

Chapter 9

Chemical Exposures

OBJECTIVES

1. Describe how to protect hospital staff and other patients from being exposed to contaminated patients.
2. Discuss when to treat nerve agent poisoning, how much initial treatment to provide and what clinical findings should guide additional therapy.
3. Describe the relationship between water solubility of a pulmonary agent and anatomic location of injury.
4. Describe the relationship between time to onset of symptoms and amount of exposure to a chemical agent.

I. INTRODUCTION

Whether it is due to an industrial accident or terrorist attack, a chemical exposure will likely involve large numbers of casualties—possibly in the thousands—depending on the method of agent dispersal. If it involves an explosion, then healthcare providers will see chemical injuries along with conventional ones. Consequently, those treating critically ill patients must understand the basic principles of decontamination, including the most appropriate personal protective equipment (PPE). To ensure their own safety, HCWs must also be familiar with mechanisms of action, clinical presentations, diagnoses and treatments for chemical agents.

II. OVERVIEW OF CHEMICAL AGENTS

Chemical agents that cause injury and death through their toxicological effects include nerve agents or anticholinesterases, blood agents or cyanogens, choking or lung-damaging agents and blister agents or vesicants. Examples of chemical agents that may trigger a mass casualty event are nerve agents such as GA (tabun), GB (sarin), GD (soman) and VX. Blood agents or cyanogens include hydrogen cyanide (AC), cyanogen chloride (CK) and arsine (SA). Choking or lung-damaging agents that have the potential to effect large numbers of people include chlorine (Cl), phosgene (CG) and diphosgene (DP); both chlorine and phosgene are potentially toxic industrial chemicals as well as potential chemical warfare agents. Nitrogen mustard (HN), phosgene oxime (CX) and lewisite (L) are examples of blister agents or vesicants. Each of these categories of chemical agents will be discussed in greater detail later in the chapter.

Lethal agents are typically used as a liquid or vapor. In liquid form, chemical agents have a slower onset compared with vapors that have a fast onset. The greater the exposure and amount of chemical absorbed, the more severe the effect on the victims. This is also true in cases of direct dermal and inhalational exposure. For example, larger exposures cause loss of consciousness, seizures, apnea and death whereas low-dose exposures cause slowness in thinking and decision making, sleep disturbances, poor concentration and emotional problems. Small to moderate direct exposures cause localized symptoms such as blanching, sweating and fasciculation followed by gastro-intestinal (GI) symptoms. Symptoms of a direct, large exposure are the same as those caused by vapor exposure. Generally, the greater the amount of chemical exposure, the faster the onset of symptoms.

Hospital providers who are faced with an influx of patients suffering from a similar symptom complex should be highly suspicious that a chemical incident has occurred.

Such an event may or may not be accompanied by an explosion. To help make this determination, HCWs should collect pertinent information from the injured individuals, bystanders and emergency medical services (EMS) personnel. Not only will HCWs need a high index of suspicion to come to this conclusion, hospital providers will need to take quick action to treat the victims and minimize the contamination risk to others.

III. MANAGEMENT OF A CHEMICAL INCIDENT

A. FIRST RECEIVERS VERSUS FIRST RESPONDERS

Hospital providers who receive contaminated victims for treatment during a chemical incident are considered "first receivers." This group is a subset of the "first responders," who are typically firefighters, law enforcement personnel, hazardous material team members and EMS personnel who act at the site of the incident. Therefore, potential exposure of first receivers is limited to the quantity of the chemical on the victims, as well as victims' clothing and personal effects.

B. RISKS POSED BY CONTAMINATED VICTIMS

Hospital providers must be prepared for potentially contaminated patients to present to the facility. In fact, up to 85% of victims of a hazardous materials incident go to the hospital without having undergone any prior decontamination. Following the release of sarin gas in the Tokyo subway system in 1995, 641 casualties were received at St. Luke's International Hospital, the nearest facility. No attempt was

made to decontaminate the patients before they entered the hospital. Subsequently, 20% of hospital staff became symptomatic.

C. MOVEMENT OF PATIENTS

Victims will need to be transported from the incident site to the hospital. Once there, they must be decontaminated before being admitted to the emergency department (ED), which should have a separate entry for contaminated patients. The hospital may consider establishing a "fast track" decontamination line for patients with severe or life-threatening symptoms enabling them to receive basic life-saving treatment during decontamination. Another option would be to establish a separate "lane" for patients arriving by ambulance who have been decontaminated on the scene enabling them to be more quickly assessed for adequate decontamination and triaged to medical screening.

Establishing a patient flow scheme in advance will help keep patients move along rapidly from decontamination through the ED to the appropriate floor or unit (**Figure 1**). The scheme assumes that all areas outside the hospital are contaminated and all areas inside the facility are clean. Ambulances bringing victims are unloaded at a triage point. The physicians and nurses running this station must decide if the patient can walk or whether he/she needs to be intubated. The patient may also need immediate intervention but not intubation – eg, fluid resuscitation, fracture stabilization, etc. Walking patients are considered only mildly injured and are sent to decontamination. Following that, they will be sent to a holding area for observation. Ideally, this holding area will be located in a building adjacent to but separate from the main facility to prevent overcrowding in the main part of the hospital. The

remaining patients, who are considered moderately to severely injured, will be intubated, if necessary, and sent to decontamination.

