cornea
  (a) Epithelium: Fluorescein staining/cell loss
  (b) Stroma
    (i) Tissue loss
    (ii) Thickening
    (iii) Opacity
      Haze, but iris detail visible
      Haze blurs iris detail
      Haze obscures view of iris or pupil
  (c) Descemet's: Folds
(3) Anterior chamber
  (a) Depth
  (b) Foreign body
  (c) Red blood cells layered
  (d) White blood cells layered
  (e) Inflammation

C. Additional Information

| | | | |
|---|---|---|---|
| 1. Intraocular pressure: | Low | Normal | High* |
| 2. Lens: | Clear | | Clouded* |

*Elevated intraocular pressure or loss of lens clarity suggests significant intraocular penetration

slower-growing conjunctival epithelial cells and fibrosed and vascularized tissue.[24] In less-severe injury, corneal epithelial stem cells that survive a chemical injury act as progenitor cells for epithelial cell division and subsequent migration of the cells to cover the epithelial surface.[25] Promotion of a healthy microenvironment for these processes is the mainstay of therapy.

The preocular tear film is normally rich in moisture, lipids, mucus, and mineral cofactors. Treatment is usually aimed at replacing the aqueous portion of the tear film with preservative-free artificial tears, ointments, and antibiotics that are relatively nontoxic to the epithelium. If the eye is significantly damaged or eyelid closure is not sufficient to maintain a healthy tear surface, prevention of tear evaporation is aided by eyelid closure with a patch, eyelid taping, or tarsorrhaphy. Again, control of inflammation is important because significant inflammation immediately after a chemical injury inhibits reepithelialization. Corticosteroids should be used if there is no evidence of coexisting infection.

The second priority in the acute phase of healing after a chemical injury is maintaining a positive balance between collagen synthesis and collagenase activity. This balance is necessary for achieving the removal of damaged collagen tissue while rebuilding the stroma proper. Recent studies of chemical eye injuries[26–28] have indicated the importance of the stroma and epithelial interactions in the modulation of corneal wound healing, and thus the achievement of an intact epithelium is vital. These same studies have also shown that treatment with citrate and ascorbate eye drops with oral supplementation of ascorbate (vitamin C) can enhance collagen synthesis.

Limiting adverse sequelae is the third goal in the triad of care for the ocular chemical injury. Reducing the risk of infection is accomplished with an antibiotic that presents little toxicity to the epithelial cells. Control of IOP by suppression of aqueous production is often effective. Oral and intravenous medication may be preferred in the acute setting to minimize the amount of drops administered to the eye. Control of pain should never be taken lightly, as chemical injuries are often severely painful. Long-acting cycloplegics help in pain management, because they prevent the repeated movement of the pupillary muscles. Again, oral, intramuscular, and intravenous pain control are preferred.

Limitation of conjunctival scarring can be one of

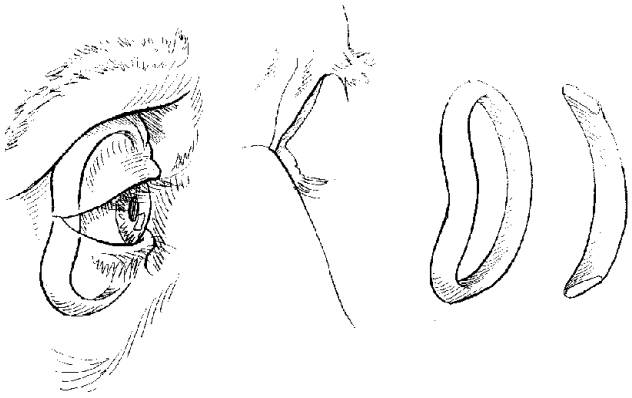

**Fig. 7-3.** A plastic symblepharon ring surrounds the globe and maintains the conjunctival fornices. Drawing prepared for this textbook by Gary Wind, MD, Uniformed Services University of the Health Sciences, Bethesda, Md.

the most challenging tasks for the physician. Prevention or breaking of formed symblepharon requires almost daily diligence. A symblepharon ring (conformer) is often helpful in these situations (Figure 7-3).

