CHAPTER 12

Emergency Preparedness: Identification and Management of Chemical and Radiological Exposures

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KEY CONCEPTS

1. In mass casualty events with chemical or radiologic exposure, the majority of victims can be managed with decontamination, observation and supportive care. Antidotal therapies should be reserved for more critically injured victims.
2. Nerve agent poisoning is similar to organophosphate insecticide poisoning with atropine and pralidoxime being the primary antidotes.
3. Cyanide gas exposure can be rapidly fatal but most victims that are conscious upon arrival to the hospital will not require antidote therapy.
4. Respiratory problems caused by pulmonary agents with low water solubility may take several hours to develop thus requiring extended observation.
5. Vesicant chemical weapons are less lethal than other chemical weapons but cause significant morbidity leaving many survivors that need extensive care.
6. Therapeutic agents are available that can block the uptake or enhance the elimination of radioactive contamination.
7. Clinicians, especially pharmacists need to be prepared to take an active role in the design and operationalization of disaster plans for their workplace and community. Pharmacists may participate on established disaster response teams that may be deployed to assist in the care of individuals outside of their local area.

Life-threatening hazardous material exposures may happen anywhere and at any time. The exposure may be due to an unintentional release or at the other extreme be the result of an intentional and catastrophic act of terrorism.[1–6] A hazardous material is defined as any substance that poses a substantial risk to the health or safety of individuals, or the environment when improperly handled, stored, transported, or disposed.[1] The specific risks are dependent on the quantity and concentration of the substance exposure and the physical, chemical, or infectious characteristics of the material. Many of these substances have the potential to be used as weapons. Small quantities of hazardous materials are used in many commercial products, such as pesticides. Larger and more concentrated quantities are found at industrial sites and in their waste byproducts. Injuries from hazardous materials are relatively common as evidenced by the tens of thousands of hazardous material incidents recorded by the U.S. Environmental Protection Agency during the last decade. The majority of these incidents occur during transport rather than at the site of manufacture or use and represent a complex and significant danger for emergency healthcare workers.[1] At the other extreme, a hazardous material exposure may be the result of an intentional and catastrophic act of terrorism. Historically, acts of chemical or radiologic terrorism have been rare but have had very high visibility and marked psychological impact. Terrorism represents a profound threat to many countries around the world. Terrorists, whether representing foreign governments, organized religious sects, or individuals, have the capacity to endanger our communities with hazardous materials. Even a single patient contaminated with a hazardous material has the potential to overwhelm an unprepared healthcare facility.

1 A common thread in all disasters is that community healthcare systems are severely strained by limited communication, lack of personnel with disaster training or experience, lack of plans for facility surge capacity and limited availability of medical supplies. If chemical or radiologic contamination occurs the system is strained even further because of a lack of decontamination training and equipment at hospitals. Preplanning and early detection systems need to be in place to facilitate early recognition of the event and the substances involved if the community has any likelihood of being able to mount an effective response to a chemical or radiologic disaster. In all disasters, the normal flow of care is disrupted and the influx of victims becomes the major focus of the healthcare community. Preplanning for acute care needs for large numbers of patients, may include devising a method for expanding bed and surgical capacity as well as preparing specialized antidotes. Even if only minor injuries result from the event a significant portion of the affected population will need access to critical every day medications, such as insulin and personal needs, such as food and shelter.

This chapter discusses the major groups of hazardous materials that have been used as weapons (Table 12–1). Chemical and radio-

TABLE 12-1 Examples of Chemical and Radiologic Agents That May Be Used as Weapons

NATO Chemical Weapon Designations	Common Examples
Nerve agents	Tabun, sarin, soman, VX, organophosphate insecticides
Blood agents	Hydrogen cyanide, cyanogen chloride
Pulmonary agents	Phosgene, chlorine, ammonia, mace/pepper spray
Vesicant agents	Mustard, lewisite, phosgene oxime
Radiologics	Dirty bombs and fallout, including radioactive cesium, iodine, plutonium, strontium, tritium and uranium

Adapted from Zajtckuk R, ed. Textbook of Military Medicine–Medical Aspects of Chemical and Biological Warfare. Bethesda, MD: Office of The Surgeon General, Department of the Army, United States of America, 1997.

logic events that have occurred in recent years are reviewed to provide an understanding of the scope, size, and complexity of such events. The clinical presentation, mechanisms of toxicity, and relevant diagnostic approaches are discussed for each type of agent. The community and individual preventative measures that can be taken to minimize the risks associated with the major types of chemical and radiologic threats are reviewed and the nonpharmacologic and pharmacologic treatment options are critically evaluated. Because controlled clinical trial data is lacking in this area the majority of treatment recommendations in this chapter are based on animal studies, anecdotal experience, and expert opinion. Finally, the ways in which clinicians can actively participate in disaster planning and response at the local, state and national level are presented.

CHEMICAL HAZARDS

NERVE AGENTS

Organophosphate chemicals that affect the cholinergic nervous system are the most potent of the chemical weapons. They are often referred to as nerve gases but this is a misnomer as they are aerosolized liquids rather than true gasses. The military designation for this group of weapons is nerve agents. The best-known terrorist use of a nerve agent occurred in Tokyo, Japan, in March 1995. A group called the Aum Shinrikyo released a dilute form of sarin nerve agent in the Tokyo subway. The sarin was placed in plastic bags, which were then covered with newspaper. The members of the Aum Shinrikyo then placed the sarin packages on the floor of the crowded subway and punctured them with the sharpened tips of umbrellas. The Sarin then flowed out upon the floor of the subway. This is a very ineffective delivery route for this chemical, however; the attack affected approximately 5,500 victims and resulted in 11 deaths. The nearest hospital received 640 of the victims and their experience is documented in the medical literature.[5] The majority of these patients arrived at the hospital without decontamination. They subsequently contaminated 23% of the emergency department staff, many of whom required medical attention. Identification of the causative agent took approximately 2 hours and the delay of appropriate treatment contributed to the morbidity and cross-contamination. Even though a dilute form was used and the delivery was inefficient, this event highlights the dramatic impact of a nerve agent attack on the public and healthcare systems.

Clinical Presentation

2 Although nerve agents are similar to organophosphate chemicals that are used as insecticides, they are much more potent and typically delivered as vapors. As a consequence, the clinical presentation of nerve agents is slightly different than that of organophosphate insecticides, despite the same mechanism of action as described in Chap. 10.

PRESENTATION OF NERVE AGENT POISONING

General

- Mild: miosis and rhinorrhea
- Moderate: vomiting, profound sweating, possible altered mental status
- Severe: unconscious or convulsing

Symptoms

- Nausea, vomiting, diarrhea, and dyspnea may be present

Signs

- Wheezing, rales or rhonchi
- Bowel sounds are hyperactive
- Bradycardia or tachycardia
- Muscle fasciculation may be noted

Laboratory Tests

- Acidosis will be present with severe poisoning

Other Diagnostic Tests

- Plasma or red blood cell cholinesterase activity

With a nerve agent release there will be a highly contaminated area surrounding the point of release where victims will be affected instantaneously and the probability of survival will be low. The size of this area will depend on factors such as the type of dispersal device and ventilation of the area. At the point of release there will be a high concentration of vaporized agent that will result in rapid absorption via the respiratory tract. Victims in this area will rapidly loose consciousness and develop seizures and apnea. On the periphery of the lethal area there will be a casualty zone where toxic but potentially survivable exposures will occur. These victims will likely develop sublethal toxicity but be able to leave the contaminated area. Victims who are able to leave are likely able to reach a healthcare facility for treatment.