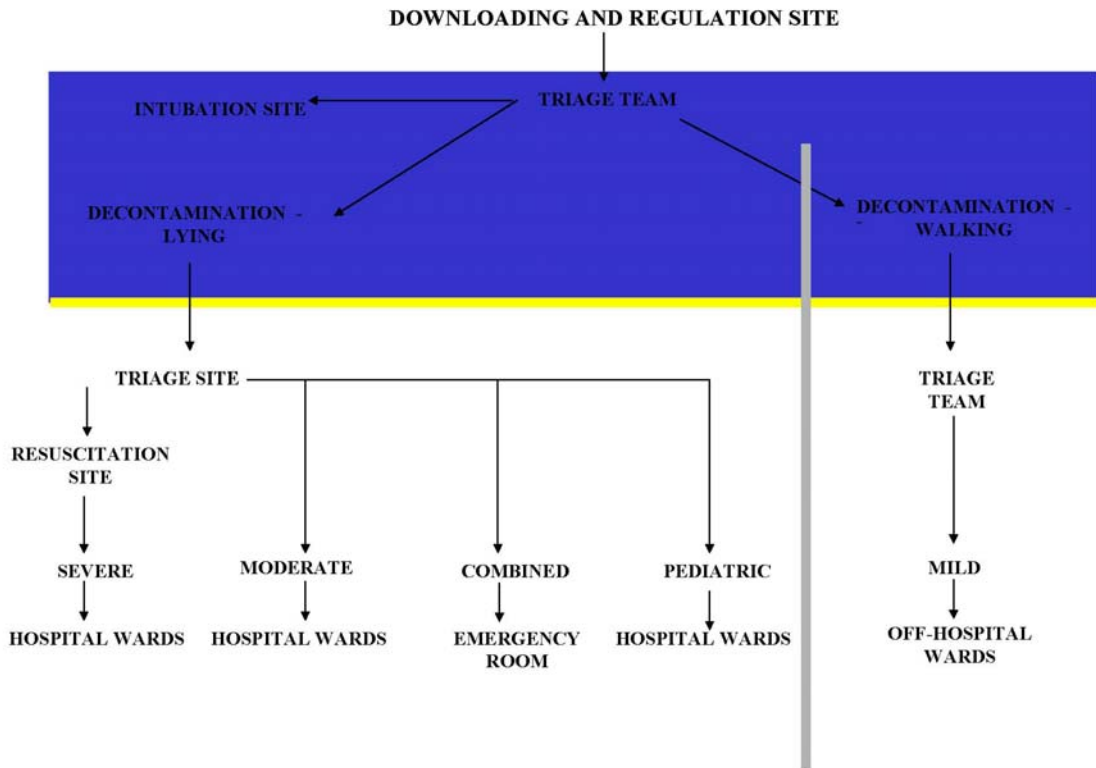


Figure 1: Patient Flow Scheme (Source: Farmer JC, Jimenez EJ, Rubinson L, Talmor DS (Eds): *Fundamentals of Disaster Management, Second Edition*, Society of Critical Care Medicine, 2003, Pg 76)

Following decontamination, patients are again triaged into groups with moderate, severe and pediatric injuries and those with combined conventional and chemical injuries. Only patients in the last category will need to go to the ED for further evaluation. All other patients will have been diagnosed and intervention started, which can be continued on the floor or in the intensive care unit (ICU) as appropriate. This flow of patients optimizes limited resources and allows the ED to concentrate on the most critically ill victims.

D. MEDICAL RESPONSE

The medical response will focus on activities employed daily by critical care clinicians. Most patients will have been quickly diagnosed and received initial treatment in the ED. Thereafter, care from the second hour onward will be the province of the critical care provider. They have familiarity with the pathophysiology involved and the drugs necessary for treatment and the ability to triage patients and to provide airway management/intravenous (IV) placement (**Table 1**).

Table 1: Medical Response to CW Threats

Pre-exposure	Latent Period	
Clinical Effect Seen	(seconds to days)	
<u>Primary Prevention:</u>	<u>Secondary Prevention</u>	
<u>Tertiary Prevention</u>		
The most important phase!	After failure of 1* prevention	After
failure of 1*/2* failure		
Intelligence/warning	Continued 1* prevention	
Continued 1*/2* prevention		
Detection in nearby areas	Early diagnosis	
Intervention to ameliorate		
True pretreatment	Early decontamination	clinical
effects and to prevent		
Skin protectants	Evacuation as appropriate	or minimize
sequelae		
Protective clothing	Treatment to prevent or	
General supportive care		

Mask	minimize later effects	Specific
antidotal therapy		
Training (what to do)	as possible	Antidotal
enhancement*		
Education (why to do it)		
National emphasis!		
		*Given before
exposure		

E. PLANNING, TRAINING, AND LOGISTICS

In addition to the medical response, chemical incidents require a great deal of pre-event planning and staff training; they also raise a host of logistical issues for the hospital.

Without a prearranged chemical response plan, it will be nearly impossible for a facility to respond effectively. The plan must take into account the types of agents anticipated in an encounter, the expected number of casualties and available resources. Everybody involved must be aware of at least the principle points of any plan. Planning must include the provision for decontamination of casualties before they enter the hospital. As discussed, a pre-planned patient flow scheme enables victims to be diagnosed and treated rapidly. The decontamination team[†] should be identified and accessible. Sources of additional manpower should be identified as well. Large numbers of support personnel from throughout the organization will be needed to transport patients and perform decontamination as well as provide support

[†] A hospital decontamination team typically consists of an emergency physician, ED nurses and aides, a nursing supervisor, an occupational health and safety officer, and a staff member from both security and building maintenance.

to several shifts to prevent heat/fatigue casualties (**Figure 1**). Staff will also be needed to manage security activities such as controlling access in and out of the hospital, directing patients and their families to the appropriate designated areas and controlling the crowd.

Clinicians need to be trained in the rapid diagnosis and treatment of the different chemical threats. Support staff must be trained in activities surrounding the care of contaminated victims, duties that may not be similar to their regular responsibilities. A hospital decontamination team typically consists of an emergency physician, ED nurses and aides, a nursing supervisor, an occupational health and safety officer and a staff member from both security and building maintenance. Additionally, the hospital will need many aides, not necessarily clinical, to do actual decontamination and administrative clerks to record and admit patients. As mandated by the Occupational Safety and Health Administration (OSHA), staff involved in decontamination should receive operations training. At the very least, all ED employees should have a basic understanding of the steps involved in decontamination. Ideally, the hospital will conduct periodic drills to give staff an opportunity to practice their roles in a chemical incident.

Logistical considerations for the hospital involved in treating contaminated patients are numerous. Three areas that will be especially strained during a chemical event are decontamination, medications and patient care support systems. Even if decontamination areas will be set up at the site of exposure, the hospital should anticipate individuals arriving untreated. A decontamination facility is best located outside the hospital in an adjacent area such as a parking lot. It will need to be equipped with showers or hoses. Thousands of gallons of water will be necessary for decontamination. Provisions for operating the site in cold weather need to be

considered. Each patient will need new clothes after discarding the contaminated ones they came in. All personnel working outside the hospital itself will require protective clothing, which requires the hospital to stockpile adequate supplies of PPE for all of its HCWs, not just critical care providers. Regarding medications, the hospital will be required to stock adequate supplies of specific antidotes for nerve agents and cyanogens. The amounts stocked should be based on the expected number of casualties. Up to 15 mg of atropine may be required per nerve gas victim. In the case of the Tokyo sarin release, with 640 patients seeking treatment, a grand total of 9,600 mg of atropine would have been needed to treat them all.

Patient care support systems will be taxed because all moderately to severe injured patients will require supplies ranging from stretchers to IV access. A significant number of patients may require intubation followed by mechanical ventilation. Since it is likely that the hospital will not have enough ventilators and critical care beds, alternatives should be worked out in advance. Using bag-mask devices for ventilating patients and operating room beds for ICU patients are reasonable options.

Bed space will not be the only kind of space in high demand. In addition to making room for a decontamination area, the hospital will need to designate an area where patients' relatives can wait to learn about their family members' conditions. This is especially true for parents of injured children.

F. DECONTAMINATION

Decontamination serves 3 purposes. It protects the following:

- patients from further injury due to residual agent on their clothing and skin

- hospital providers from injury by coming in contact with residual agent
- the facility itself from contamination, thus providing clinicians with a place to continue treating casualties

A decontamination area located outside the facility is preferential because it eliminates the need for contaminated individuals to come inside, thus minimizing the risk of ED and facility contamination.