**Early Reparative Phase Treatment**

An intact epithelium should have already been achieved by the third phase of therapy. If it has not been, aggressive therapy is instituted by the use of lubrication, punctal plugs, punctal occlusion with cautery, bandage contact lens, or tarsorrhaphy. If the epithelium is not intact, corticosteroids are prescribed in a tapering dosage to be discontinued by the 14th day after injury. If significant inflammation remains, progestational steroids (eg, medroxyprogesterone) may be substituted or added to the regimen.[29,30] Ascorbate and citrate are continued. Antiglaucoma therapy is continued as required. If the epithelium is not intact, antibiotics are maintained. Examination for the formation of symblepharon is continued.

**Late Reparative Phase Treatment**

The patient whose injured eye has not achieved an intact epithelium by the 21st day, is at significant risk of permanent vision loss. Furthermore, long-term reduction in the amount of tear and mucus production, decreased corneal sensation, and the risk of sight-threatening infection place the patient at risk for loss of the globe. Aggressive surgical intervention is usually required in eyes that have not epithelialized within 3 weeks. Progressive thinning is treated as required with tissue glue, lamellar keratoplasty, patch graft, or pericardial tissue graft.

**Rehabilitative Phase**

After the eye has stabilized, most surgeons prefer to wait months to years to consider rehabilitative surgery. Limbal stem cell transplantation has shown remarkable promise in rehabilitating ocular chemical injuries that have resisted treatment or were considered too great for rehabilitation.[24,31–34] Limbal stem cells can be donated from the patient's uninjured fellow eye, a blood relative, or a postmortem globe. All have shown promise in reestablishing a healthy ocular surface prior to further reconstructive surgery. Once a healthy surface is achieved, penetrating keratoplasty or a keratoprosthesis may be considered.[35]

## INJURIES OF THE EYE CAUSED BY CHEMICAL WARFARE AGENTS

The earliest military use of chemical weapons included the burning of sulfur and other choking agents to "smoke out" an enemy holding in a defensive position. Chemical weapons were later used as defensive tools. Burning oils and other noxious agents were poured from cauldrons high atop castle towers onto attackers below to repel their assault.

Modern chemical weapons were used in the attempt to break the stalemate that had developed in the trench warfare of World War I. German forces discharged chlorine gas, allowing the prevailing wind to sweep it over the British and French soldiers entrenched in Belgium in April 1915. The wartime element of surprise effectively devastated the unsuspecting soldiers, who were not wearing protective equipment, and the toxic gas killed and injured unknown numbers because of its effect on the respiratory system. Sulfur mustard was first used in warfare at Ypres, Belgium, in 1917 by German forces.[36,37] By the war's end, both sides were using choking agents (eg, phosgene) and vesicants (eg, mustard) as modern weapons of the era.[38]

The images of chemical casualties from World War I and political issues were part of the reasons that chemical agents were not used in World War II. Despite active research in chemical agents, military use of chemical weapons declined for a time. During a phase of the Vietnam War (primarily in the late 1960s), chemical defoliants such as Agent Orange were sprayed to destroy the thick jungle

