

CRITICAL CARE MANAGEMENT OF CHEMICAL EXPOSURES

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The views expressed in this article are those of the authors and do not necessarily reflect the position or policy of the Department of Veterans Affairs.



Objectives

- Review measures of preparedness and planning.
- Describe the purpose of decontamination.
- Discuss how to evaluate whether a patient has been adequately decontaminated to enter the emergency department (ED), hospital, or intensive care unit (ICU).
- Summarize the steps necessary to protect hospital staff: decontamination, personal protective equipment (PPE).
- Review specific agents: diagnosis, identification, and management.

If supposedly civilized nations confined their warfare to attacks on the enemy's troops, the matter of defense against warfare chemicals would be purely a military problem, and therefore beyond the scope of this study. But such is far from the case. In these days of total warfare, the civilians, including women and children, are subject to attack at all times.

Colonel Edgar Erskine Hume, *Victories of Army Medicine*, 1943



Case Study

A young couple was transported to your hospital's ED from a local cinema. You have been told there are many others who are being cared for by the emergency medical services and are en route. The 18-year-old male and 17-year-old female were admitted to your ICU after intubation and placement on mechanical ventilation. They are unresponsive and diaphoretic, and they have constricted pupils with excessive lacrimation, vomiting, diarrhea, and restlessness. The young man had a seizure. Copious secretions have been suctioned from their endotracheal tubes, and on auscultation coarse rales, rhonchi, and wheezes are heard.

- What should be your immediate intervention?
- What needs to be done to accommodate other victims?

I. INTRODUCTION

The term *chemical agent* has traditionally been defined as a substance intended for use in military operations to kill, seriously injure, or incapacitate humans (or animals) through its toxicological effects. These agents have been used in warfare for thousands of years but came to the forefront of modern warfare during World War I. German forces released 150 tons of chlorine gas from 6,000 cylinders on the afternoon of April 15, 1915, near Ypres, Belgium, in an attempt to help end the trench warfare. This release resulted in 800 deaths and caused the retreat of 15,000 Allied troops, largely due to the psychological terror it produced. Two years later, on July 12, 1917, again near Ypres, German forces used weapons containing a new agent, sulfur mustard, which resulted in 20,000 casualties. Although less than 5% of the casualties died as a result of the attack, many had debilitating injuries.



A chemical agent is a substance intended for use in military operations to kill, seriously injure, or incapacitate humans (or animals) through its toxicological effects.



Since then, chemical agents have been used intermittently in skirmishes and in warfare between nations, such as in the Iran-Iraq war of the 1980s, when both mustard and nerve agents were employed. In 1997, the Chemical Weapons Convention, which had the goal of eliminating state production, storage, and use of chemical weapons, was ratified by more than 160 nations. However, a new development, the use of chemical weapons by independent terrorist organizations, appeared on June 27, 1994, in Matsumoto, Japan, when the Aum Shinrikyo Cult released the nerve agent sarin, resulting in 600 people exposed, 58 admitted to the hospital, and 7 deaths. Their more famous and destructive release on March 20, 1995, in the Tokyo subway system resulted in 5,500 people exposed and 3,227 seeking care at hospitals, with 550 transported via emergency medical services. The closest hospital to the largest concentration of casualties, St. Luke's International Hospital, received 641 casualties in a short time: 5 critically ill, 106 with mild to moderate injuries, 530 with mild injuries, and eventually 2 deaths. Essentially none of

the patients were decontaminated prior to arriving at the hospital. Consequently, 20% of ED personnel, including 11 physicians, were affected by off-gassing of the victims. Once the problem was recognized, the removal of victims' clothing prevented further effects on the ED staff.

Owing to the local potential for earthquakes, St. Luke's International Hospital had previously conducted exercises in disaster response. In managing this chemical event, hospital staff learned the following lessons, among others:

1. A chemical incident requires quick recognition.
2. A pre-event disaster plan helps both preparation and response.
3. A moderately well-prepared hospital can save most patients.
4. Even under ideal conditions for the use of chemical agents, most victims of nerve gas may be only mildly to moderately affected.
5. If no attempt is made to decontaminate patients before they enter the hospital, staff and the facility will be contaminated.

In short, to properly plan for the decontamination and care of victims of chemical exposure, the presence of such agents and other toxins, such as biological agents, must be recognized. Common clues prompting concern are summarized in **Table 4-1**.

Table 4-1. Clues Signaling a Chemical (or Biological) Attack^a

- Large number of ill persons with a similar syndrome
- Large number unexplained diseases or deaths
- Unusual illnesses in a population or among individuals
- Disease with an unusual geographic or seasonal distribution
- Higher than usual morbidity and mortality in a common disease or syndrome
- Similar genetic type among agents isolated from distinct sources at different times/locations
- Unusual, atypical, genetically engineered, or antiquated agent strain
- Stable endemic disease with an unexplained increase in incidence
- Simultaneous clusters of a similar illness in noncontiguous areas
- Atypical disease transmission through aerosols, food, or water
- Point source of a disease outbreak with a compressed epidemic curve
- Patterns of illness related to ventilation systems
- Unusual animal deaths or illness preceding or accompanying human disease

^a Data from Biological Warfare and Terrorism Medical Issues and Response [Satellite Broadcast]. Fort Detrick, MD: United States Army Medical Research Institute for Infectious Diseases. September 26-28, 2000.