Dry decontamination is not generally recommended because wiping may drive the agent into the skin or wounds or may smear it over previously unexposed areas. It is, however, performed before wet decontamination usually if wet resources are unavailable or delayed. Under those circumstances, it is best to use resins from a decontamination kit or products such as fuller's earth, clay or flour to adsorb the agent. Dry decontamination must be followed by mechanical removal.

Wet decontamination is the only practical solution in a mass casualty event because it is effective for all chemicals and can remove 95% of the agent, but it requires large amounts of water. Various governmental agencies and organizations recommend a shower time of 5 minutes as adequate for decontamination purposes. Water and soap with good surfactant properties work better. Victims will need assistance in removing contaminated clothing, a place to dispose of them and new clothes. Patients who are incapacitated and/or ventilated will have to be decontaminated by specially trained and protected personnel. The area and equipment used for patients will need to be cleaned and decontaminated afterwards. Additionally, contaminated tissues will have to be disposed of following the hospital's existing hazardous waste management procedures. The facility may choose to arrange with a state-approved hazardous waste contractor to remove the contaminated materials **(Figure 1)**.

G. PERSONAL PROTECTIVE EQUIPMENT

Ensuring that HCWs have the appropriate level of PPE is essential during a chemical incident. PPE selection should be based on the type of chemical exposure that has occurred.

PPE has been categorized into 4 levels of protection. Level D is the minimum level of protection required for securing, isolating and denying entry of an ambulatory victim. This PPE would be appropriate if no staff contact or exposure to the chemical is anticipated or the chemical is known and is a low-risk contaminant. Level D offers liquid splash protection as it calls for the use of a full face shield, hood or hair covering, gloves, water-repellant gown, and water-repellant boots/shoe covers. At this level, respiratory protection is unnecessary. Level C provides protection when victims require direct assistance and staff contact or exposure to the chemical is anticipated. It offers liquid splash protection, plus respiratory protection in the form of a powered air purifying respirator (PAPR), an air purifying respirator (APR) or a supplied air respirator with a loose fitting hood. Level C is adequate unless there is a known contraindication for the filter cartridge in the PAPR or APR. Levels A and B are considered specialized protection for when staff contact with victims or the agent is anticipated and there is a known contraindication for the use of the PAPR or APR. Level A calls for liquid splash protection to include a vapor protective suit while Level B calls for a chemical-resistant suit with hood and chemical-resistant gloves. Both Levels A and B require waterproof-chemical resistant boots. Respiratory protection consists of an atmosphere supplying respirator such as a supplied air respirator or a self-contained breathing apparatus (**Table 2**). Although Level C is the recommended hospital protection level in chemical decontamination scenarios, the

PPE should be modified or augmented as necessary to provide adequate protection against a specific chemical once one is identified.

Table 2: Personal Protection Equipment (PPE) levels

- A
 - Uses:
 - MAXIMUM level of protection
 - FULL encapsulation of wearer (front and back)
 - Mainly used in HOT zones that present immediate danger to life and health
 - NOT used routinely in WARM hospital areas due to its complexity

- B
 - Uses:
 - PREFERRED level of protection for WARM zone
 - ACTUAL staff exposure anticipated
 - UNKNOWN and/or HIGH-RISK contaminant
 - Liquid protection
 - Full face shield
 - Chemical-resistant gloves
 - Chemical-resistant suit with hood
 - Waterproof, chemical-resistant boots
 - Excellent FRONTAL splash protection
 - Back is not fully encapsulated
 - Respiratory protection
 - Supplied Air Respirator (SAR), or
 - Self-contained Breathing Apparatus (SCBA)

- C
 - Uses:
 - INTERMEDIATE level of protection
 - POTENTIAL staff exposure anticipated
 - KNOWN, LOW-RISK contaminant
 - Liquid protection
 - Full face shield

- Chemical-resistant gloves
 - Chemical-resistant suit with hood
 - Waterproof, chemical-resistant boots
 - Respiratory protection
 - Air Purifying Respirator (APR), preferably powered
- D
 - Uses:
 - MINIMUM level of protection
 - When NO staff exposure anticipated
 - Can be used to DIRECT traffic of ambulatory patients – NO Decon procedures
 - Can be used in Decon ONLY for a KNOWN, LOW-RISK contaminant
 - Liquid protection
 - Full face shield
 - Hood or hair covering
 - Gloves
 - Water-repelling gown
 - Rubber boots
 - Respiratory protection
 - None needed
- Protective respiratory devices
 - SCBA – Self-contained breathing apparatus
 - Portable source of compressed air
 - Positive pressure system
 - SAR – Supplied air respirator
 - Air source away from area, connected via air hose
 - Positive pressure system
 - APR – Air-purifying respirators
 - Can be powered or nonpowered
 - Nonpowered units offer less protection as they rely on negative pressure to function (wearers respiratory effort)
 - PAPR – Powered air-purifying respirator
 - Positive pressure system
 - Filtered ambient air
 - Chemical cartridges/canisters

- Efficient against many chemicals (acid, organic agents)
 - HEPA filters
 - Remove close to 100% of biological aerosols
 - Incorporated to PAPR
 - Surgical masks
 - Offer NO protection
- Physical barriers
 - Make sure that equipment used is CHEMICAL-RESISTANT
 - Usual latex gloves and hospital gowns used for “Universal Precautions” are effective against biological agents but offer little or NO protection against chemical agents

(Source: Farmer JC, Jimenez EJ, Rubinson L, Talmor DS (Eds): *Fundamentals of Disaster Management, Second Edition*, Society of Critical Care Medicine, 2003, Pg 48)

IV. NERVE AGENTS

Nerve agents are organophosphorous compounds that produce a biological effect by inhibiting acetylcholinesterase resulting in excess acetylcholine. Some of the most toxic chemical agents, nerve agents include GA (tabun), GB (sarin), GD (soman), GF and VX. Their structure and biological action is similar to commonly used insecticides. At room temperature, nerve agents are clear and usually colorless liquids (except GA, which may be brownish) and can be dispersed as either a vapor or a liquid. The 4 G-agents are relatively odorless (except GA and GD may smell fruity) and more volatile than VX. GB has the greatest degree of volatility—similar to that of water—followed by GD, GA, and GF. VX is a persistent substance, commonly found in an oily state, which allows for greater stability on surfaces. In either liquid or vapor phase, nerve gases are able to penetrate both clothing and skin. Toxicity occurs at varying exposures for each agent depending on quantity, volatility, mode of release and environmental conditions (**Table 3**).

Table 3: Differentiates toxic dosages among various nerve agents

	LCt ₅₀ mg-min/m ³	LD ₅₀ g/70kg
GA	400	1,000
GB	100	1,700
GD	70	50
GF	50	30
VX	10	10

Exposure: Concentration x Time

Unit: mg/m³ x Minutes

LCt₅₀: Lethal exposure to kill 50% of those exposed

The lethal amount of an agent is often difficult to conceptualize. The green dot on the U.S. penny pictured below (**Figure 2**) represents the amount of VX that would be lethal to 50% of those exposed (LCt₅₀).