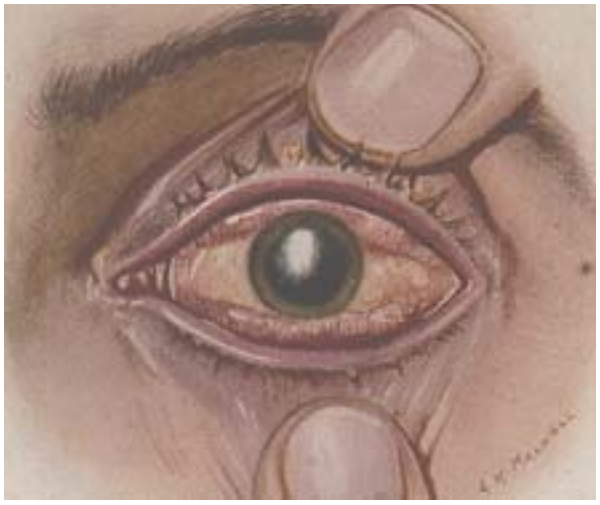

**Fig. 7-4.** (**a**) Although the vesicular effects of mustard agent on the skin of the casualty's back are impressive (the casualty's head is seen in the upper right of this photograph), (**b**) the eyes are significantly more sensitive to mustard's effects; the eye involvement seen here is relatively severe even though the skin is only minimally affected. (**c**) In 1918, the British prepared for the American Expeditionary Force a series of color drawings and descriptions of injuries by chemical warfare agents. This drawing depicts a severely burned eye in the acute stage after exposure to mustard vapor. A portion of the original description follows:

> [Severely burned eyes] may be recognized by certain characteristic features … . Whenever a dead white band crosses the exposed area of the conjunctiva, while the parts of this membrane covered by the upper and lower lids are red and oedematous, serious injury from the burning is likely to have occurred.
>
> In the case illustrated, the caustic effect of the vapour is seen chiefly in the interpalpebral aperture. On each side of the cornea there is a dead white band due to coagulative oedema, which compresses the vessels, impairs the circulation, and thus acts as a menace to the nutrition of the cornea. The swelling in the region of this white band is slight, while the protected conjunctiva above and below it is greatly swollen and injected and may even bulge between the lids.
>
> The exposed portion of the cornea is grey and hazy; it has lost its lustre, and when viewed with a bright light and a magnifying glass it shows a blurred "window reflex" and a typical "orange skinned" surface. The haze gradually faces off above in the region of the protected part of the cornea where the surface is bright and smooth. The pupil is at first contracted as a result of irritation and congestion. In this drawing it is shown as artificially dilated by atropine ointment, which should always be used early in severe cases or where there is much pain and blepharospasm.

Photograph b: Courtesy of Dr Luis Requena, Universidad Autónoma de Madrid, Spain. Reproduced from Bennion SD, David-Jabar K. Cutaneous reactions to nuclear, biological, and chemical warfare. In: James WD, ed. *Military Dermatology*. In: Zajtchuk R, Bellamy RF, eds. *Textbook of Military Medicine*. Washington, DC: Department of the Army, Office of The Surgeon General, Borden Institute; 1994: 95. Drawing c: Reproduced from *An Atlas of Gas Poisoning*. 1918: Plate 11A. Handout provided by the American Red Cross to the American Expeditionary Force. In: Joy RJT. Historical aspects of medical defense against chemical warfare. In: Sidell FR, Takafuji ET, Franz DR, eds. *Medical Aspects of Chemical and Biological Warfare*. In: Zajtchuk R, Bellamy RF, eds. *Textbook of Military Medicine*. Washington, DC: Department of the Army, Office of The Surgeon General, Borden Institute, 1997: 99.

plants and thereby deny the enemy concealment. Whether antipersonnel chemical agents were used during the Vietnam War continues to be debated.

A sharp rise has been seen in the distribution and use of chemical weapons in events around the world. Chemical injuries have increased both on and off the battlefield in recent decades. For example, as many as 45,000 casualties may have oc-

curred when Iraq employed mustard agent during its war (1982–1988) with Iran[39,40]; Iraq also deployed vesicants in its suppression of the 1988 rebellion in Kurdistan (Figure 7-4).

Military-strength chemical injuries have also occurred outside the classically defined boundaries of warfare. In the United States, highly toxic agents, both industrial and weapons grade, are commonly transported throughout the country. A significant industrial toxic chemical spill from a tanker truck in the Washington, DC, area required almost 24 hours for HAZMAT (hazardous material) team operations to completely decontaminate a major highway and the surrounding residential area.