II. CHEMICAL DECONTAMINATION

The objectives of decontamination are to:

- Prevent further injury to the patient
- Protect hospital staff
- Protect the hospital environment

All patients who have been exposed to chemical agents must go through decontamination. It cannot be assumed that decontamination at the scene will result in 100% of patients being decontaminated. Experience has shown that many casualties of a chemical exposure will arrive directly at a healthcare facility without having been decontaminated, as occurred following the 1995 sarin gas attack in Tokyo.

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Decontamination of mass chemical casualties is best handled with water or soap and water.

The importance of an established decontamination plan and readily available equipment cannot be overemphasized. Decontamination of mass chemical casualties is best handled with water or soap and water. Although absorbing powders are also available, 95% of a chemical agent can normally be removed simply by washing with water. Resins can be used to absorb and inactivate mustard gas and many other oily chemical agents. Calcium chloride, magnesium oxide,

activated charcoal, and other substances—even powdered milk, flour, and clay—have also been utilized or suggested. Dry decontamination, however, is labor intensive and complex. Wiping can be dangerous and may smear the agent over unexposed areas. The most important aspects of decontamination are removal of the patient from the contaminated environment and removal of clothing and foreign bodies. The number of casualties must be effectively communicated from the scene of the chemical incident to receiving healthcare institutions so that adequate patient care and flow can be facilitated, even though communication may be difficult for people wearing protective masks.

All decontamination necessitates that the victim's clothing be removed, bagged, and labeled. This can be complicated by inclement weather and the need to maintain modesty for victims and the integrity of family units. Incapacitated victims who have organ failure or require mechanical ventilation will need specially trained personnel to manage their decontamination. Tents and other temporary facilities may be set up to efficiently decontaminate many individuals in production-line fashion. Makeshift facilities have even been created by hanging tarps over 2 fire trucks parked closely together. Generally, 2 lanes are required: 1 for walking victims who can pass through a shower area on their own, and 1 for more seriously injured and nonambulatory victims who will be placed on stretchers and passed through the shower area. Attention should be given to eye injuries, and supplies for eye flushing should be readily available. Blankets or heaters must be on hand to prevent hypothermia.



Decontamination facilities are best located outside the hospital in an area such as a parking lot.



Unless on-scene decontamination can be verified, all victims must be decontaminated prior to entering the hospital ED, acute care setting, or ICU. Hospital-based decontamination facilities are best located outside the building in an area such as a parking lot. These external decontamination facilities need not be elaborate and may be constructed with tarps and water hoses, if necessary. Of concern is the effluent and wash from decontamination, which should be placed

in large drums, if at all possible, to avoid contaminating the soil and surrounding area. A large, impermeable ground covering can be placed in such a way that contaminated drainage can be collected and prepared for proper disposal.

III. HOSPITAL ORGANIZATION FOR A CHEMICAL EVENT

A. Managing Patients' Arrival

Just as there is an organized response for a mass casualty incident in the field, there must be a similar organization at the level of the first receiver. A hot zone, which must be considered contaminated, exists outside of the facility. The inside of the facility must be kept clean for patient care and for central command to direct the facility's response. No one who is potentially contaminated should be allowed to enter the hospital. Patients must first pass through a triage area, where vital signs are assessed and casualties are simply designated as walking or lying. Here, 2 basic questions must be addressed: Can the patient walk? Does the patient need to be intubated? Walking patients must remove their clothing, proceed through decontamination, and receive fresh clothing or other suitable garments prior to being admitted into the hospital or an observation unit. The more seriously injured pass through decontamination on stretchers and require more expert management.

After decontamination, patients pass through a secondary triage station. Based on severity of illness or injury, individuals are assigned to an ICU or other acute care setting, or to a holding/observation area. Patients with complex injuries, such as blast injuries along with chemical exposure, normally proceed to the ED for further stabilization and management. An observation unit could be established outside the hospital to keep hospital beds and ED facilities as available as possible. Finally, counseling should be available for victims in need.



No one who is potentially contaminated should be allowed to enter the hospital.



B. Protecting Staff and Facilities

Staff protection from chemical contamination is of utmost importance. Adequate PPE must be supplied to healthcare providers working with victims of chemical exposure. Various hoods and masks are available, from passive breathing equipment to powered inhalation devices. Occupational Health and Safety Administration (OSHA) Level C protection, including a full face mask, powered or nonpowered hood, canister filtration device, and a chemical barrier suit with gloves and boots, will most likely suffice for the majority of responders at the hospital decontamination site. Attention should be paid to taping gloves and boots to the chemical barrier suit to provide an adequate seal.