Figure 2: Representation of lethal VX amount

A. MECHANISM OF ACTION

Nerve agents are organophosphorous cholinesterase inhibitors that inhibit butyrylcholinesterase in the plasma, acetylcholinesterase on the red cell and acetylcholinesterase at cholinergic receptor sites in the tissues. This leads to acetylcholine accumulation and binding to the cholinergic receptor sites.

Acetylcholine accumulates and continues to stimulate the affected organ producing various symptoms (**Figure 3a-d**).

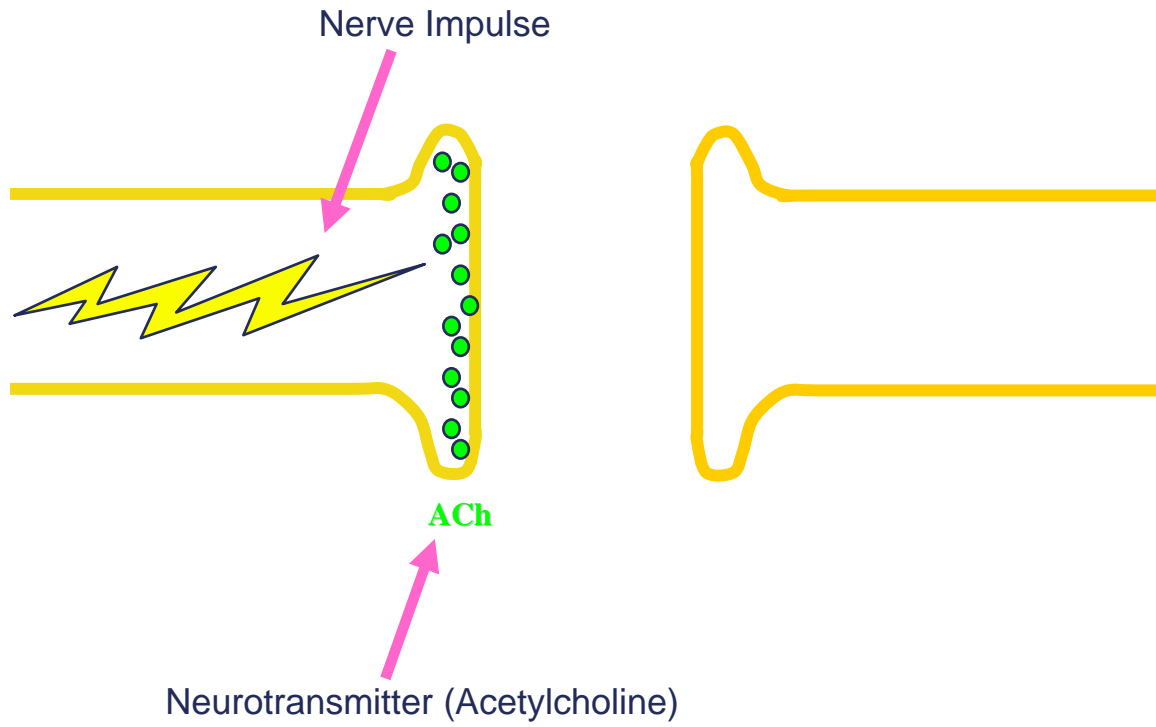


Figure 3a: Nerve Transmission: Nerve to Nerve

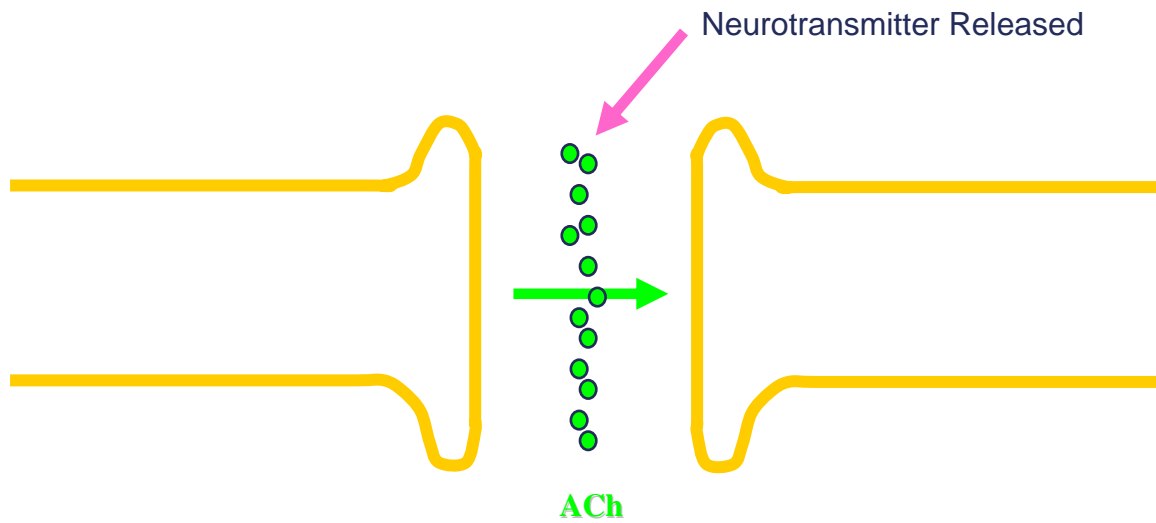


Figure 3b: Nerve Transmission: Nerve to Nerve

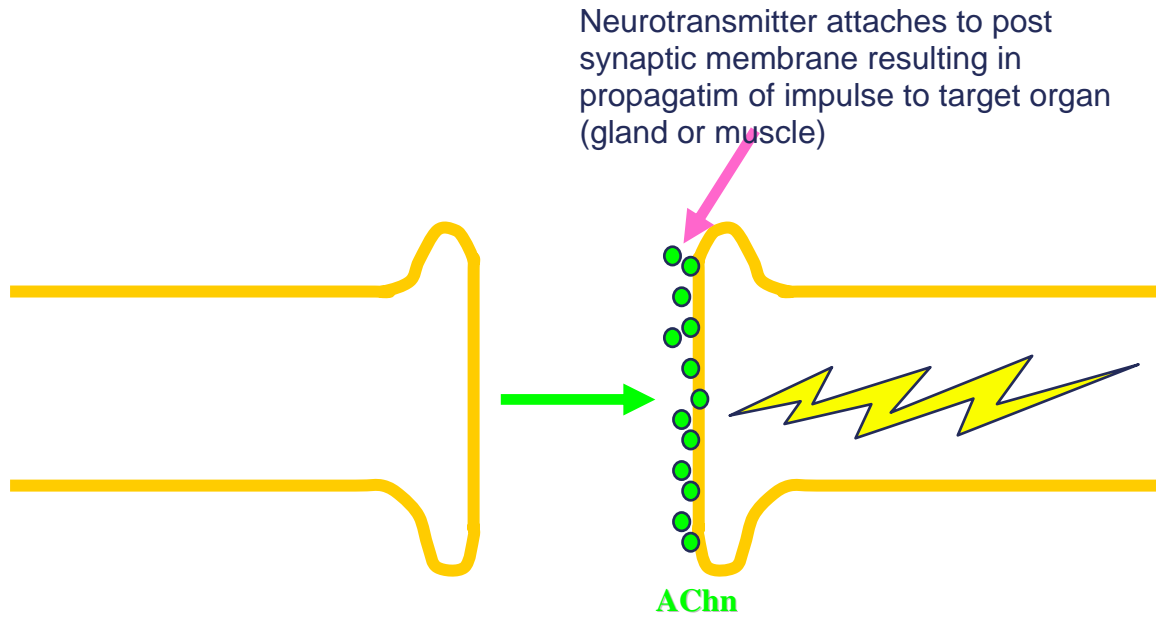


Figure 3c: Nerve Transmission: Nerve to Nerve

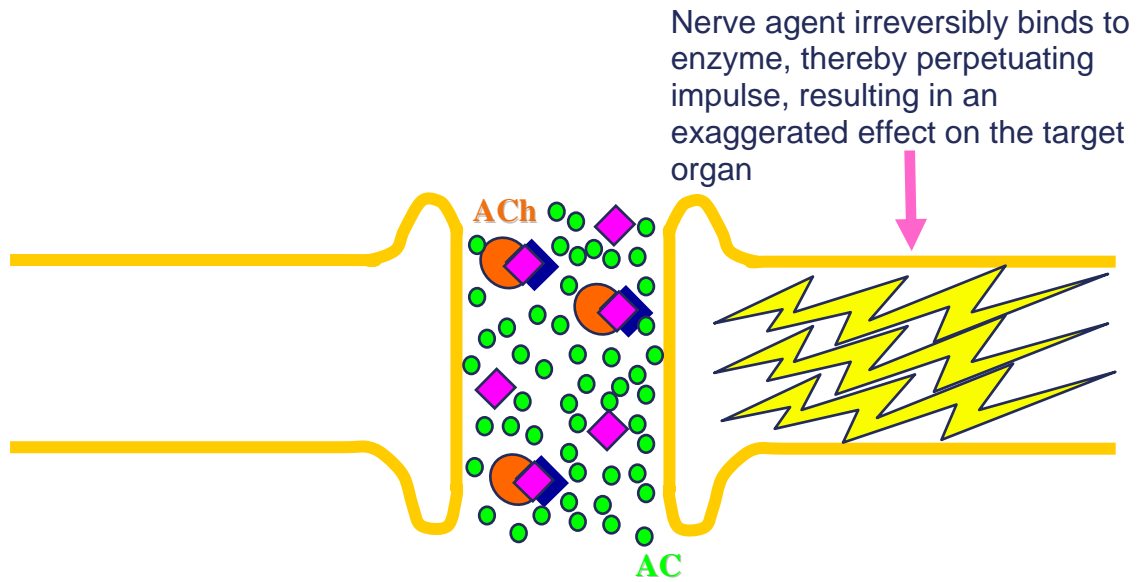


Figure 3d: Nerve Transmission: Nerve to Nerve

The onset of action is shorter following vapor exposure than liquid exposure. After being inhaled, the agent rapidly crosses the alveolar interstitial space into the bloodstream. Although able to penetrate the skin, reaching the bloodstream this way takes more time and, therefore, has a delayed onset of signs and symptoms. Symptoms of vapor exposure have an onset of seconds to minutes compared with liquid exposure, which has an onset of minutes to hours. Poisoning may also occur through ingestion of the agent via the GI tract.

B. SYMPTOMS AND DIAGNOSIS

Nerve agents induce numerous effects throughout the body. The ultimate effect and speed of onset depends on the size of the droplet contacted and the method by which it entered the body. Any organ with cholinergic receptors is a potential site of action for nerve agents; thus, they exert their effects on the airway, eyes, nose, GI tract, skeletal muscles, central nervous system (CNS) and skin. Respiratory symptoms include severe breathing difficulty, gasping and irregular breathing compounded by excessive secretions. The eyes will be injected and miosis will be present. Vision will commonly be dim, blurred and painful. Significant rhinorrhea usually occurs. Gastrointestinal symptoms will include increased motility characterized by vomiting, pain, and diarrhea. The muscles will demonstrate fasciculations, twitching and weakness. Victims will salivate and drool from the mouth and sweat profusely. They will experience bradycardia and/or tachycardia and hypotension in extreme cases. Paradoxically, symptoms may initially be less with direct skin exposure to nerve agents than through inhalation.

Low-dose exposure typically will affect the eyes, nose and oropharynx. Direct contact to glands will result in lacrimation, salivation, rhinorrhea and chest pressure. Miosis