The most common clinical presentation for victims who arrive at the hospital includes miosis, rhinorrhea, cough, and mild shortness of breath as a result of vapor exposure.[7] Localized areas of sweating or muscle fasciculation may also be seen if droplets have come in contact with the skin. Those individuals who had more direct or pronged exposure will have more significant symptoms; including exaggerations of the common findings and possibly altered mental status, muscle weakness or seizures. Most victims that are able to make it to a hospital will have a low mortality but often suffer varying levels of morbidity from long term effects. Infants and young children exposed to organophosphates often will have a different clinical presentation than adults; central cholinergic effects predominate and thus pronounced weakness, altered mental status and fewer secretions are more common.[8]

Long-term effects of nerve agent exposure are less-well studied, but it appears that survivors have an increased incidence of neuropsychiatric problems. Organophosphate insecticides and nerve agents cause behavioral and cognitive dysfunction in animal studies and in human case reports. Studies of occupational exposure and acute poisoning with organophosphate insecticides further substantiate the likelihood of undesirable changes in cognitive and behavioral function, as well as peripheral neuropathies.[9–11] Survivors of terrorism with the nerve agent sarin in Japan report an increased prevalence of such disorders.[12–15] Similarly, a recent study indicates that soldiers who were exposed to very low doses of nerve agents while burning captured munitions during the 1991 gulf war had decreased white matter and increased brain cavity size.[16] Cholinesterase enzyme polymorphisms can influence individual response to different organophosphates and may affect susceptibility to neuropsychiatric problems and neuropathies.[17–20]

Mechanism of Toxicity

Nerve agents bind to various cholinesterase enzymes and prevent the breakdown of acetylcholine (see Fig. 12–5 later in this chapter). The resulting excess of acetylcholine leads to acute hyperstimulation of muscarinic and nicotinic receptors. There is variation between the effects of different nerve agents in terms of potency and kinetic parameters. Peripherally, the muscarinic excess results in increased secretions, while nicotinic excess leads to muscle weakness and fasciculation. Centrally, the excess nicotinic and muscarinic activity leads to altered mental status and seizures. Rapid fatality with high-dose exposures appears to be the result of

TABLE 12-2 Properties of Nerve Agents

Agent	Sarin	Soman	Tabun	VX	Household Organophosphate
Aging time	5 hours	5 minutes	14 hours	48 hours	12–24 hours
Dermal LD_{50}	1,700 mg	100 mg	1000 mg	10 mg	>35,000 mg
Inhaled LCt_{50}	100 mg/m^3	50 mg/m^3	400 mg/m^3	10 mg/m^3	>250 mg/m^3
Volatility	High	High	High	Low	Very low
Environmental persistence	Low	Low	Low	High	Intermediate

LCt, lethal concentration in air when inhaled; LD, lethal dose on contact with skin.
Adapted from Sidell FR.[22]

centrally mediated seizures whereas fatalities as a consequence of lower doses stem from hypoxia as a result of noncardiogenic pulmonary edema.[21] Over time the organophosphate binding may become irreversible through a process called *enzyme aging* where a covalent bond is formed between the enzyme and organophosphate molecule. The time required for aging can be as short as a few minutes or as long as a few days, depending on the organophosphate. Once aging occurs the affected cholinesterases will never become functional again and must be replaced. Because the majority of cholinesterases are produced by red blood cells, it will take about 120 days, the typical red blood cell life span, before cholinesterase levels will return toward "normal." However, within 60 to 90 days, when cholinesterase levels recover to approximately 80% of normal, most individuals are able to function without any clinical consequences.[22]

Causative Agents

Organophosphate chemicals are widely used as insecticides and certain highly toxic organophosphate compounds have been developed for military use. Commercially available insecticides for consumer use are relatively dilute but more concentrated versions are available to registered pesticide applicators. Insecticides could potentially be used by terrorists as weapons but are difficult to disperse effectively. The nerve agents are classified and differentiated by several different properties that characterize their effectiveness as weapons. The most important of these are aging time, potency, and volatility. Table 12–2 lists the characteristics of common organophosphate insecticides used in the home. Nerve agents are liquids at room temperature but the highly volatile agents are more easily dispersed. The high volatility agents have low viscosity while VX has high viscosity, making it harder to aerosolize. VX is the most potent of the agents but it has low volatility and a long aging time. As little as 1 drop on the skin can be lethal but absorption may be delayed and thus allow time for treatment. The rapid aging time associated with the agent soman is very concerning because there is little opportunity for intervention.

Risk Factors

If the exposure occurs in an enclosed space that is poorly ventilated the agent will be concentrated and result in increased potential for morbidity and mortality. Outdoor release generally produces less concentrated exposures and thus less mortality and varying rates of morbidity. The presence of rain, sunlight, or wind reduces the effectiveness of these agents, especially the volatile ones. Individuals who are the most heavily exposed will be at the greatest risk as well as pose the greatest risk to first responders and healthcare workers. They can present direct contact hazards but also be a respiratory hazard as vapors are volatilized through a process know as off-gassing. Off-gassing is most likely to be problematic in warm and poorly ventilated spaces. Contaminated victims that present to the hospital with residue on their clothes, hair, or skin also represent a significant risk to healthcare professionals.

TREATMENT

Nerve Agents

DESIRED OUTCOME AND GENERAL APPROACH TO TREATMENT

The initial goals for treatment of nerve agent poisoning are detecting the exposure, mitigating ongoing exposures, stabilizing immediate threats to the airway, breathing, or circulation, and initiating appropriate antidotal therapies. After stabilization, the patient should be monitored for ongoing antidote needs. Followup evaluation is needed to assess for the development of long-term neuropsychiatric problems.

NONPHARMACOLOGIC THERAPY

Decontamination of nerve agent exposure victims, and most other hazardous chemical exposures, is of critical importance. Exposed victims should not be allowed to enter the emergency department of a hospital or any other secondary facility until they have been decontaminated. Personnel working around contaminated victims need to wear protective equipment that at a minimum complies with Occupational Safety and Health Administration's level C requirements.[2] This includes a respiratory protection device (powered air purifying respirator), chemical resistant suit, double-layered gloves, and boots. For victims of a vapor exposure with minimal symptoms on arrival, removal of their clothes is likely all that will be needed to prevent contamination of others. However, because it is unlikely that the specific agent will be known at the time the person arrives at a care area or institution, wet decontamination also should be initiated. Wet decontamination consists of washing from head to toe with water and mild soap.

PHARMACOLOGIC THERAPY

There are three primary reasons to use pharmacologic therapy for the management of acutely exposed people: to treat excessive secretions, to control seizures, and to protect cholinesterase enzymes from aging. The standard antidotes, which include atropine, a muscarinic antagonist, pralidoxime, a peripheral nicotinic antagonist and cholinesterase protectant, and benzodiazepines, for seizure control are discussed in detail in Chap. 10.

Although the general approach to treatment for individuals who have been exposed to nerve agent as the result of a terrorist action on a large population are the same as those for insecticide poisoning, there are a few subtle differences. Nerve agent exposures paradoxically require lower total doses of atropine than insecticides. Also, because nerve agents may rapidly "age" the use of pralidoxime is more urgent than in insecticide poisonings.

Drug Treatments of First Choice

Currently, the standard antidote regimen for organophosphate poisoning used in the United States includes atropine, pralidoxime,

and benzodiazepines if needed for seizure control. Atropine competitively antagonizes muscarinic cholinergic receptors to relieve symptoms of cholinergic excess and a starting dose of 2 mg IV should be promptly administered and then rapidly titrated upward until secretions stop and the patient can easily be ventilated.[23] Because it freely crosses the blood–brain barrier, atropine acts both centrally and peripherally. In the CNS atropine blocks muscarinic receptors but simultaneously stimulates acetylcholine release. Pralidoxime is a nucleophilic oxime that acts as a reversible inhibitor of acetylcholinesterase that can also bind peripheral nicotinic cholinergic receptors. By binding to acetylcholinesterase it can prevent or displace organophosphate from binding to the enzyme and prevent enzyme aging. By binding to peripheral nicotinic cholinergic receptors, pralidoxime is thought to improve muscle weakness within minutes of administration. Pralidoxime, however, has poor CNS penetration and primarily acts only on peripheral enzymes.[24] Other oxime compounds, such as obidoxime, that offer greater CNS penetration are used in other countries but are not FDA approved.[24] When used alone, pralidoxime offers a limited survival benefit. However, in combination with atropine it offers a synergistic effect that improves survival beyond that associated with either agent alone.[23] By preventing enzyme aging, the combination is also thought to greatly reduce the duration of atropine therapy. The major limitation of such treatment is that central nicotinic receptors are unprotected. This gap in protection may contribute to the long-term neuropsychiatric problems that have been observed.