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Adequate PPE must be supplied to healthcare providers.
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In regard to chemical exposures, the battle dress overgarment has been preferred by the US military. It has an inner layer that is charcoal-impregnated and absorbs biological agents, chemical toxins, and radioactive alpha and beta particles. Over that is a tightly woven outer layer. A hood, mask, and protective rubber gloves, as well as shoe covers, complete the garb. Civilian garb normally includes an impermeable, waterproof suit with hood, mask, gloves, and boots.

Clinicians must be familiar with the PPE they will need for various chemical agents. Support staff must be trained in their duties and, ideally, issued job descriptions detailing their roles in a mass casualty incident.

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Disaster response plans must anticipate needs for special equipment such as ventilators, intravenous access supplies, and pharmaceuticals, and for bed allocation in units such as critical care, acute care, isolation, and observation.
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All planning and training should be validated by drills and exercises in which everyone participates. Drills and exercises should not stop at triage and care in the ED. An essential element of planning is anticipating the need for special equipment such as ventilators, intravenous access supplies, and pharmaceuticals, and for bed allocation in units such as critical care, acute care, isolation, and observation. Planning must also ensure adequate communication between the hot, contaminated zone and cold or clean zones. When a chemical attack occurs, the possibility of multiple similar attacks must be considered as well as the likelihood that a chemical assault may be

mixed with other forms of attack, such as the release of biological agents, blasts, and/or radiation exposure. Safe transport of patients through the hospital decontamination zone and within the hospital must be addressed as well as security issues and other ways to protect the hospital environment from contamination. If the hospital becomes contaminated, it will be necessary to shut it down, and it will no longer be available to treat victims. Staff must be similarly protected to ensure both their own safety and adequate care of victims.

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If a hospital is contaminated, it must be shut down and prevented from treating victims.
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C. Stockpiling Supplies

Materials that must be stockpiled in preparation of a chemical-related mass casualty incident include Mark 1 kits or the drugs those kits contain—atropine and pralidoxime chloride (2-PAM). Large amounts of these drugs, especially atropine, must be kept on hand. Bronchodilators and steroids will be necessary to treat bronchospasm that occurs with respiratory tract irritants. Cyanide antidote kits must be kept on hand, or alternatively, the individual components of the kit, including amyl nitrite, sodium nitrite, and sodium thiosulfate, must be available. Readily available hydroxocobalamin may be another useful antidote for cyanide. Diazepam and/or lorazepam should also be kept on hand to treat seizures and agitation. Materials for establishing an airway as well as intravenous access are necessary. An adequate number of ventilators must be available for those who require mechanical ventilation.

Many hours may pass before state and federal agencies can provide supplemental medications, unless they were included in pre-positioned push-packs. Until emergency supplies arrive, all facilities must triage and use their equipment in an effective, efficient manner. With adequate planning, training, stockpiling of materials, and repetitive drills, morbidity and mortality can be drastically reduced.

D. Caring for Patients in the Intensive Care Unit

Ultimately, the most seriously ill and injured will be cared for in an ICU. The skills of critical care professionals are exactly those that will be most needed in any chemical incident. Patients will initially be diagnosed, triaged, stabilized, and treated in the ED. The intensivist, members of the critical care team, and nonspecialists participating in the expanded critical care team will eventually care for these patients in the ICU or in areas designated to increase ICU surge capacity. All healthcare providers who participate in the expanded critical care team must be familiar with the pathophysiology of various forms of chemical exposure and with the antidotes and drugs needed to treat them. Triage abilities and basic airway and vascular access skills are essential.

Only the most seriously ill or injured should be triaged to the ICU. Only those who have a possibility of recovery should be placed on mechanical ventilation, and only those with potentially reversible shock and multi-organ failure should be admitted into the intensive care setting. Sophisticated ventilators capable of pressure control ventilation—airway pressure release ventilation or oscillators—should be reserved for patients with acute respiratory distress syndrome, a common result of pulmonary agents. Other forms of respiratory failure can be treated with simple ventilators, even transport ventilators and ventilators provided through the Strategic National Stockpile. When an overwhelming number of patients require critical care, resources must be rationed in atypical ways.



Information that must be readily available includes number of ICU beds that can quickly be made available, number and types of ventilators available, and existing quantities of antidotes.



To ensure optimal patient care, specific information must be readily available. This includes the number of ICU beds that can be made available at a moment's notice, the number and types of ventilators available, and the existing quantities of antidotes such as atropine, 2-PAM, sodium nitrite, amyl nitrite, and sodium thiosulfate. In addition, it must be determined if current hospital supplies will suffice until the arrival of a push-pack.