also will occur from vapor exposure to the eyes, producing a change in vision, usually accompanied by pain. Fatigue, slurred speech and nausea may also occur.

Increasing levels of exposure manifest themselves in the airway, GI and genitourinary tracts. Bronchoconstriction and increased secretions may occur manifesting with cough and dyspnea. Abdominal cramping and loss of bladder and bowel control will follow. As the level of exposure increases, weakness, tremors and seizures will become apparent. With even higher exposure levels, fasciculations and twitching, which progress to muscle weakness and flaccidity, are seen.

Cardiovascular changes may present as either increased or decreased heart rate secondary to anxiety or vagal involvement. Heart block may also occur. Blood pressure is commonly within normal limits until terminal decline.

High levels of exposure may have a rapid onset, not allowing time for the previously mentioned low- and moderate-exposure symptoms to occur. High-dose exposures may manifest as rapid loss of consciousness and possible seizures. Death from apnea results after respiratory muscle paralysis and respiratory center depression of the CNS.

Although tissue enzyme activity can be tested to make a diagnosis, during a mass casualty event diagnosis will need to be made based on clinical signs and symptoms alone. Most clinical laboratories do not have the capacity of testing enzyme levels or activity

C. TREATMENT

The treatment of nerve agents has many components. They are decontamination, assessment of the airway, breathing, and circulation, antidotes and supportive care. These treatments should not necessarily be provided in that order.

Decontamination protects the patient from experiencing further injury.

Assessing the patient's airway, breathing, and circulation will help determine whether the patient is at risk of developing a life-threatening illness, which will impact the type of supportive care required.

Antidotes for nerve agent poisoning are atropine and pralidoxime chloride (2-PAM). Atropine is an anticholinergic that works by blocking excess acetylcholine at the postsynaptic membrane. It dries secretions and reduces smooth muscle constriction. However, it will not have an effect on muscles or treat miosis. The initial dose should be 2 to 6 mg given intravenously or intramuscularly. Give a repeat dose of 2 mg every 5 to 10 minutes until the secretions are drying and ventilation improves. In severe casualties, the usual dose is 15 to 20 mg (**Table 4**).