Alternative Drug Treatments

Pyridostigmine In situations where there may be a high risk of exposure, such as military operations or for first responders entering a contaminated environment, pretreatment of individuals can be considered. A pretreatment regimen of oral pyridostigmine 30 mg administered every 8 hours in humans can protect the acetylcholinesterase enzyme from organophosphate binding and aging. This therapeutic regimen blocks 20% to 40% of peripheral cholinesterase enzymes.[25] As such, this blockade protects a critical mass of acetylcholinesterases against nerve agent binding. In animal studies, pretreatment with pyridostigmine followed by postexposure therapy with atropine and pralidoxime improved survival against high doses of nerve agents.[26] Although pyridostigmine appears to improve survival against lethal doses of all nerve agents it's most dramatic effect is against the rapidly aging agent soman. For soman it improved the protective ratio almost 40-fold in rhesus monkeys versus treatment with atropine and pralidoxime alone.[26] Against other nerve agents pyridostigmine offered more modest benefits, increasing protective ratios by approximately 50%. The benefit of pyridostigmine is somewhat limited because it does not cross the blood–brain barrier and offers no CNS protection. Additionally, it is theoretically possible that pyridostigmine may actually potentiate acute toxicity with low-dose organophosphate exposures.[26–28] Central-acting agents are impractical because they can impair cognition. An ideal pretreatment that would offer peripheral and CNS protection without disrupting cognition or enhancing toxicity is currently not available.

Special Populations Young children exposed to organophosphates often will have an unusual clinical presentation as compared to adults—the degree of emesis and other excess secretions is markedly reduced. Rather, they often present with profound weakness and altered mental status. Their appearance is often described as "floppy" or like a rag doll. However, once appropriately diagnosed, the treatment is the same as in adults. Pediatric autoinjectors with smaller needles, containing 0.5 or 1 mg of atropine are available. Pediatric atropine autoinjectors may offer enhanced safety in small children but if they are not available, adult-size autoinjectors can be used in life-threatening situations.[8] It is important to remember that dosing in this situation is based on neutralizing the excess acetylcholine and not on body weight, so dosing will be titrated in the same manner as adults and will require similar total doses.

PHARMACOECONOMIC CONSIDERATIONS

The Strategic National Stockpile and CHEMPACK programs (which are discussed in detail in Strategic National Stockpile/CHEMPACK Program below) may augment local supplies of antidotes but will take hours to days to arrive and be distributed. Thus plans need to be made at the local level for responding to the initial need for antidotes. Antidote stocking of an initial cache for nerve agent exposures can be quite expensive. Given the infrequency of such events stocking the drugs with appropriate expiration dates may be problematic. Several authors suggest keeping a stock of powdered atropine on hand for rapid reconstitution. Powdered atropine can be used to rapidly prepare several hundred doses of atropine at a very low cost.[29–31] Prefilled autoinjector syringes containing atropine, pralidoxime, and diazepam are available for use in the prehospital and decontamination settings. They are included as part of the strategic national stockpile and CHEMPACK programs. Pralidoxime from autoinjectors appears to be stable if reformulated for intravenous use.[32]

EVALUATION OF THERAPEUTIC OUTCOMES

The assessment of nerve agent exposures is mainly clinical. As described above atropine dosing should be titrated to drying of secretions and ease of ventilation. Frequent assessments should be made to determine the required duration of atropine therapy. If atropine cannot be weaned within the first 48 hours it is likely that enzyme aging has occurred or there is ongoing exposure due to incomplete decontamination. If muscle weakness persists or returns additional pralidoxime (1 g) is warranted. Routine laboratory studies, such as electrolytes, glucose, and blood cell counts should be followed daily in patients who require hospitalization. These studies and blood gasses may be performed more frequently based on the patients clinical condition, Measurement of serum and red blood cell cholinesterase function may assist in developing a prognosis for moderate to severely poisoned patients. Unfortunately these tests are not universally available and may be difficult to obtain during mass casualty incidents.

CYANIDE AND ASSOCIATED AGENTS

Cyanide compounds comprise the group of chemical weapons known as blood agents that impair oxygen use for aerobic energy production.[4,33] Cyanide salts have been used as oral poisons in numerous cases of suicide and mass poisoning. In 1980, cyanide was inserted into Tylenol products in the Chicago area by an unknown terrorist. This event led to requirements for tamper-evident packaging. Hydrogen cyanide gas has been used to execute condemned prisoners and was used in the Nazi death chambers. Cyanide gas is released in smaller, but still toxic, amounts during fires when plastics and other types of organic materials are burned. Terrorists attempting to kill a large number of people with cyanide will most likely use the gaseous form. Similar to the nerve agents, there will be a zone of high lethality at the release site. Victims outside this zone are likely to present to healthcare facilities. Most victims who are able to transport themselves to a healthcare facility or a hospital have a low likelihood of morbidity or mortality.

Clinical Presentation

The clinical presentation of cyanide poisoning can vary in severity depending on dose, time since exposure, and route of exposure.

Signs and symptoms are consistent with global hypoxia, ranging from headache to convulsions.

PRESENTATION OF CYANIDE POISONING

Symptoms

- Mild: headache, dizziness, possible vomiting
- Moderate: agitation or lethargy
- Severe: unconscious, convulsing

Signs

- Rapid heart rate
- Rapid respiratory rate
- Skin will be normal color to flushed
- Arrhythmias may be present

Laboratory Tests

- Metabolic acidosis will be present with poisoning
- Serum lactate will be elevated
- Venous oxygen will be elevated

Other Diagnostic Tests

- Plasma cyanide concentration, if available

Victims of cyanide inhalation in the severest form may be unconscious and near death; in contrast, those at the periphery of the exposure may be asymptomatic. Some may have a noticeable odor of "bitter almonds" that is frequently described as a musty odor. Because approximately 40% of the population does not carry the gene necessary to detect this odor, it is not a reliable sign.[4] If ingested the onset of toxicity may be delayed with signs and symptoms that mimic anxiety. Dizziness, headaches, weakness, flushing, diaphoresis, dyspnea, hyperventilation, and tachypnea are also commonly seen in those with moderate to severe exposures.[4] Hydrogen cyanide and cyanogen chloride gas may cause mucus membrane irritation as well. As cellular hypoxia worsens, victims will experience loss of consciousness with fixed dilated pupils, hemodynamic compromise, arrhythmias, seizures, apnea, secondary cardiac arrest, and finally death. Organs with high oxygen demands are the most sensitive to cyanide poisoning (Fig. 12–1). The most prominent laboratory finding in cyanide toxicity is metabolic acidosis with dramatically elevated lactate levels. Cyanide blocks mitochondrial oxygen use, causing a shift from aerobic to anaerobic metabolism. This increases production of lactate and produces a high anion gap metabolic acidosis. Several reports indicate that lactate levels may be used as markers of severity of cyanide toxicity.[34] However, numerous processes in a critically ill patient contribute to elevations in lactate and limit the specificity of this marker. In the case of an unknown exposure, check both venous and arterial blood gases to determine if there is a supranormal venous oxygen content, which would strongly indicate cyanide toxicity.[34] As the mitochondria cease to use the supplied oxygen, a disproportionate oxygen concentration builds up in the venous blood supply. Oxygen saturation measurements by pulse oximetry remain high as the blood has good oxygen content.