IV. CHEMICAL AGENTS

Chemical warfare agents are classified by their physiologic action or military use. A summary of those agents can be found in **Table 4-2**. The 5 categories based on physiologic action are nerve agents, vesicants, cyanides, pulmonary agents, and riot-control agents. The nerve agents, vesicants, cyanides, and pulmonary agents are also classified according to their military uses. Each class of agents has different pathophysiologic signs and symptoms and requires different treatments. The management of the effects of chemical warfare agents requires specific knowledge of their biological effects and clinical experience in the diagnosis and treatment of intoxications. The identity of the toxin is usually unknown during the initial phase of exposure. Thus, it is essential to recognize the signs and symptoms of chemical warfare agents, obtain information on the type of agent used, and begin specific treatment.

The initial steps in the general treatment of exposure to chemical warfare agents include the distribution of PPE to rescue personnel and the decontamination of casualties, as discussed above. Antidotes should be given intramuscularly in the field, if available. Because porous foreign bodies in wounds may contain active agents, the removal and immediate decontamination of inanimate objects, usually in concentrated hypochlorite solution, is necessary.

A. Nerve Agents

Nerve agents were first developed in the 1930s in Germany for military use. They are chemically related to organophosphate insecticides and produce their effects by inhibiting the enzyme acetylcholinesterase. The resulting accumulation of excessive concentrations of acetylcholine at the cholinergic synapses causes overstimulation of nerve impulses and cholinergic crisis. Cholinergic receptors are located in the central nervous system, eye, respiratory tract, gastrointestinal tract, bladder, cardiac muscle, sweat glands, and blood vessels. The toxicity of these agents is mainly dependent on their power to inhibit acetylcholinesterase. The inhibition is initially reversible, but the bond between the agent and acetylcholinesterase may undergo a secondary reaction known as *aging*, which results in an irreversibly inactivated enzyme. The nerve agents their codes include the following:

- Sarin (GB)
- Tabun (GA)
- Soman (GD)

■ Cyclosarin (GF)

■ Methylphosphonothioic acid (VX)

Table 4-2. Chemical Warfare Agents

Nerve Agents	Signs	Symptoms	Treatment
Sarin Tabun Soman Cyclosarin Methylphosphonothioic acid	Pinpoint pupils, bronchoconstriction, respiratory arrest, hypersalivation, increased secretions, diarrhea, decreased memory, poor concentration, confusion, loss of consciousness, seizures	<i>Moderate exposure:</i> diffuse muscle cramping, runny nose, difficulty breathing, eye pain, dimming of vision, watery eyes, blurred vision, sweating, cough, chest tightness, headache, muscle tremors <i>High exposure:</i> Same as above plus sudden loss of consciousness, seizures, flaccid paralysis	Atropine 2 mg IM/IV every 5 minutes Oxygen Ventilatory support Pralidoxime 600-1,800 mg IM or 1 g IV over 20-30 minutes (maximum 2 g IM/IV per hour) Repeat atropine and pralidoxime as needed based on symptoms Benzodiazepine to treat seizures
Vesicants Sulfur mustard Lewisite Nitrogen mustard Phosgene oxide	Asymptomatic latency period (mustard), skin erythema and blistering, watery swollen eyes, upper-airway sloughing with pulmonary edema, metabolic failure, bone marrow suppression	Burning, itching, red skin, mucosal irritation (prominent tearing, burning, and redness of the eyes), eyelid edema, shortness of breath, nausea and vomiting, cough, chest tightness, sore throat	Mustards: no antidote Lewisite: British anti-Lewisite (BAL or dimercaprol), if available Supportive therapy for burns
Cyanides Hydrogen cyanide Cyanogens chloride	<i>Moderate exposure:</i> metabolic acidosis, venous blood O ₂ level above normal, hypotension, pink skin color <i>High exposure:</i> same as above plus coma, seizures, respiratory and cardiac arrest	<i>Moderate exposure:</i> giddiness, palpitations, dizziness, nausea and vomiting, headache, eye irritation, hyperventilation, drowsiness, restlessness <i>High exposure:</i> immediate loss of consciousness, seizures, respiratory failure, and death within 15 minutes	Oxygen Amyl nitrate by inhalation 1 ampule (0.2 mL) every 5 minutes Sodium nitrite 300 mg IV over 5-10 minutes Sodium thiosulfate 12.5 mg IV Repeat sodium nitrite based on hemoglobin level and patient weight Hydroxocobalamin 5-10 g IV as clinically indicated
Pulmonary Agents Chlorine Phosgene Diphosgene Chloropicrin	Pulmonary edema with some mucosal irritation, acute respiratory distress syndrome or noncardiogenic pulmonary edema, pulmonary infiltrates	Shortness of breath, chest tightness, wheezing, laryngeal spasm, mucosal and dermal irritation, coughing, burning sensation of eyes and throat, blurred vision	No antidote Oxygen Manage secretions
Riot-Control Agents Chloroacetophenone Ortho-chlorobenzylidene-malononitrile	Lacrimation, erythema, corneal injury, rhinorrhea, cough, dyspnea, tachypnea, wheezing or rales, hypoxemia, pulmonary edema, skin erythema and blistering	Eye irritation and redness, blurred vision, cough, hoarseness, shortness of breath, sore throat, dysphagia, salivation, oropharyngeal and nasal burning	No antidote Remove clothing Eye irrigation Respiratory support

Abbreviations: IM, intramuscularly; IV, intravenously.