Table 4: Nerve Agent Management – Atropine

- An anticholinergic
- Blocks excess acetylcholine
- Clinical effects at muscarinic sites
 - Dries secretions
 - Reduces smooth muscle constriction
- Not for skeletal muscle effects
- Given systemically it will not treat miosis
- Side effects in unexposed

- Starting dose 2 to 6 mg
- Repeat with 2 mg every 5 to 10 minutes until
 - Secretions drying
 - Ventilation improved
- Usual dose: (severe casualty) 15 to 20 mg

Atropine does cause side effects in individuals who were not exposed to nerve agents. Unless aging (the time it takes for the agent to irreversibly bind to the enzyme) has occurred, 2-PAM works by removing the nerve agent from the enzyme. It should be given in a 600 to 1800 mg dose either intramuscularly or in a slow IV. Although 2-PAM will have an effect on the nicotinic sites (eg, relating to the stimulating action of acetylcholine and other nicotinic agents on autonomic ganglia, adrenal medulla and the motor-end-plate of striated muscle) by increasing skeletal muscle strength, it will not have an effect on the muscarinic sites (eg, those that produce effects that resemble post ganglionic parasympathetic stimulation) (**Table 5**).

Table 5: Nerve Agent Management – Oximes

- Pralidoxime Chloride (2-PAM Cl) most used in US
- Remove agent from enzyme, unless aging has occurred
- Effects at nicotinic sites
 - Increase skeletal muscle strength
- No clinical effects at muscarinic sites

Re-evaluate the patient every 3 to 5 minutes until secretions decrease and breathing becomes easier. If the patient is experiencing significant respiratory distress, intubate him/her. All severely injured patients demonstrating seizure activity should

receive a benzodiazepine, which will decrease brain damage from prolonged seizures, as it has been shown to improve outcome following lethal doses of soman in animal models. In the case of a large exposure, it may prevent secondary anoxic brain injury. Diazepam should be given in 5 to 10 mg doses in a slow IV (**Table 6**).

Table 6: Nerve Agent Management – Diazepam

- Any benzodiazepine used as an anticonvulsant to decrease brain damage from prolonged seizures
- In animal models has been shown to improve outcome following lethal doses of soman
- Should be given to all seriously injured patients
- Dose = 10 mg

Alternatively, an equivalent dose of either lorazepam or midazolam can be administered. One must be aware that the antidotes may interact with other drugs. For example, they can interact with succinylcholine, which may be given to control paralysis during surgery or for patients with traumatic injuries. Patients will also require supportive care such as mechanical ventilation. Clinicians should use the symptoms to guide treatment options.

Recovery will depend on the specific agent and level of exposure. Although data regarding nerve agent exposure is lacking, patients without complications were conscious and breathing spontaneously within 3 to 4 hours of exposure to sarin. With more persistent agents (eg, VX), or complications (eg, anoxic brain injury),

neurological symptoms could require mechanical ventilation and persist for weeks. Long-term outcome is unknown.

V. CYANOGENS

Cyanide is a rapidly acting volatile gas or colorless liquid, which has the odor of bitter almonds. It exists as hydrogen cyanide (AC) and cyanogen chloride (CK), with AC having a slightly faster onset of action. Ubiquitous in low concentrations, cyanogens are poisonous in higher concentrations.

A. MECHANISM OF ACTION

Cyanide has an increased affinity for inhibiting metal-containing enzymes such as the iron-containing cytochrome oxidase and some sulfur-containing compounds. The cyanide ion combines with the iron molecule in the cytochrome A3 component of the cytochrome oxidase complex. This binding interrupts cellular respiration in the mitochondria, thus forcing the cell to use anaerobic metabolism. This creates a metabolic acidosis through the increased production of lactic acid. Cyanide also has an increased affinity for the iron ion in methemoglobin, which can be used therapeutically.

B. SYMPTOMS AND DIAGNOSIS

The signs and symptoms of cyanide toxicity are related to the body's inability to utilize oxygen. The body's homeostatic mechanisms interpret this situation as

hypoxemia and attempt to increase peripheral oxygen delivery by increasing the heart rate and minute ventilation. As these compensatory mechanisms fail in the face of increasing oxygen debt and metabolic acidosis, the heart rate and minute ventilation will fall and deteriorate to cardiac arrest.

The route, total dose and exposure time drive the severity of systemic poisoning. Restlessness and increases in respiratory rate follow inhalation of cyanide as the initial symptoms. Vomiting, convulsions, respiratory failure and unconsciousness follow quickly. Severe and rapid inhalation of lethal dose exposure to cyanide causes the onset of symptoms, such as hyperpnea, within 15 seconds followed by seizures in 15 to 30 seconds. Respiratory and cardiac depression usually occur within 6 to 8 minutes, resulting in death.

The ingestion of cyanide produces a more delayed onset and progression of signs and symptoms than inhaled cyanide. The onset of symptoms may require minutes rather than seconds. Anxiety, agitation, vertigo, weakness and muscular trembling may follow an increased respiratory rate. As with inhalation exposure, respiratory depression, convulsions and cardiac dysrhythmias may occur. Hypertension and bradycardia are followed by hypotension and tachycardia, and finally bradyarrhythmias occur prior to asystole.

C. TREATMENT

The goal of treatment for cyanide poisoning is to increase the body's ability to detoxify and excrete cyanide as well as prevent its re-entrance into the cell and inhibit the cytochrome oxidase complex. This is accomplished through the creation of thiocyanate with sodium thiosulfate, which is excreted through the kidneys.

Thiocyanate is formed from the conversion of cyanide and sodium thiosulfate via the enzyme rhodanese. Sodium nitrate assists in the formation of methemoglobin, which binds cyanide ions with greater affinity than cytochrome oxidase. Intravenous sodium thiosulfate can be given in a dose of 12.5 g IV following IV injection of sodium nitrite. Intravenous sodium nitrite can be given in a dose of 300 mg IV in 10 mL of diluent, injected over a 2- to 4-minute period. General supportive therapy may include providing 100% oxygen, correction of metabolic acidosis and observation for at least 24 to 48 hours (**Table 7**).

Table 7: Cyanogens Specific Antidotal Therapy

- Displacement of CN^- from cytochrome a3
 - Reaction of CN^- with methHb generated by nitrites or others
 - Amyl Nitrite ($\text{C}_5\text{H}_{11}\text{NO}_2$)
 - Sodium Nitrite (NaNO_2), 10 ml IV of a 3% solution = 300 mg
- Enzymatic conversion of CN^- to thiocyanate
 - Administration of a sulfate as a sulfur donor:
 - Sodium Thiosulfate ($\text{Na}_2\text{S}_2\text{O}_3$) 50 ml IV of a 25% solution (ie, 12.5 g)

Recovery is generally quite rapid after acute exposure, usually requiring a few days before returning to baseline activity.