In addition to the immediate effects, chemical injuries produce long-term problems with reduced vision, as well as employment and rehabilitation issues.[41] One patient who was exposed to mustard agent during the 1988 attack in Iraq presented 10 years later with delayed mustard gas keratopathy.[42] This and the recent examples above are just a few of the readiness issues for chemical injury that the military physician must be prepared to identify and treat whether in combat or everyday life.

Chemical munitions currently available include blister agents (vesicants), nerve agents, irritants, and blood agents (Tables 7-4 and 7-5). These agents can affect different organ systems, producing temporary incapacitation, temporary illness, permanent disability, or even death. The eyes can be very sensitive to many chemical agents (Table 7-6); permanent damage to the eye with loss of vision may occur.

### Blister Agents

The major agent in the vesicant, or blister agent, class is sulfur mustard. During World War I, there were as many as 400,000 chemical casualties, but fewer than 3% died of their chemical wounds.[43] Of the casualties of mustard agent, 86% had ocular involvement, and many had skin involvement, especially in warm, moist areas such as the scrotum, buttocks, axillae, neck, face, and areas that were

**TABLE 7-4**

**CHEMICAL AGENTS**

| US Army Code | Name of Agent |
|---|---|
| Vesicants | |
| H | Sulfur mustard, munitions grade (30% impurities) |
| HD | Distilled sulfur mustard |
| HN | Nitrogen mustard (once used in chemotherapy) |
| L | Lewisite (an arsenical) |
| Nerve Agents | |
| GA | Tabun |
| GB | Sarin |
| GD | Soman |
| VX | *o*-Ethyl *S*-[2-(diisopropylamino)ethyl] methylphosphonothiolate |
| Irritants (Tear Gas) | |
| CN | 2-Chloro-1-phenylethanone (also known as Mace) |
| CS | 2-Chlorobenzalmalononitrile |
| Vomiting Gas | |
| DM | Adamsite |
| Other Agents | |
| CG | Phosgene (alveolar toxicity) |
| AC | Hydrogen cyanide |
| CK | Cyanogen chloride |
| BZ | 3-Quinuclidinyl benzilate (anticholinergic agent with psychoactive properties) |

**TABLE 7-5**

**MILITARY CHEMICAL AGENTS OF OPHTHALMOLOGICAL INTEREST**

| Military Designation | Agent | Onset of Symptoms | Odor at Higher Concentrations |
|---|---|---|---|
| H | Sulfur mustard $S(CH_2–CH_2–Cl)_2$ | 4–12 h | Garlic or mustard |
| HN* | Nitrogen mustard $N(CH_2–CH_2–CL)_3$ | 1–6 h | Fishy |
| L | Lewisite $ClCH=CH–As–Cl_2$ | Immediate | Geranium |
| CX | Phosgene oxime $CCl_2=NOH$ | Immediate | Low concentrations: newly mown hay; higher concentrations: acrid, pungent, disagreeable |

*Although HN has previously been used only as a chemotherapeutic agent, it might be used as a weapon in the future.

**TABLE 7-6**

**OCULAR EFFECTS OF CATEGORIES OF CHEMICAL WARFARE AGENTS**

| Category of Agent | Ocular Effects | Category of Agent | Ocular Effects |
|---|---|---|---|
| Vesicants (Blister Agents) | Conjunctivitis | Riot Control Agents | Burning/irritation |
| | Irritation blepharospasm | | Conjunctival injection/ conjunctivitis |
| | Photophobia | | Lacrimation |
| | Corneal clouding and vascularization | | Blepharospasm |
| | Inflammation | | Photophobia |
| | Symblepharon | | Keratitis |
| | Lid burns | Phosgene | Pain |
| | Corneal perforation | | Keratitis |
| Nerve Agents | Miosis | | Conjunctivitis |
| | Pain | Cyanide | Irritation |
| | Dimming of vision | | Difficulty focusing (late mydriasis) |
| | Ocular pain | | |
| Mycotoxins | Tearing | | |
| | Pain/burning | | |
| | Decreased vision | | |
| | Conjunctivitis | | |
| | Keratitis | | |