1. Diagnosing Exposure to Nerve Agents

The appearance of symptoms varies with the route of exposure. Symptoms may appear within seconds after inhalation exposure and up to 30 minutes after dermal exposure, or they may be delayed for as long as 18 hours. Whereas respiratory symptoms are usually first to appear after inhalation, gastrointestinal symptoms are usually seen first after ingestion, as often occurs when organophosphate insecticides are ingested in suicide attempts or by accident.

Acetylcholine receptors are divided into 2 classes, muscarinic and nicotinic. Both kinds of receptors are overstimulated by acetylcholine, resulting in the constellation of symptoms that are seen in nerve gas poisoning. The muscarinic effects are manifested by complications of the eye, respiratory tract, gastrointestinal tract, and cardiovascular system. Stimulation of the nicotinic receptors results in increased fatigability and generalized weakness as well as scattered muscle fasciculations, twitching, and cramps.

Miosis is the earliest ocular sign following direct eye exposure. The pupil size depends on the balance between sympathetic and parasympathetic stimulation. Therefore, the pupillary constriction may be different in each eye, or the pupils may be wide in the beginning and become miotic later in the course of intoxication. Redness of the eyes may occur within minutes after exposure. Additional ocular effects include pain behind the eyes, headache, and twitching of the eyelids.

Following minimal respiratory exposure, the early effects include a watery nasal discharge, nasal hyperemia, chest tightness, and wheezing. Tightness of the chest is an early symptom of respiratory exposure that progressively increases as the agent is absorbed into the systemic circulation. Although bradycardia may result from cholinergic stimulation, in reality tachycardia may develop due to increased sympathetic activity stemming from stimulation of the nicotinic ganglia. Central nervous system effects include tension, anxiety, jitteriness, restlessness, emotional lability, and giddiness. In more severe exposures, headache, tremor, drowsiness, difficulty concentrating, and memory impairment may be present. This may be followed by coma, loss of reflexes, and Cheyne-Stokes respirations. Death results most directly from respiratory failure caused by paralysis of respiratory muscles, loss of airway control, and profuse bronchorrhea.

The acronym SLUDGE can be used to remember the basic clinical syndrome produced by nerve agents: *Salivation, Lacrimation, Urination, Defecation, Gastric distress, and Emesis.*

2. Managing Exposure to Nerve Agents

Removing patients from the toxic environment is one of the most important steps in managing exposure to nerve agents. Decontamination prevents patients' further absorption of the nerve agent and secondary exposure to healthcare providers. Dermal exposure requires formalized decontamination in the field and/or before entering the hospital. Endotracheal intubation with assisted ventilation is normally required to manage ventilatory failure. Because

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Atropine therapy resolves rhinorrhea, salivation, and lacrimation; controls bradycardia and circulatory depressions; dilates the bronchi; and abolishes bronchorrhea.
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high airway resistance necessitating pressures up to 50 to 70 centimeters of water may complicate ventilatory support, field personnel often prefer esophageal-tracheal double-lumen airway devices over laryngeal mask airways.

The speed of both the onset of symptoms and aging has a great impact on treatment and the effectiveness of antidotes. Atropine and 2-PAM are the 2 primary antidotes for nerve gas exposure. Atropine is a competitive antagonist at muscarinic receptors which resolves rhinorrhea, salivation, and lacrimation; controls bradycardia and circulatory depression; dilates the bronchi; and abolishes bronchorrhea. Nausea, vomiting, and diarrhea will cease, and constipation will occur. Seizures can be blocked by atropine for a very limited time after exposure to nerve agents. Because other neurotransmitter systems become involved in cholinergic overstimulation in the brain (eg, gamma-aminobutyric acid, glutamate), the neuromuscular transmission cannot be restored by atropine, which means that spontaneous respiration remains insufficient.

The recommended atropine dose is 2 mg by intravenous (IV) access repeated every 5 to 10 minutes and titrated until ventilation is easy and bronchial secretions have dried up. Patients with severe poisoning will require initial doses of 6 mg. Total doses of 40 mg or higher have been seen in organophosphate insecticide ingestion, a figure that may be useful in planning amounts of medication to have on hand. Dosing should be based on clearing of respiratory secretions. However, in the elderly and those with heart disease, caution is necessary to avoid provoking cardiac ischemia even though treatment with large doses of atropine is necessary. In the field, atropine should be administered intramuscularly (IM) if IV access is not available. Topical homatropine will be required to treat the miosis because systemic atropine will have no effect. Benzodiazepines may be administered to treat seizures.