VI. LUNG-DAMAGING OR CHOKING AGENTS

Lung-damaging agents include chlorine (CI), chloropicrin (PS), phosgene (CG) and diphosgene (DP). These agents attack lung tissue causing pulmonary edema. Both

CG and DP are colorless with the odor of green corn or freshly mown hay. Lung-damaging agents are distributed as aerosols or gases/vapors.

A. MECHANISM OF ACTION

Although only slightly soluble in water and aqueous solutions, CG hydrolyzes to form carbon dioxide and hydrochloric acid. It then participates in an acylation reaction, which damages the alveolar-capillary membrane leading to leakage of fluid into the lung causing PE. This effect will not occur with exposure by any other route.

B. SYMPTOMS AND DIAGNOSIS

Inhalation usually occurs hours before the onset of symptoms after a symptom-free period. Symptom onset may be delayed hours to days. Objective signs follow symptoms.

Pulmonary edema can be profound. After a latent period, which may last anywhere from 20 minutes to 24 hours, the body's lymphatic draining ability to clear the lungs of fluid is overcome. Exertion can shorten this period and/or exacerbate the symptoms. This pattern mimics that seen in acute respiratory distress syndrome (ARDS). Dyspnea is the first symptom and progresses to a productive cough with chest tightness. These initial symptoms alone are relatively nonspecific and of little aid in diagnosis. Vomiting, headache and lacrimation may or may not occur. The onset of symptoms of pulmonary edema within 4 hours is an indicator of poor prognosis. As dyspnea worsens and pulmonary edema continues to develop, hypoxemia and lung crackles appear. Frothy sputum may also develop. Infectious bronchitis/pneumonitis typically occurs 3 to 5 days following exposure. Fever and

elevated white blood cells will occur but may not always result from an infection. As the condition worsens, shock-like symptoms will appear. Fluid loss through the lungs may be profound and contribute to hypovolemia and hypotension. Any of these complications in addition to respiratory failure may be solely or in part responsible for the victim's death. An increase in hematocrit may be reflective of loss of fluid into the lungs, as may an arterial blood gas. Higher concentrations of exposure may cause a sudden laryngeal spasm and death (**Table 8**).

Table 8: Pulmonary Agents Clinical Considerations

- These agents cause pulmonary edema or ARDS
 - Damage alveolar – capillary membrane
- Latent Period
 - Symptom onset may be delayed hours to days
 - Objective signs appear later than symptoms
- Sudden Death may occur
 - Laryngeal obstruction (edema/spasm)
 - Bronchospasm
- Infectious Bronchitis/Pneumonitis common
 - Usually occurs 3 to 5 days post-exposure
 - Fever, elevated WBC, infiltrates – not always infection
 - Prophylactic antibiotics not indicated
- Effects exacerbated by exertion
 - Compensatory mechanisms overwhelmed
 - Strict rest, even if asymptomatic
- No specific therapy exists

No specific diagnostic sign or test exists. The diagnosis will have to be made based on the appearance of a number of patients with ARDS following a suspicious exposure.

C. TREATMENT

No specific therapy exists to treat pulmonary agents. Supportive care includes oxygen and positive pressure ventilation. The patient will have not only excessive secretions but also an airway possibly sensitive to bronchospasm. Consequently, one should consider both bronchodilators and steroid therapy. Hypotension may be treated with IV fluids and vasopressors as needed. Most victims will likely develop symptoms mimicking ARDS, so mechanical ventilation will be necessary. A bacterial super-infection is common 3 to 5 days following exposure. While serial cultures should be followed, prophylactic antibiotics are not indicated. Patients can benefit from strict rest, even if they are asymptomatic because the symptoms are exacerbated by exertion.

Patients who demonstrate the onset of pulmonary edema within 4 hours of exposure demonstrate a poor prognosis. Individuals who survive more than 48 hours usually recover. For uncomplicated cases, no longer-term sequelae exist.

VII. VESICANTS

Vesicants include sulfur and nitrogen mustards, lewisite (L) and phosgene oxime (CX). They cause destruction of the skin resulting in blister formation and damage respiratory tissues if inhaled or intestinal mucosa after ingestion or systemic absorption. Some vesicants are more insidious than others.

Mustard agents are the prototypical vesicants. They may be colorless or vary from pale yellow to dark brown. They may lack odor or smell of garlic, fish, fruit or soap. Mustard agents possess a great deal of persistence and stability in both cold and temperate climates. Because of this, they are effective agents for contact contamination in civilian settings. Vesicants are relatively easy to manufacture and can be made more persistent by incorporating them into nonvolatile solvents.

A. MECHANISM OF ACTION

It takes approximately 2 minutes for the mustard agents to enter the body through the skin. There, they react with the body's enzymes, proteins and deoxyribonucleic acid (DNA). The DNA undergoes alkylation and crosslinking, particularly in rapidly dividing cell lines. This DNA damage leads to cell inflammation and eventual cell death.

B. SYMPTOMS AND DIAGNOSIS

Mustard agents quickly cross both skin and mucous membranes to target the eyes, skin, lungs, mucous membranes and blood-forming organs. Mustard agents are destructive to the spleen, lymphatics and precursor cells in the bone marrow, causing decreases in red and white blood cells as well as in platelets (**Table 9**).

Table 9: Vesicants – Targets

- Skin: Ranges from erythema to skin necrosis
- Eyes: Mild conjunctivitis in most cases; 0.1% may be legally blind

- Airway: Both upper and lower airway disease; in massive exposure, hemorrhagic pulmonary edema
- Bone marrow: Stem cell damage and pancytopenia
- GI tract: A late, severe cytotoxic effect
- CNS: Ranges from apathy through convulsions to coma depending on the dose
- Cellular interaction: Occurs in 1 to 2 min
- Clinical effects: Evident in 2 to 48 hours, usually 4 to 8 hours

The mustard agents have an insidious onset of signs and symptoms: exposure is apparent only after the onset of signs and symptoms, which can appear anywhere from 2 to 24 hours later. No immediate signs or symptoms occur on contact, inhalation, or ingestion. Warm, wet skin hastens the onset and increases exposure severity, making areas of the body such as the groin and armpit at increased risk. Initially the exposed skin will demonstrate rubor and erythema with blister formation appearing later. Lewisite has similar effects but its onset is immediate.