constricted by clothing, such as the waist.[43] The British reported many thousands of eye casualties, with 75% mildly affected (2 wk on average before casualties were returned to duty); 15% were intermediate (incapacitated, 4–6 wk); and 10% were severe (their ocular injuries remained active for 4–6 mo before stabilizing). Fifty-one soldiers were blinded, and 180 were given vision-related pensions.[43] On the other hand, the Americans reported 1,500 chemical casualties, with 15% recovering in 10 to 14 days and 80% recovering in 5 to 8 weeks. They also reported cases of panophthalmitis.[44,45]

The apparent discrepancy between the British and American experience in World War I is hard to explain. The important fact remains that most patients recovered without significant damage but were incapacitated for a long time. The symptoms of photophobia, grittiness, pain, and blepharospasm effectively immobilized those affected. Keep in mind that 10% to 20% of those evacuated from the front during World War I for ocular injuries were suffering a combat reaction (gas hysteria) and either did not sustain a physical injury or demonstrated symptoms far in excess of their injuries. Today, our troops are better trained and equipped to deal with the chemical threat, and medical therapy for these types of exposures has been improved.

Between 75% and 90% of vesicant casualties can be anticipated to have ocular involvement,[44,46] with symptoms usually peaking 6 to 12 hours after exposure. Of these, 90% should have no significant corneal involvement.[47,48] They may present with a gritty sensation, conjunctivitis, chemosis, lid edema, blepharospasm, photophobia, blurred vision, tearing, and exudates.[39,48] The 10% with corneal involvement may additionally demonstrate corneal edema, keratitis, ocular pain or headache, temporary blindness, tissue necrosis, iridocyclitis, glaucoma, vascularization, delayed keratopathy, and rarely ulceration or perforation.[39,49–52]

### *Mechanisms of Injury*

The vesicants are alkylating agents that have a pronounced intracellular effect, especially on replication of deoxyribonucleic acid (DNA).[53] Irreversible histological changes occur within 10 minutes, and these changes become pronounced at 30 minutes. Additionally, the arsenical Lewisite liberates hydrochloric acid. The acid lowers the pH of the eye to 1.3, which causes superficial opacities, but arsine oxide is its main toxin.

Lewisite, developed in the United States at the end of World War I but never used, was nevertheless extensively studied in World War II, revealing the following facts[50,54]:

- the corneal surface is free of toxins within 2 to 4 minutes,
- toxins are in the stroma within 2 minutes,
- toxins are in the anterior chamber within 1.5 minutes,
- the anterior chamber is free of toxins within 30 minutes, and
- some stromal toxins are present for 1 to 26 hours.

Research with mustard agent shows similar penetration, with the eye being free of toxins within 15 minutes.[50] The delay in symptoms with mustard thus makes timely decontamination difficult. Early detection and prevention of injury become critical.

### *Signs and Symptoms*

Exposure to minute quantities (0.001 mg/L) of mustard agent for periods up to 1 hour does not affect the skin or the respiratory tract significantly. Yet, within 4 to 12 hours, lacrimation occurs, and a sandy sensation in the eyes becomes manifest. The conjunctivae and lids become swollen and edematous. Exposure to increased concentrations shortens the latent period, causes more damage with corneal involvement, and prolongs recovery to 2 to 6 weeks. Hot, humid weather increases the rapidity of action but also decreases the persistence of the agent.

The skin shows erythema similar to a sunburn after a latent period, and then large, thin-walled bullae usually form. Irritating these affected areas (eg, by scrubbing during decontamination), can promote vesicle formation in casualties who might not have developed them otherwise. The fluid in these vesicles is not contaminated and may safely be drained when necessary. These lesions behave much like second-degree burns and heal in several weeks, depending on the area affected.