Atropine does not regenerate acetylcholinesterase. Pralidoxime chloride reverses the binding of the nerve agent to acetylcholine, regenerating acetylcholinesterase and allowing the enzyme to metabolize acetylcholine. It can reactivate acetylcholinesterase in the whole nervous system (to a lesser extent in the central nervous system), provided the enzyme is not yet aged. Once aging has taken place, only generation of new acetylcholine will result in clinical improvement, a process that may take days to weeks. Soman undergoes aging in 2 minutes, whereas sarin ages in 5 hours. Typical 2-PAM doses range from 600 to 1,800 mg IM or 1 g IV over 20 to 30 minutes (maximum 2 g IM or IV per hour). Additional doses of atropine and 2-PAM may be administered depending on the severity of exposure.

Diazepam has historically been the anticonvulsant of choice for the management of seizures associated with nerve agent exposure. Centrally acting anticholinergics may also be effective adjuncts if given within 5 minutes of seizure onset. In the hospital setting, diazepam may be given intravenously until seizures resolve, normally in an adult dose of approximately 5 to 10 mg every 10 to 20 minutes, but not to exceed 30 mg in an 8-hour period. Even large doses may be ineffective if treatment is delayed. For use in the field, diazepam is available in auto-injectors containing 10 mg. Because ventilatory failure can result from use of diazepam, patients require close monitoring. The more commonly used benzodiazepines lorazepam and midazolam can normally be employed in the critical care setting. Some data suggest that midazolam may be more effective than diazepam, and recent literature has shown lorazepam to be the most effective agent to terminate seizure activity. Phenytoin, fosphenytoin, carbamazepine, valproic acid, and other common seizure medications have no effect on seizures induced by nerve agents.

B. Vesicants

Mustard gas is the most commonly known agent of the vesicant group. It was first used as a chemical weapon during World War I and was used as recently as the Iran-Iraq conflict in the 1980s. These compounds work by binding to a variety of molecules via a reactive sulfonium ion. They have high affinity for nucleic acids and sulfur and sulfhydryl groups in proteins. They act as alkylating agents affecting the biologic processes such as cell division and DNA synthesis. The vesicants and their codes include the following:

- Sulfur mustard (mustard gas, HD)
- Lewisite (L)
- Nitrogen mustard (HN)
- Phosgene oxime (CX)

1. Diagnosing Exposure to Vesicants

Vesicants burn and blister the skin or any part of the body they contact and may seriously destroy the epidermal layer of the skin. They act on the eyes, mucous membranes, lungs, skin, and blood-forming organs. They damage the respiratory tract when inhaled and cause vomiting and diarrhea when ingested. Pure sulfur mustard is a colorless liquid that is nearly odorless but may have an odor resembling garlic or mustard.

The organs most affected are the skin, eyes, respiratory tract, and occasionally the gastrointestinal tract. These agents are highly lipophilic and easily penetrate mucosal surfaces. Severity and duration of symptoms are related to the concentration of the agent and the length of exposure.

The eyes react relatively quickly to vesicant exposure because the cornea can be more easily penetrated and is more sensitive than the skin. Eye symptoms can develop within 30 minutes to 3 hours after exposure. Initially photophobia, lacrimation, irritation, and blepharospasm will appear, followed by hemorrhagic conjunctivitis. Corneal changes develop more slowly than conjunctival ones and begin with surface erosions followed by a clinical latent period of about 8 hours, after which corneal opacities may occur.

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The hallmark of dermal exposure to mustard is a prolonged asymptomatic period before symptoms appear.

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The hallmark of dermal exposure to mustard is a prolonged asymptomatic period before symptoms appear. The latent period may be as short as an hour after liquid contamination or as long as several days after mild vapor exposure. In temperate climates the latent period for most vapor exposures is usually 6 to 12 hours. This may result in delayed decontamination or even a failure to decontaminate.

The duration of the asymptomatic period and severity of the lesions are dependent on the mode of exposure, environment, and patient temperature. High temperature and wet skin are associated

with more severe lesions and shorter latent periods. Lesions appear preferentially in areas covered by clothing. Skin damage is characterized by generalized painful inflammation followed by blistering and desquamation. Blisters filled with fluid develop in relation to the dose and may appear within hours after the skin is exposed. The blisters may rupture if they are large enough and leave deep ulcers.

The inhalation of vesicant vapor results in lesions of the bronchial system. Airway damage begins with sinus pain, irritation of the nose, sore throat, and hacking cough. It can progress to hoarseness and loss of voice. Inhalation of large doses can damage the lower airways, causing shortness of breath and productive cough. Purulent bronchitis and patchy pneumonia may follow. Pseudomembranes that may eventually develop can obstruct the bronchi or trachea and lead to suffocation.