Long term neuropsychiatric effects from an acute exposure are not frequently addressed, but can contribute a significant morbidity. These effects are similar to carbon monoxide-induced neuropsychiatric disorders that arise from oxidative stress and lipid membrane peroxidation caused by hypoxia.[4] Chronic low-level cyanide exposure is thought to contribute to or cause several neurologic disorders. Although management of an acute exposure is well defined, little is known about prevention of long-term effects from low-dose cyanide exposure.

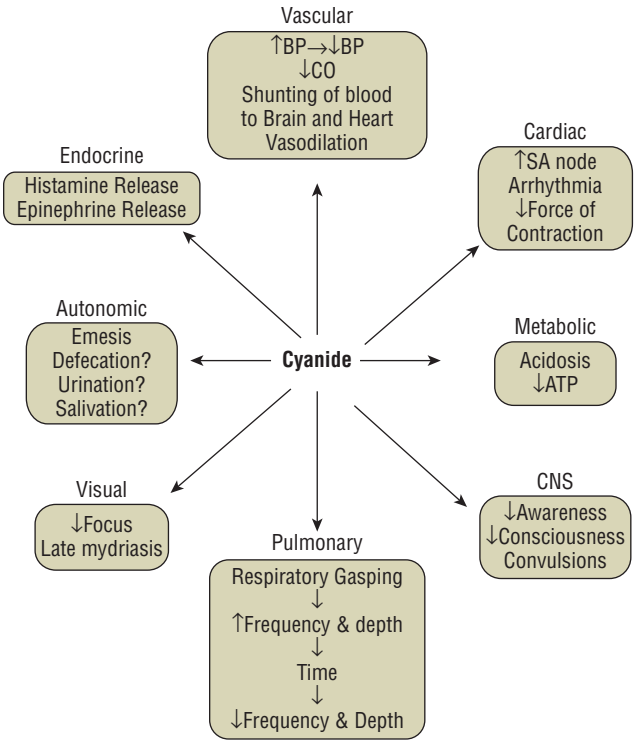


FIGURE 12-1. Signs and symptoms of cyanide poisoning. (↓, Decrease; ↑, increase; ATP, adenosine triphosphate; BP, blood pressure; CO, carbon monoxide; SA, sinoatrial.) *(From reference 33.)*

Mechanism of Toxicity

Cyanide is known to inhibit many metabolic processes but the most notable toxic effects seem to originate from the inhibition of the terminal enzyme in the respiratory chain.[4] Normally, sulfane and cyanocobalamin reactions will rapidly metabolize endogenously produced cyanide. The body can detoxify about 0.017 mg of cyanide/kg/min.[35] When these pathways of metabolism are overwhelmed and conjugate substrates depleted, cyanide accumulates, resulting in toxicity. The accumulated "free" cyanide binds cytochrome oxidase within the mitochondria, resulting in abrupt cessation of aerobic metabolism (Fig. 12–2).

Essentially, the body can no longer use oxygen to make energy. Cyanide has a high binding affinity for the ferric ion (Fe^{3+}) on the aa_3 complex. This effectively stops electron transport. Because cyanide is occupying the binding site, oxygen no longer is able to reoxidize the reduced cytochrome a_3. This uncoupling of oxidative phosphorylation terminates the synthesis pathway of adenosine triphosphate. Although the mitochondria continue to be exposed to an adequate oxygen supply, there is impaired oxygen extraction and use. This disruption of aerobic metabolism leads to increased glycolysis via anaerobic pathways.

Binding to the mitochondrial cytochromes often takes several minutes to occur, but early signs of cyanide poisoning are seen within seconds. This observation leads to the theory of additional mechanisms of toxicity. Because cyanide exists predominately in the unionized form within the body, it readily diffuses across membranes. Rapid effects seen after inhalation may be a result of the near instantaneous diffusion across the blood–brain barrier. Cyanide appears to alter neuronal transmission following absorption into the CNS possibly through a glutamate pathway. It also appears to increase vascular resistance early in poisoning which increases cerebral blood flow thereby enhancing CNS penetration.

Causative Agents

Cyanide Cyanide is both widely available and easily accessible in a variety of forms. Historically, cyanide was used as a warfare agent

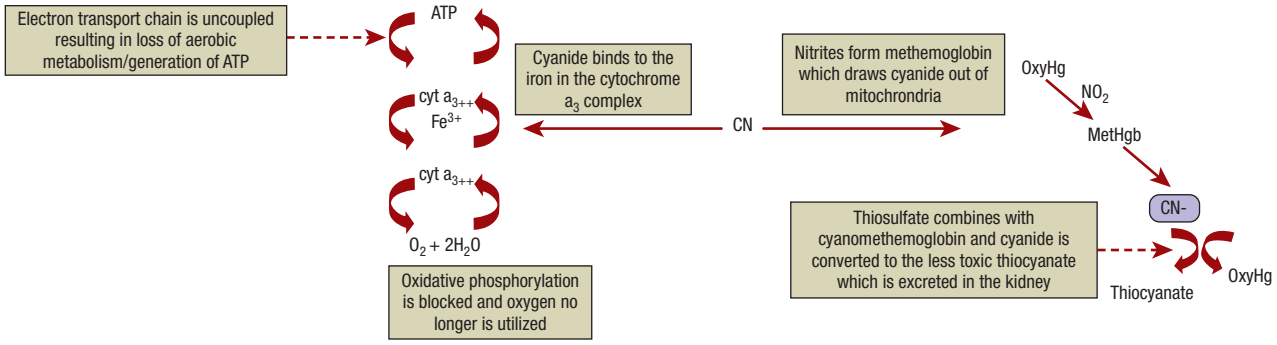


FIGURE 12-2. Mechanisms of cyanide toxicity. (ATP, adenosine triphosphate; cyt a_3, cytochrome a_3; MetHgb, methemoglobin; OxyHg, oxyhemoglobin.) *(From reference 4.)*

in the volatile, water soluble, liquid forms of hydrogen cyanide and cyanogen chloride. Potassium cyanide and sodium cyanide are highly reactive salts that are used in many industrial applications ranging from photograph developing solution to gold mining to production of explosives. Mixing these salts with a strong acid produces hydrogen cyanide gas.[4] The plant-derived cyanide precursor, amygdalin, is an unlikely source of mass exposures but is reported to cause acute toxicity if eaten in very large quantities.

A more frequently encountered source of cyanide exposure is fires. Cyanide gas may be released in the combustion of many synthetic polymers and natural materials. Any material that contains carbon and nitrogen is a potential source of cyanide during a fire. Victims of smoke inhalation are also at high risk for both carbon monoxide and cyanide poisoning.[4] Both carbon monoxide and cyanide will cause hypoxic damage and the effects will be additive and possibly synergistic. Some studies even suggest that the toxicity from cyanide may be more contributory to death in some fire victims than the carbon monoxide.[4]

Incidence and Risk Factors

Suicide attempts and smoke inhalation are the primary events associated with the development of cyanide toxicity. In these situations the number of individuals affected has usually been small. Terrorist use of cyanide can take several forms. Oral poisoning of a small number of influential people as the result of adulterated food or medications can lead to public unrest. However, an act of terrorism using cyanide gas could harm a much larger group of people and strain or overwhelm community resources. Such an attack would likely occur by releasing cyanide gas into a building or crowded public place such as a subway system.

TREATMENT

Cyanide

■ DESIRED OUTCOME

The initial goals for treatment of cyanide poisoning are detecting the exposure, mitigating ongoing exposures, stabilizing immediate threats to the airway, breathing or circulation, and using antidotal therapies appropriately. After stabilization the patient should be monitored for sequela of hypoxic injury.