Respiratory tract effects begin with hoarseness and a persistent cough that can progress to bronchopneumonia; these effects usually do not reach maximum severity for several days. This delay should prompt us to carefully observe those with ocular or facial burns for subsequent signs of pulmonary damage.

Working with casualties of mustard agent puts medical personnel at risk. Exhibit 7-3 lists some properties of mustard that healthcare personnel must keep in mind while aiding casualties who have

**EXHIBIT 7-3**

**FACTS TO KEEP IN MIND WHEN WORKING WITH CASUALTIES OF MUSTARD AGENT**

1. Mustard agent sensitizes, and reexposure to it—even to a small amount—may cause a more severe reaction.
2. Mustard agent is toxic in concentrations so slight that it may not be detected by its odor.
3. Contact with mustard agent is initially painless. Casualties may be produced hours or days after contaminated areas were exposed. (Lewisite, in contrast, causes immediate symptoms.)
4. Mustard-contaminated clothing, weapons, and the like may produce severe lesions for some time after the initial exposure. Contact with persons who were injured and with clothing unrecognized as contaminated with mustard has accounted for many secondary casualties among medical personnel.
5. Mustard agent is easily soluble in organic solvents and lipids but poorly soluble in water. Therefore, it can easily penetrate clothing and shoes and be absorbed into the skin. Decontaminate with water because organic solvents may actually promote its absorption.
6. Vaporized mustard agent is denser than air.
7. Mustard agent is persistent and is used to deny terrain to the enemy. This persistency varies from weeks in a cold climate to days in hot weather.
8. Mustard can be combined with other chemical agents such as Lewisite, phosgene, or nerve agents to enhance the toxicity. Keep this in mind if you are treating apparent nerve-agent casualties to avoid contaminating yourself and others.
9. Mustard agents can be delivered by airplane sprays, bombs, artillery and mortar shells, and by missiles. Mustard's boiling point is 220°C, and thefore to be effective, it must be atomized or vaporized by the munition.
10. Mustard agent that is not vaporized can contaminate the area as a contact poison with a long persistence and can serve as an inhalational poison as it evaporates.
11. Mustard agent can be destroyed by chlorination, but only dilute chlorine preparations should be used because of the great heat and sometimes flame that are generated by the chemical reaction. Decontaminating solutions are toxic to the eyes and should not be used.

Source: Blewett WK. *Defense Against Mustard: A P2NBC2 Review and Analysis*. Aberdeen, Md: Aberdeen Proving Ground, Physical Protection Directorate; 1992. Chemical Research and Development Engineering Command Technical Report 3270.

been exposed to mustard agent. Wounds per se are unlikely to be sources of mustard contamination of medical personnel, given the rapid fixation of mustard by tissues.

***Treatment***

There is no specific treatment used for mustard injuries; the treatment described above for alkali injuries should prove beneficial in dealing with such casualties. If decontamination is not performed within the first 5 minutes or certainly within the first 15 minutes, however, it is probably inconsequential to the outcome of the ocular injuries. The delay in the onset of symptoms probably precludes effective decontamination of the eyes, but decontamination of the casualty's clothing, skin, and hair can help prevent recurring exposure and secondary casualties. When a casualty with an injury caused by mustard agent arrives at a 3rd- or 4th-echelon medical treatment facility with an ophthalmology service, medical personnel may find it necessary to use a standing operating procedure (SOP) for mustard injuries of the eye (Exhibit 7-4).

However, a specific treatment for Lewisite injuries is available. British anti-Lewisite (BAL), which is dimercaprol, is extremely effective against Lewisite but *only* if administered topically within 2 to 10 minutes after exposure. Treatment for as long as an hour after exposure may have some benefit in an otherwise destructive lesion. Subsequent treatment of injuries caused by Lewisite and other vesicants should also follow the recommendations given for the treatment of alkali injuries.