2. Managing Exposure to Vesicants

Treatment of exposure to vesicants is primarily supportive, and the majority of mustard gas casualties survive. Early decontamination is the only effective means of preventing the toxic effects of these agents. Healthcare providers should wear protective clothing when treating these patients. Burn units may be the most appropriate places for managing the most severely affected patients because infection is the most important complicating factor in the healing of vesicant burns. Topical antibiotics should be applied to blisters and skin ulcers; the use of steroids in this context is controversial. Ocular complications may be treated with ophthalmic antibiotics, steroids, and lubricants. Mild respiratory tract injury usually requires no treatment, but bronchodilators may be beneficial if bronchospasm is present. Antibiotics may be required to treat pneumonia, but prophylactic antibiotics are not recommended. The chelating agent British anti-Lewisite (or dimercaprol) may be used if the vesicant is lewisite, which resembles mustard in symptoms, signs, and management, except for its relatively abrupt onset of findings. Bougienage may eventually be required for airway pseudomembranes.

C. Cyanides

The cyanide agents are often called blood agents because they are taken up by the blood or lymphatics and systemically distributed to all tissues and organs of the body. The cyanides interfere with aerobic respiration by inhibiting mitochondrial cytochrome oxidase, resulting in tissue hypoxia and lactic acidosis. The cyanide ion forms a stable complex with ferric iron (Fe^{+3}) in the cytochrome oxidase enzymes, thereby inhibiting cellular respiration. The final step of electron transfer between the substrate hydrogen and oxygen in the mitochondria is therefore blocked. This stops the production of adenosine triphosphate, leading to a loss of energy needed for metabolism. The consequence is a metabolic breakdown despite normal oxygen supply. The cyanides and their codes include the following:

- Hydrogen cyanide (AC)
- Cyanogen chloride (CK)
- Cyanide salts (eg, sodium cyanide and potassium cyanide)

1. Diagnosing Exposure to Cyanides

The symptoms of cyanide toxicity depend upon the agent's concentration and the duration of exposure. The feeling after cyanide inhalation is similar to that of a cold in the nose and throat, followed by a burning sensation. Although debated, in some it may also be associated with the smell of bitter almonds. After exposure to lower concentrations of cyanide, symptoms appear within seconds to minutes, with hyperventilation being one of the initial signs of toxicity. The clinical syndrome mimics hypoxemia and hypoxia, with the exception that cyanosis is absent. The diagnosis is made on clinical grounds, but a high venous PO_2 relative to arterial PO_2 results from the inability of the tissues to use oxygen. Exposure to high concentrations of cyanide results in gasping for breath within seconds, immediate loss of consciousness, convulsions, and respiratory failure leading to death within 1 to 15 minutes.

Other symptoms of cyanide poisoning include headache, transient central nervous system stimulation, and dizziness. Vertigo and pink skin color are seen in the early stages of moderate cyanide exposure. Coma and seizures may develop later. Early respiratory arrest with tachycardia changing to bradycardia and cardiac arrest are the most severe and dramatic findings associated with cyanide.

2. Managing Exposure to Vesicants

The primary treatment for exposure to vesicants is to remove the patient from the source of exposure and provide oxygen and assisted ventilation if necessary. Medical treatment includes amyl nitrate administered by inhalation, 1 ampule (0.2 mL) every 3 to 5 minutes. Administer sodium nitrite 300 mg IV over 5 to 10 minutes and sodium thiosulfate 12.5 g IV over 10 minutes. Additional sodium nitrite should be based on hemoglobin level and patient weight. The sodium nitrite is given to produce methemoglobinemia, sequestering the cyanide on the methemoglobin, to which it binds preferentially over hemoglobin. Sodium thiosulfate combines with any remaining free cyanide to form thiocyanate, which is excreted in the urine.

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Hydroxocobalamin binds directly to cyanide.
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Also available to assist in the management is hydroxocobalamin, 5 to 10 g IV, as clinically indicated, which acts by binding directly to cyanide. It may be useful, especially in the prehospital setting. Anemic patients who may not tolerate the methemoglobinemia from sodium nitrite may also benefit from this therapy.

D. Pulmonary Agents

Phosgene is the primary pulmonary agent used in chemical warfare. Like mustard, its use dates back to Germany in World War I, when it caused 80% of all chemical fatalities. Phosgene is a colorless gas that when inhaled results primarily in pulmonary edema. It is not easily absorbed through the skin. These agents produce injury to the lungs and irritation to the eyes and the respiratory tract. They may also cause noncardiogenic pulmonary edema and predispose to secondary pneumonia. The pulmonary agents and their codes include the following:

- Chlorine (CL)
- Phosgene (CG)
- Diphosgene (DP)
- Chloropicrin (PS)

1. Diagnosing Exposure to Pulmonary Agents

The hallmark of phosgene poisoning is massive pulmonary edema. Initial symptoms include shortness of breath, chest tightness, wheezing, laryngeal spasm, mucosal and dermal irritation and redness, coughing, burning sensation of eyes and throat, and blurred vision. There is a latent period before the onset of more serious symptoms. Dyspnea, cough, tachypnea, and cyanosis usually precede pulmonary edema. Exertion exacerbates and hastens the onset of symptoms. If the patient survives, resolution begins within 48 hours, and in the absence of complicating infection, there may be little or no residual damage.