■ NONPHARMACOLOGIC THERAPY

All patients should undergo decontamination appropriate to the type of exposure. For ingestions, remove the victim's clothing and initiate orogastric lavage and administer activated charcoal for patients presenting within 1 hour of ingestion. Although activated charcoal poorly binds cyanide, administration may be helpful because of the relatively small lethal dose.[4] Several case reports describe secondary contamination caused by off-gassing from victims. The cyanide may be exhaled from the affected individual's lungs, or emanate from heavily soaked clothing, skin, or toxic vomitus. For inhalation victims, simply disrobing is appropriate decontamination.

Supplemental oxygen is a crucial part of supportive care in cyanide poisoning. Ventilation with 100% oxygen will increase tissue oxygen delivery but will not improve utilization by poisoned cytochromes. However, even in a case of normal measured P_{O_2}, supplemental oxygen may enhance antidote efficacy. Oxygen may serve to increase respiratory excretion of cyanide, restore the cytochrome oxidase activity by displacing cyanide, stimulate activation of other oxidative systems (such as those enzymes not yet poisoned by cyanide), and perhaps facilitate the rhodanese enzyme indirectly.

Additional supportive therapies included initiating treatment for acidosis, hemodynamic compromise, and seizures as needed throughout the clinical course. Seizures resulting from cyanide poisoning requires aggressive management and in some cases be refractory to standard benzodiazepine therapy.[4]

■ PHARMACOLOGIC THERAPY

Drugs of Choice

3 In the United States two different cyanide antidotes are available, albeit not widely. A three-part antidote consisting of nitrates and thiosulfate has been used successfully since the 1950s, while hydroxocobalamin, which became available in the United States in 2007, has been widely used in Europe since the 1970s. Both antidotes have proven to be effective for treating acute cyanide poisoning. Antidotes should be used in case of suspected cyanide exposure or an unknown exposure resulting in rapid onset of respiratory and neurologic symptoms. The differential diagnosis for acute cyanide poisoning is relatively small (see Fig. 12–1), and the antidote should be administered empirically to patients with hypoxic symptoms but lacking pallor. Initial studies with the nitrite-thiosulfate combination found that patients were responsive to therapy up to 2.5 hours after the exposure.[36]

The nitrate-thiosulfate antidote kit contains amyl nitrite, sodium nitrite, and sodium thiosulfate. Nitrites are used to induce methemoglobinemia (metHb). Cyanide appears to preferentially bind to the ferric iron of the metHb rather than in the mitochondria. It is thought that an increased amount of cyanide will then transfer to the extracellular space and be displaced from the cytochrome. The mitochondria can then reactivate electron transport.[36] The amyl nitrite is in crushable glass vials for inhaled administration and will generate approximately 5% metHb. Sodium nitrite 300 mg (10 mL of a 3% solution) is given intravenously and increases metHb to between 15% and 20% in adults. In children, the sodium nitrite will

require a dose adjustment based on hemoglobin concentration to prevent excessive methemoglobin formation.[4] Doses range from 5.8 to 11.6 mg/kg for hemoglobin concentrations ranging from 7 to 14 g/dL. This is often impractical, so the sodium nitrite component may be omitted or the other antidote used, if available.

The nitrites do cause significant adverse side effects, namely vasodilation and hypotension. These side effects can be problematic especially if compounded by coingestants or preexisting medical conditions. Although metHb is the desired end point to therapy, it may exacerbate the condition of certain patients, including those with poor cardiopulmonary reserve and those with concomitant carbon monoxide poisoning. It is recommended to avoid nitrites in smoke inhalation victims as a result of the risk of worsening the oxygen-carrying capacity deficit. The antidote for metHb is methylene blue, which will counteract excess metHb formation but may subsequently release bound cyanide.[4]

The third component of the cyanide antidote kit is sodium thiosulfate. This agent enhances clearance of cyanide by acting as a sulfur donor. Thiosulfate reversibly combines with cyanide in the extracellular space to form the minimally toxic and renally excreted thiocyanate. It may also augment mitochondrial sulfurtransferase reactions. The enzyme rhodanese is the catalyst for the direct conversion of cyanide to thiocyanate. The effectiveness of sodium thiosulfate as an antidote is limited by its delayed onset of action, short half-life, and small volume of distribution. However, in smoke inhalation cases with a suspected cyanide component, thiosulfate can be used without nitrite therapy to avoid hemoglobin problems.

Sodium thiosulfate as a short-term therapy has very few side effects. The only significant adverse reactions are idiopathic hypersensitivity and infusion rate-related hypotension. If hypertension occurs during administration, the infusion rate should be reduced. Chronic exposure to thiocyanate can cause toxicity because thiocyanate and cyanide exist in equilibrium. Toxic effects from acute treatment of cyanide exposure are rare, but may occur more frequently in the setting of severe renal failure.[4]

Hydroxocobalamin is a vitamin B_{12} precursor and acts as a chelating agent to bind cyanide in equimolar amounts directly forming cyanocobalamin (vitamin B_{12}).[37] It is available as a lyophilized powder and forms a clear red liquid when reconstituted. This antidote has proven to be highly effective as a result of its increased affinity for cyanide as compared to the cytochrome oxidase moiety. The recommended starting dose is 5 g IV over 15 minutes.[37] Additional doses of 2.5 g may be given if needed to control symptoms. No dosing adjustments are required for children. Adverse reactions to this therapy are rare and generally not severe. At recommended doses it is has very low toxicity.[37–39] The most commonly reported adverse effect is reddening of the skin, which can last for several days. Allergic reactions are rarely reported.[39] The compound's usefulness is only limited by the large dose required and its relatively short half-life because of light instability. An additional advantage of this agent is that pediatric dosing does not have to be based on hemoglobin concentration like sodium nitrite and thus it is a better option for empiric use in children. There may be a synergistic protection if the hydroxocobalamin therapy is augmented by sodium thiosulfate. Because of its low toxicity and its efficacy, it is ideal in cases where the diagnosis is uncertain or in cases where the induction of metHb may be detrimental.

CLINICAL CONTROVERSY

The use of hyperbaric oxygen for cyanide toxicity is controversial. The literature offers little corroboration as some investigations find positive effects and other studies fail to demonstrate correlations with improved clinical status.[4]

EVALUATION OF THERAPEUTIC OUTCOMES

Monitoring

The assessment of cyanide-induced hypoxia is complicated by the lack of cyanosis. Improvements in mental status and normalization of the respiratory and heart rates after oxygen or antidotes are indicative of improvement, as well as supportive of the diagnosis. Assessment of mental status, arterial blood gasses with methemoglobin, and lactate guides therapy. Oxygen saturation measurements by pulse oximetry remain high as the blood has good oxygen content; rather the problem lies in oxygen use and extraction. Of note, once therapy is initiated to induce methemoglobinemia, the pulse oximetry will depict a higher-than-actual oxygen concentration as oxyhemoglobin and methemoglobin deflect light at similar wavelengths.

PULMONARY AGENTS

Pulmonary agents were the first widely used chemical weapons. The first major use occurred in 1915 at Ypres, Belgium, where 150 tons of chlorine gas was released and resulted in approximately 5,000 casualties over a 5-mile area.[40] During World War I, pulmonary agents were responsible for thousands of casualties and deaths. Recently, insurgents in Iraq have been making crude weapons by attaching explosives to relatively small tanks of chlorine gas.[41] Larger quantities such as might be found in rail cars or tanker trucks could be devastating. A recent transportation accident illustrates this vulnerability and the effect on the healthcare system.

In January 2005, Graniteville, SC (15 miles north of Augusta, GA) was the site of one of the largest hazardous material incidents in the United States. Just before 3:00 AM two freight trains collided, releasing 80 tons of chlorine gas into the atmosphere. The derailment and release required the evacuation of 5,400 people over a large section of the town. The exact number of people affected was difficult to determine but several hundred victims underwent decontamination at secondary facilities and area hospitals. The most commonly reported symptom was minor mucous membrane irritation that rapidly resolved once the individual was removed from proximity to the contaminated area. More than 500 patients were acutely treated in local emergency departments, 69 required admission, and 9 people died as a direct result of the exposure.