When the skin comes in contact with a small amount of vesicants, over time it will become red and pruritic. Increased injury to the skin is more common in exposure of the liquid as compared to the vapor. With moderate exposure of agent, the skin will form blisters within 4 to 24 hours and peak within days. The sloughing of necrotic skin caused by damage of the dermal layer and subsequent thin-walled blisters bursting serves as a medium for bacterial overgrowth and infection. Sepsis is not uncommon with sufficient exposure. Gastrointestinal tract involvement usually begins approximately 24 hours after exposure provided that the agent was ingested or a sufficient amount was absorbed through the skin. Although GI symptoms are generally nonspecific, they do have a severe cytotoxic effect. The eyes are extremely

sensitive to mustard injury, and after approximately 1 hour of minor exposure, they will demonstrate intense pain and conjunctivitis, the latter of which will be mild in most cases. However, with increasing exposure, symptoms will continue to develop. Between 4 and 12 hours later, lacrimation and foreign body sensation in the eyes, conjunctival injection with irritation, photophobia and edema will occur. The lids may continue to swell to the point of closure, obstructive blindness, and blepharospasm. Possible corneal perforation with loss of the eye may occur after extensive exposure. Additionally, miosis may occur. Damage may result in eventual total loss of vision (Figure 4a and 4b).



Figure 4a

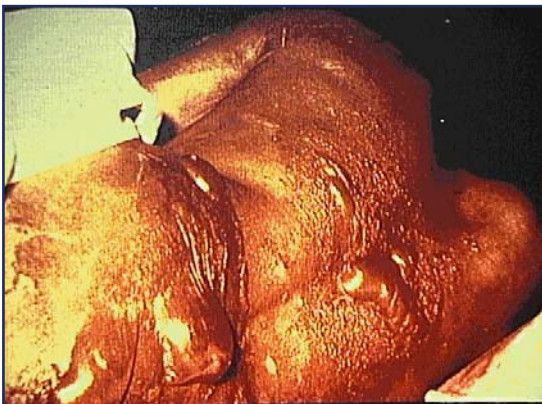


Figure 4b

Damage to the airways occurs with inhalation as the mucous membranes are attacked and slowly destroyed in a descending direction with the musculature following. After 4 to 6 hours, the membranes of the nose, throat, trachea and large bronchi become congested. A burning sensation will develop in the throat along with hoarseness. A dry nonproductive cough also will develop and later become productive. Dyspnea ensues after the production of necrotic mucous membranes and the formation of pseudomembranes. The sloughed mucosa of the lower respiratory tract will become at risk of infection, thus predisposing the victim to pneumonitis. Chemical pneumonia may also develop 2 to 3 days after heavy exposure. Airway obstruction or PE may occur and lead to eventual death.

Due to the lack of a specific antidote, it is imperative to identify the specific agent as mortality from vesicants is higher than other chemical agents.

C. TREATMENT

Because no laboratory test or specific antidote for mustard poisoning exists, prevention of exposure is the best method of preventing casualties. This form of protection, however, requires a respirator with full-face protection in addition to special protective clothing, which is unavailable to the population-at-large. If contamination occurs, decontamination and prevention of further exposure is necessary. One must remove the victim's clothes and flush his/her eyes with water for at least 5 minutes. Immediately decontaminating the skin within 2 minutes of exposure may reduce the appearance of signs and symptoms but will not prevent tissue damage. Chemical inactivation with chlorination via a paste or powder containing a substance such as Chloramine is somewhat useful for HD and Lewisite but ineffective against HN. Calamine may reduce burning and itching. Blisters larger

than 2 cm should be unroofed; smaller blisters should be left intact. Because significant fluid losses may be associated with these skin lesions, one must provide adequate fluid therapy.

Prevention of infection is critical in preventing long-term complication of skin lesions. Eighty to 90% of injured skin can be treated if infection is kept at bay. Keep skin lesions clean and free from infection by irrigating them 3 to 4 times daily and applying topical antibiotics such as silver sulfadiazine; keeping airways patent and functioning with intubation and ventilation, if necessary, and preventing blindness with frequent irrigation and topical antibiotics. Ease eye pain and skin lesions by systemic or local analgesics, if necessary. Lung injuries can be treated symptomatically, but airway maintenance should be the greatest concern. In some cases of severe exposure, mechanical ventilation will be required. If pseudomembrane formation is in question, bronchodilators may be indicated. Antibiotic prophylaxis is not indicated, but antibiotic treatment of pneumonia should be used only after determination of positive cultures (**Table 10**). Other therapies may include replacement of blood components and electrolytes as well as marrow transplants, which would only be available in isolated cases.

Table 10: Vesicants – Respiratory Management

- Oxygen, steam, cough suppressants
- Bronchodilators
- Early intubation
- Positive pressure ventilation as indicated
- Antibiotics prophylaxis not indicated

Gastrointestinal symptoms, such as nausea and vomiting, can be treated with antiemetics. Severe diarrhea suggests a high exposure and poor prognosis. Patients

with pancytopenia due to marrow damage may need blood component therapy. These patients will be at increased risk for developing infectious complications.

Acute mortality following exposure to mustard agents is relatively low. In fact, the inhalation required to kill a person is 50 times that of a typical nerve agent such as soman. However, morbidity is high. Furthermore, injuries from exposure can be expected to consume significant resources. Tissue regrowth in the blister area is slow and requires weeks to months, longer than thermal burns. Plastic surgery may be required. Recovery from pulmonary and GI damage is variable.

Although this chapter focuses on chemical agents of terror, much of the information can be extrapolated to common industrial chemicals. Issues include toxidromes, skin/eye findings, inhalational injuries and adsorption/systematic findings. Other system similarities include the role of a hazard vulnerability analysis to assess what chemicals are located locally or transported through the area via highway or rail system, facility concerns, decontamination, etc.

KEY POINTS

1. 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.

2. Most patients present to the hospital without having undergone any prior decontamination, even if it is being conducted at the incident site.
3. The unique patient management requirements of a chemical exposure, including the need for decontamination, place an incredible strain on the hospital, stressing the need for pre-event planning and staff training, as well as consideration for logistical issues related to space, supplies and medications.
4. The purpose of decontamination is 3-fold: It protects patients from ongoing injury due to residual agent on clothing and skin, HCWs from injury due to coming in contact with residual agent and the facility by allowing it to continue to function as a site for treating casualties.
5. Personal hospital protective equipment is categorized into 4 levels of protection; Level C is the preferred protection level in chemical incidents.
6. 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.
7. Cyanogens are a fast-acting volatile gas or colorless liquid whose route, dose and exposure time drive the severity of systemic poisoning. Cyanide exposure can be treated with sodium thiosulfate and sodium nitrite IVs and recovery is generally rapid.
8. Pulmonary agents, which are water soluble, damage the alveolar-capillary membrane causing significant fluid leakage in the lungs. Treatment options include decontamination, supportive care, IV fluids, mechanical ventilation and vasopressors.
9. Vesicants quickly cross both skin and mucous membranes to target the eyes, skin, lungs, mucous membranes and blood-forming organs. With the lack of a specific antidote, treatment options revolve around decontamination,

inactivation with chlorination, topical medications and antibiotics, antiemetics and supportive blood products and fluid therapy. Acute mortality is relatively low, but morbidity is high.

SUGGESTED READINGS

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