Several publications advocate using topical anesthetics for the eye to relieve pain. However, these

**EXHIBIT 7-4**

**EXAMPLE* ORDER SHEET FOR A PATIENT WITH OCULAR MUSTARD INJURIES**

ADMIT:

Dx: Chemical ocular injury. ***WARNING! MUSTARD EXPOSURE DECONTAMINATED***

COND:

VITALS:

ALLERGIES:

ACTIVITY: Restricted to room/bed (to minimize the risks of contaminating others and of infection)

MEDS (*examples only*):

Polytrim ophthalmic solution: one drop 5 times daily
Ilotycin or bacitracin *ophthalmic* ointment: 3 times daily and at bedtime
Prednisolone phosphate: one drop to affected eye every 2 hours while awake
Vitamin C: 2 g by mouth, 4 times daily
10% ascorbate: one drop to the affected eye
10% citrate: one drop to the affected eye every 2 hours while awake
Homatropine 2%: one drop to the affected eye 3 times daily
Timoptic 0.5%: one drop to affected eye twice daily
Neptazane 50 mg: one by mouth, 3 times daily

*The listed medications are for a patient with ocular injuries from exposure to mustard agent, who has no contraindications or allergies that would preclude their use. This example is *only* a guide.

anesthetics *should be avoided* except as needed for periodic examinations, as they can have serious deleterious effects on the eye if used frequently. The use of systemic analgesics would be appropriate as needed.

**Nerve Agents**

The nerve agents are organophosphates that bind cholinesterase. Tabun (GA), sarin (GB), and soman (GD) are essentially volatile, nonpersistent agents used for their immediate effect, but they can be combined with a thickener for more persistence. They are clear, colorless, and odorless—except for tabun, which is said to have a slightly fruity odor. In March 1995, a terrorist attack with sarin in the Tokyo, Japan, subway system injured many civilians, 12 of whom died. Another nerve agent, *o*-ethyl *S*-[2-(diisopropylamino)ethyl] methylphosphonothiolate (VX; no common name), is oily with little volatility except in high temperatures and is used as a persistent agent.

These agents are mentioned here in the discussion of ocular injuries because they can cause miosis of the pupils, blurred vision, dimmed vision, and ocular pain. Atropine (as much as 20 to 100 mg may be needed in severe intoxication) and pralidoxime chloride (2-PAM Cl), which can remove the agent from sites on the enzyme acetylcholinesterase only if the nerve agent is not "fixed" on the enzyme molecule, are used to counter the effects of these nerve agents. Atropine is given as long as signs of intoxication are present and is usually titrated by minimizing nasal, bronchial, and salivary secre-

tions. The miosis or pupil size should not be used as an index of atropinization.

**Mycotoxins**

Trichothecene mycotoxins—the most memorable example is the infamous "yellow rain" from the Vietnam War era—are produced by certain strains of *Fusarium* fungi. They seem to inhibit synthesis of proteins. Symptoms appear from 1 hour (pulmonary route) to 24 hours (cutaneous route) after exposure and include vomiting, weakness, hypotension, and burns in exposed areas including the cornea.[55] Microgram quantities can cause irreversible corneal injury. Victims have complained of tearing, eye pain, conjunctivitis, a burning sensation, and blurred vision.[56,57]

## SUMMARY

Despite advances in treatment for chemical injury, knowledge of risks and prevention remain the best ways to avoid the often-long therapeutic course for recovery of vision. When a patient with a chemical ocular injury presents to the treating physician, early recognition and prompt treatment remain the standards to minimize ocular tissue damage and provide hope for preservation of vision.

Military chemical agents are usually not part of the daily training environment of civilian physicians, but chemical warfare agents remain a real threat on the battlefield. Knowledge of battlefield chemical munitions, their characteristics, and expected treatment is important for patient care as well as protection of medical personnel.

Chemical ocular injuries—whether they happen on the battlefield, in the military industrial base, or at home—will occur. When they do, knowledgeable physicians can minimize tissue destruction and enhance healing throughout all phases of treatment.

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