The biggest clinical challenge for first responders to this event was determining what chemicals were involved and the potential risks associated with the exposure of the community and healthcare professionals. This compromised the ability of physicians to ascertain who had been significantly exposed, to diagnose the initial exposure conditions, and to anticipate sequelae. It also impacted the response of public health officials and pharmacists who were faced with providing immediate specific treatments. Additionally, patients were distributed to hospitals in a random fashion rather than on the basis of hospital resources and capacity. This resulted in several hospitals being overwhelmed and others, such as the regional trauma center, receiving only a small number of the casualties despite having the greatest capacity for casualty decontamination and patient care.

Clinical Presentation

Victims of pulmonary agents present with symptoms ranging from mild mucous membrane irritation to chemical burns and apnea.[40] The severity of presentation will vary with different chemical properties, air concentrations, durations of exposure and patients underlying health status.

PRESENTATION OF PULMONARY AGENT POISONING

General

- Skin is erythematous and varying sizes of blisters may be present

- Onset is delayed with low-water-solubility agents

Symptoms

- Nonproductive cough to respiratory distress
- Burning of eyes and mucous membranes
- Nausea vomiting

Signs

- Pulmonary: rales, decreased breath sounds, dullness to percussion
- Skin: irritation and mild erythema
- Eyes: irritation, conjunctivitis

Laboratory Tests

- Arterial blood gasses: respiratory acidosis may be present and oxygen levels may be low in symptomatic patients

Other Diagnostic Tests

- Chest radiography looking for bilateral infiltrates
- Findings may be delayed 12 to 24 hours

Low-level exposures can result in minimal irritation to the eyes and airway, and may have a delayed onset of initial respiratory toxicity. Low-level exposures can be problematic in victims with preexisting lung disease such as asthma or chronic obstructive pulmonary disease. Higher doses result in significant toxicity almost immediately and often have effects on the eyes and skin, as well as the lungs. Severe exposures will manifest as upper airway irritation leading to increased secretions, productive cough, dyspnea, and possibly laryngospasm. Auscultation may reveal rales and crackles as a result of pulmonary edema. After leaving the contaminated area and medical intervention most patients will have an apparent improvement but are at risk of delayed (up to 24 hours later) worsening of lower airway problems. Following a mass exposure the majority of victims will present with mild mucous membrane irritation and self limiting coughing and choking.

Mechanism of Toxicity

Pulmonary agents may cause damage in one or more of the following ways: asphyxiation, allergic reactions or direct irritant/corrosive effects. Asphyxiation may result from displacement or dilution of oxygen by other gasses. Typically this only occurs in enclosed spaces or other poorly ventilated areas. Allergic response to an inhaled toxicant may result in a pulmonary or systemic reaction, which may be mediated by one or more of a variety of immunoglobulins.[40] Direct irritant effect is the main mechanism of toxicity. Topical damage to the respiratory tract may occur because of direct toxic inhalational injury to the airways or alveoli.[40,42] The chemicals in this class combine with water to produce acids or bases. Cellular damage with consequent airway obstruction, pulmonary interstitial damage, surfactant loss or alveolar–capillary damage can result in impaired oxygen–carbon dioxide exchange.

Causative Agents

The pulmonary agents are grouped below by their water solubility, which impacts where in the airway injury occurs and the rapidity of onset.

High Water Solubility Ammonia, formaldehyde, hydrogen chloride, and sulfur dioxide are common examples of highly water-soluble irritant gases. These chemicals react rapidly with moisture in the upper airways to form corrosive compounds. In patients exposed to these agents, chemical burns affecting the upper airway and eyes, as well as laryngospasm, are the primary concerns. These patients often need aggressive airway management. Any hint of airway compromise exhibited by stridor may be an indication of impending airway obstruction.

Intermediate Water Solubility Chlorine is the prototypical example with intermediate water solubility. When inhaled into the moderately size airways, it combines with the water there to form hydrochloric and hypochlorous acid. Chemicals in this category are capable of affecting the entire respiratory tract. Consequently, the patients have some upper airway involvement but also have significant wheezing and bronchospasm as a result of the moderate-size airway involvement.[43] Like the highly water-soluble agents, irritant effects occur rapidly and are dose dependent.

Low Water Solubility 4 The low-water-solubility agents penetrate deeper into respiratory tissues because they react slower with water to form corrosive compounds. Examples of low-solubility agents include various oxides of nitrogen and phosgene. Oxides of nitrogen have numerous industrial applications and also are produced by crops in silage. These compounds react with water to form nitric acid. Phosgene also has numerous industrial uses relating to plastics and polymer production. Phosgene reacts with water to form modest amounts of hydrochloric acid. Low-level exposures to these agents can result in a significant delay in the onset of toxicity and progression of the injury may last for several days before reaching a nadir.[40]

Among this group, phosgene is probably the most concerning agent. Toxicity can occur at concentrations below the odor threshold. Because it smells like freshly mown hay even at detectable concentrations, victims often will not recognize the hazard. In addition to poor recognition, phosgene also has additional toxic mechanisms. Besides water, phosgene also reacts with cellular constituents. Acylation reactions occur with sulfhydryls, amines, and hydroxyl groups that produce hydrochloric acid. Additionally, the process of acylation can damage cell membranes, disrupt enzymatic processes, impair energy production, and promote free radical formation.[40]

Incidence and Risk Factors

Respiratory exposures to irritant chemicals are fairly common. Minor exposures often occur in the home or work place when cleaning chemicals are inappropriately mixed. Combining household bleach with acidic or ammonia based chemicals will result in the generation of chlorine or chloramine gas, respectively. Such exposures are usually self-limiting once the victim is removed to fresh air. Large-scale releases resulting in multiple casualties typically are the result of industrial accidents or illegal activity. Whatever the cause, exposures that occur in enclosed spaces with limited ventilation are more likely to produce significant injuries than exposures that occur outside. Victims with preexisting lung disease such as asthma or chronic obstructive pulmonary disease may have significant problems even with minor exposures.

TREATMENT

Pulmonary Agents

■ DESIRED OUTCOME AND GENERAL APPROACH TO TREATMENT

The primary goal of therapy is to limit further exposure, maintain respiratory function, and monitor for delayed complications.[40,42] The initial goals are detection of the exposure source, mitigation of ongoing exposure, stabilize immediate threats to the airway, breathing, or circulation, and appropriate use of antidotal therapies. After stabilization the patient should be monitored for the late onset of complications, especially if a poorly water-soluble agent is believed

to have been involved. Followup evaluation may be needed to assess for the development of long-term respiratory complications in more severe cases.

■ NONPHARMACOLOGIC THERAPY

Removal from the contaminated atmosphere is the initial priority of therapy. Dry decontamination or removal of all of the clothing is usually adequate for treatment of irritant gas exposures unless the patient has mucous membrane irritation. For any patient with mucous membrane irritation water should be applied to those areas. If there is any doubt, the patient should receive full-body decontamination. The treatment of irritant gas exposure is primarily supportive in nature with aggressive early airway management for patients with high and moderately water soluble exposures.[40] Airway compromise is the most common cause of death in these patients. The method of delivery and flow rate of supplemental oxygen should be modified based upon severity of clinical presentation.