2. Managing Exposure to Pulmonary Agents

There is no specific treatment for phosgene or chlorine poisoning. Bronchodilator therapy with a nebulized β_2 -agonist, perhaps with the addition of nebulized ipratropium, is the mainstay of therapy for bronchospasm. Corticosteroids may be useful in the treatment of severe bronchospasm, particularly in individuals who have a history of reactive airway disease. There is, however, no definitive clinical evidence for their efficacy in reducing the severity of acute lung injury or pulmonary edema. Oxygen should be administered with humidification.

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There is no specific treatment for phosgene or chlorine poisoning.

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E. Riot-Control Agents

Riot-control agents are typically used to temporarily incapacitate, not to kill or injure. They characteristically act on the eyes and mucous membranes, causing intense pain and lacrimation. High concentrations irritate the upper respiratory tract and skin and may cause nausea and vomiting. The riot-control agents and their codes include the following:

- Chloroacetophenone (Mace, CN)
- Ortho-chlorobenzylidenemalononitrile (CS)

1. Diagnosing Exposure to Riot-Control Agents

The effects of riot-control agents are felt almost immediately, usually within seconds to minutes after exposure, and may last up to 5 to 10 minutes. The diagnosis of these agents is made by their odors and the presence of ocular and respiratory effects. The ocular effects include lacrimation,

erythema, corneal injury, and blepharospasm. Respiratory signs include rhinorrhea, cough, dyspnea, tachypnea, wheezing or rales, hypoxemia, and pulmonary edema. These agents may exacerbate preexisting pulmonary disease. Skin effects include stinging sensation, erythema, dermatitis, and, rarely, blistering.

2. Managing Exposure to Riot-Control Agents

Riot-control agents usually have short-lived effects and are unlikely to cause fatalities. Treatment usually includes clothing removal and eye irrigation. Respiratory support consists of supplemental oxygen and bronchodilators if severe respiratory injury is present. Erythema and the stinging sensation of the skin are transient and do not require treatment. More severe skin reactions may be treated with topical products such as calamine lotion or corticosteroid cream.

Key Points

CRITICAL CARE MANAGEMENT OF CHEMICAL EXPOSURES

- Healthcare workers should be highly suspicious that a chemical incident has occurred if the hospital receives an influx of patients suffering from a similar symptom complex.
- Most patients present to the hospital without having undergone prior decontamination, even if decontamination is being conducted at the incident site.
- The unique patient management requirements of a chemical exposure, including the need for decontamination, place a strain on the hospital, stressing the need for pre-event planning and staff training as well as consideration of logistical issues related to space, supplies, and medications.
- The purpose of decontamination is 3-fold: it protects patients from ongoing injury due to residual agent on the clothing and skin, it guards healthcare workers from injury caused by contact with the residual agent, and it enables the facility to remain uncontaminated and thus continue to treat casualties.
- Personal protective equipment, preferably OSHA Level C, must be worn by healthcare providers working with victims of chemical exposure.
- The severity of patients' symptoms is related to the toxicity of the chemical and its concentration.
- Symptoms of nerve agent contamination vary depending on the route and dose of exposure. Treatment options include decontamination; assessment of the airway, breathing, and circulation; supportive care; and antidotes. Atropine treatment should be titrated to secretions. Death is usually secondary to asphyxiation.
- The route, dose, and exposure time of cyanides, whether as a fast-acting, volatile gas, or a colorless liquid, drive the severity of systemic poisoning. Cyanide exposure can be treated with sodium thiosulfate and sodium nitrite IVs, and recovery is generally rapid. Hydroxocobalamin is a new alternative.

- Vesicants quickly cross both skin and mucous membranes and target the eyes, skin, lungs, mucous membranes, and blood-forming organs. Given the lack of a specific antidote, treatment options revolve around decontamination, topical medications and antibiotics, antiemetics, supportive blood products, and fluid therapy. Acute mortality is relatively low, but morbidity is high.
- Pulmonary agents damage the alveolar-capillary membrane, causing significant fluid leakage in the lungs. Treatment options include decontamination, supportive care, IV fluids, mechanical ventilation, and vasopressors.



Suggested Readings

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Chemical Weapons Elimination. Centers for Disease Control and Prevention. <http://www.cdc.gov/nceh/demil/>.

National Library of Medicine/NIH. <http://sis.nlm.nih.gov/enviro/chemicalwarfare.htm#a1>.

Medical Management Guidelines for Acute Chemical Exposures. Agency for Toxic Substances and Disease Registry. <http://www.atsdr.cdc.gov/MHMI/mmg.html>.

US Army Medical Research Institute of Chemical Defense. <http://chemdef.apgea.army.mil/>.