■ PHARMACOLOGIC THERAPY

Drug Treatments of First Choice

There is no specific antidote for the treatment of casualties exposed to these agents. The general approach to pharmacotherapy is similar to the treatment of asthma (see Chap. 28). Initially, administer 100% humidified oxygen and then adjust oxygen concentration downward as tolerated. An oxygen saturation of 90% or greater is the usual goal of therapy. β_2-Adrenergic agonists should be administered if bronchospasm develops. Typically, albuterol is given as a nebulized solution containing 2.5 mg (0.1 to 0.15 mg/kg/dose in young children) over 5 to 15 minutes.[40,42] Inhaled corticosteroid treatment with budesonide is often used in combination with albuterol for victims with symptomatic chlorine exposures but clinical data on efficacy are inconclusive.[40,42] In a randomized controlled study, pigs were exposed to chlorine gas and the effects of terbutaline, budesonide, or combination therapy revealed that there was improvement in the terbutaline and the budesonide alone groups, which was enhanced with combination therapy.[43]

Alternative Drug Treatments

Theoretically, the use of sodium bicarbonate may neutralize the acidic products formed when the chlorine gas reacts with water. There have been no controlled studies in humans evaluating the safety or efficacy of sodium bicarbonate inhalation.[43] There is limited evidence to suggest that repletion of glutathione reduces and/or prevents lung damage by phosgene. This may provide an opportunity for therapeutic intervention with inhaled *N*-acetylcysteine, 1 to 10 mL of a 20% solution every 2 to 6 hours.[42]

■ EVALUATION OF THERAPEUTIC OUTCOMES

Victims should be observed for improvements in mucous membrane irritation and respiratory functions. Those that had significant acute injury can have persistent pulmonary abnormalities (e.g., a decrease in total lung capacity, functional residual capacity, and vital capacity and a significant increase in residual volume and airway resistance over several years and persistent reactive airways disease syndrome). After the initial hospitalization follow up for pulmonary function monitoring and evaluation of the medication regimen should be addressed in the care plan.

VESICANT AGENTS

5 The vesicants are often referred to as blistering agents. They have produced more casualties that any other type of chemical weapon. It is estimated that during World War I more than 300,000 casualties resulted form the use of sulfur mustard vesicant.[40,44] It is estimated that sulfur mustard was responsible for 50,000 casualties during the Iran–Iraq war in the 1980s. Vesicants have lower lethality than nerve agents but cause injuries that often disable survivors for weeks to months. Often victims have permanent effects such as loss of vision, respiratory problems, and physical disfigurement. Because of the psychological impact of seeing such injuries and the large amount of resources required to care for victims vesicants are considered ideal terrorist weapons.

Clinical Presentation

The clinical hallmark of the vesicant agents is the formation of fluid-filled blisters and bullae on the skin (Fig. 12–3).[44,45]

PRESENTATION OF BLISTER AGENT EXPOSURE

General
- Skin will be erythematous and varying sizes of blisters may be present
- Onset is delayed with low-dose exposures
- Eyes and mucosa are most sensitive

Symptoms
- Burning pain and itching at the affected areas
- Mucosal irritation
- Nausea, vomiting

Signs
- Skin: erythema to bullae
- Eyes: irritation, conjunctivitis, ophthalmitis
- Pulmonary: mild cough to respiratory distress

Laboratory Tests
- High fluid and electrolyte loss is not expected
- Immune suppression may occur

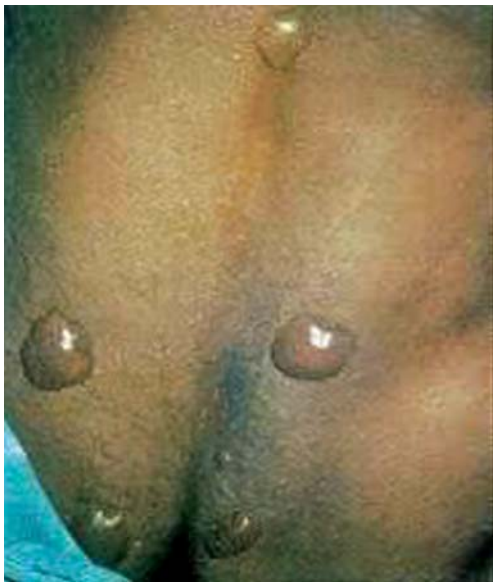
Other Diagnostic Tests
- Blood and urinary arsenic concentrations for lewisite exposures, if available

Available data suggests that mortality is low among vesicant casualties but they will consume considerable medical resources and require lengthy hospitalization. Initial signs of vesicant exposures usually appear rapidly, although they may occasionally be delayed for up to 24 hours depending on the agent and degree of exposure.[44,45] This initially starts off as erythema which progresses to vesicles that may come together to form bullae. In very large exposures, nausea, vomiting, and CNS depression also may be seen early in the course of the exposure. Patients with very high exposures may develop a central zone of coagulation necrosis in the exposed area. The eyes are very sensitive to vesicants with exposure often resulting in chemosis conjunctivitis. Systemic effects can also be seen with vesicants.[44,45] The mustards can produce bone marrow suppression as a delayed consequence. Lewisite contains arsenic, which, when absorbed systemically, can impair cellular energy production. In the long-term vesicants can cause changes in pigmentation or scarring of affected areas. Also restrictive respiratory disorders may result from inhalation exposures.[40,42]

Mechanism of Toxicity and Causative Agents

The vesicants include sulfur mustard, lewisite, and phosgene oxime. Vesicants bind irreversibly to cell structures within minutes of exposure, this process is referred to as "fixing." The mechanisms of action for the three agents are discussed below.

A



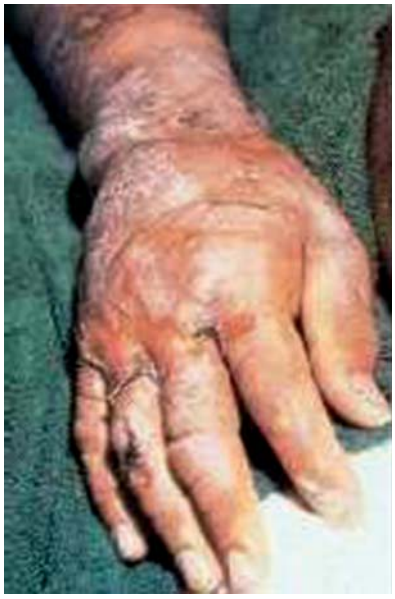


FIGURE 12-3. Examples of injury caused by *(A)* sulfur mustard in the eye, *(B)* bullae on a patient's back, and *(C)* scarring of the arm and hand of a patient of 5 days after exposure. *(From reference 44.)*

Mustard Mustard along with the nerve agents represents the most important of the chemical weapons. Mustard is an oily, tan-colored liquid that has low volatility, except at higher temperatures. Allegedly, mustard received its name from its smell or taste and/or its color. Mustard when vaporized is approximately five times heavier than air. Pure mustard freezes at 13.9°C (57°F) but can be combined with other chemicals to lower the freezing points. This allows its use in colder environments.

Mustard rapidly penetrates cells and generates toxic intermediates that damage tissues through a poorly understood process.[44,45] Within the cells, mustard alkylates DNA, RNA, and proteins. These reactions disrupt cell function by preventing transcription and translation of genetic material to assemble proteins necessary for maintaining the cell. Similar to what is seen with nitrogen mustard chemotherapy, rapidly dividing cells are most susceptible. Mustard will also create stable bonds with thiol and sulfhydryl groups. These reactions may lead to an inability to detoxify free radicals, resulting in lipid peroxidation, and impairment of the activity of thiol-containing enzymes.[44,45]

Lewisite Lewisite is an arsenical compound with vesicant properties. Lewisite is much more volatile and persistent in colder climates than mustard. Lewisite hydrolyzes rapidly and has very limited activity in humid environments. It was synthesized by the U.S. military during World War I but was not used and has seen little or no battlefield use.

Lewisite is similar to mustard in that it damages the skin, eyes, and airways. However, its clinical effects appear within seconds of exposure.[44,45] Fortunately, the recovery time is also shorter than for mustard. Lewisite shares many biochemical mechanisms of injury with the other arsenical compounds. It inhibits many enzymes that are important for energy production: in particular, those with thiol groups, such as pyruvic oxidase, alcohol dehydrogenase, succinic oxidase, hexokinase, and succinic dehydrogenase.[44,45] Inactivation of carbohydrate metabolism, primarily because of inhibition of the pyruvate dehydrogenase complex, is thought to be a key factor.

Phosgene Oxime Phosgene oxime is the third chemical designated by the U.S. military as a vesicant agent. It is important to note that phosgene oxime is a vesicant and is not the same as the phosgene gas that was described earlier. However, it is not a true vesicant because, unlike mustard and Lewisite, it does not produce fluid-filled blisters; rather, it produces solid wheal-like lesions resembling urticaria. There has been no verified battlefield use of this compound, and there has been little study of it in the Western world.[44]

Phosgene oxime's exact mechanism of action is unknown.[44,45] It might produce biologic damage because of corrosive effects of the chlorine moiety, because of the direct effect of the oxime, or because of the carbonyl group. The skin lesions, in particular, are similar to those caused by a strong acid.

TREATMENT

Vesicants

■ DESIRED OUTCOME AND GENERAL APPROACH TO TREATMENT

The primary defense against vesicants is protective garments and decontamination. Removal of contaminated clothing and thorough washing need to be initiated as soon as possible. Decontamination is only effective if performed within 2–5 minutes of contact with the skin. Unfortunately, in many cases the exposure will not be recognized in time to perform effective removal. [44,45] Recently there has been work evaluating various creams to protect against sulfur mustard. Although the data are limited it appears that creams with drugs designed to actively neutralize the agent are superior to simple barrier creams. Experimental studies have found that metal oxide nanocrystals and perfluorocarbon compounds in creams reduced lesion size in exposed animals.[45]

■ PHARMACOLOGIC THERAPY

Drug Treatments of First Choice

Current therapy for vesicant exposures is primarily supportive care.[45] For skin lesions less than 1 cm, topical soothing agents, such as calamine, are all that is needed. Larger lesions should be deroofed and treated with topical antibiotic ointment. Victims with large dermal exposures may appear similar to burn victims. However, fluid loss is significantly lower than in burn victims. To prevent overhydration, rehydration should be based on the patient's fluid and electrolyte status rather than using formulas based on affected surface area.[45]

Ocular exposures should be irrigated with saline for 15 minutes. Lubricating eye drops may be used to reduce discomfort but severe cases may require systemic pain medications. Ophthalmic preparations of antibiotics, such as 10% sulfacetamide ointment three times daily for a week, can be used to prevent secondary infections in the eye. Ophthalmic steroids, such as 0.1% dexamethasone drops twice daily for 2 days, can be used to reduce inflammation early in the course of therapy. Atropine 1% drops four times a day for 2 days can be used reduce to scarring and blepharospasm.

Respiratory effects should be treated as described in the section on pulmonary agents. If bone marrow suppression occurs, transfusions or growth factors may be used to treat anemia or immunosuppression.

Sulfur Mustard Currently, there is no approved antidote for mustard. There are several compounds that are under investigation but they are not yet commercially available; indeed, FDA approval is unlikely within the next 2 to 3 years.[45] The one currently approved drug that may offer some benefit is *N*-acetylcysteine, a glutathione precursor and sulfhydryl donor that has been evaluated as a treatment against sulfur mustard exposure.[46] In several animal studies it appears to minimize lung injury associated with low to moderate exposure to mustard gas, which is believed to be related to glutathione depletion.[47,48] In one study it reduced lung injury by 70% in rats when given 10 minutes before exposure, and administration up to 90 minutes after exposure was also associated with some benefit.[48] It is by no means a perfect antidote, but it has a track record of human safety and further studies may be warranted.

The most common adverse effects following oral administration of *N*-acetylcysteine are nausea and vomiting, but this is not significantly higher than placebo. The U.S. military recommends prophylactic administration with an oral dose of 1,200 mg four times a day for persons who are likely to have mustard exposure for as long as they are in a high-risk environment.[46] For postexposure treatment, either oral or IV *N*-acetylcysteine may be used. Although there are no human studies, animal data suggest that doses between 50 and 150 mg/kg are a reasonable emergency measure. The intravenous route may achieve better tissue penetration and distribution but currently there is no published data indicating either route is superior.

British Anti-Lewisite British anti-Lewisite, also known as dimercaprol, is a chelating agent that contains sulfhydryl groups that bind the arsenic moiety of the lewisite molecule.[45] It comes in a peanut oil vehicle and should be avoided in patients with peanut allergy. British anti-Lewisite can be used topically as a barrier or to assist in decontamination. The injectable product can be compounded into topical products for immediate dermatologic or ocular use. In cases where there is greater than 5% body surface area affected or evidence of systemic arsenic poisoning, British anti-Lewisite should be administered intramuscularly.[44] Recommended dosing for children and adults is 2.5 to 3 mg/kg IM four times per day for 2 days, twice a day on day 3, and then once daily until recovery. Typically, the course of therapy will last for 7 to 10 days. If renal impairment develops, the drug should be discontinued or the dose reduced if the drug remains clinically necessary. IM administration of British anti-Lewisite is painful because of its peanut oil vehicle. Hypertension, tachycardia, and a sense of chest tightness are common during administration. Other common complaints include lacrimation and rhinitis, headache, paraesthesia, tremor, and GI.

Succimer may be considered as an alternative to British anti-Lewisite for systemic toxicity. Succimer is a chelating agent that is indicated for pediatric lead poisoning but has been reported to be useful for systemic arsenic poisoning.[45] Typical dosing is 10 mg/kg orally every 8 hours for 5 days, then 10 mg/kg every 12 hours for 14 days. Common adverse effects include GI upset, rash, and elevations of aspartate aminotransferase and alanine aminotransferase. Less commonly, significant neutropenia has been reported.

■ EVALUATION OF THERAPEUTIC OUTCOMES

Victims of vesicant exposures should be monitored for resolution of lesions, respiratory function and resolution of any systemic toxicities. Good wound care and appropriate antibiotic selection are critical for managing vesicant exposures, particularly if immunosuppression occurs. Blood cell counts should be monitored daily and colony-stimulating factors should be considered for those with severe leucopenia.[45]

RADIOACTIVE AGENTS

Mass casualties from ionizing radiation can come from industrial accidents or weapons that release radioactivity. Potential radioactive weapons include concentrated isotopes, radiation dispersal devices and nuclear bombs. In either case, care issues are similar.

One of the largest and most studied radiologic disasters occurred in 1986 near Kiev, Ukraine, at the Chernobyl nuclear reactor site.[3] An explosion and subsequent fire occurred in the core of one of the site's four reactors. A very high level of radiation was released at the reactor site, resulting in acute radiation injuries in approximately 200 people with 30 deaths. The fire released large amounts of radioactive iodine-131 and cesium-137 into the atmosphere. Fallout spread contamination in low, but significant, amounts over the Ukraine region and into Poland (up to 300 miles away). The event resulted in the eventual evacuation of more than 200,000 people. In this situation, thousands of people needed acute decontamination and treatment with potassium iodide.[49] Victim exposures and contamination of the environment and food supply created significant long-term public health problems in Belarus, Russia, and the Ukraine. Within contaminated parts of the Ukraine, the incidence of thyroid cancer increased from 5 cases per million children in the years before the event to 46 cases per million in the 10 years after.[50] National registries from these countries estimate that more than 1 million people were possibly affected by the fallout. The scope of this event, which involved several countries, highlighted the need for the provision of good information in a coordinated fashion. Clinically, it highlighted the difficulty of clinicians to identify who needed treatment without the aid of radiation detection devices.

CLINICAL PRESENTATION

Radiation poisoning is a complex clinical process that can affect any part of the body. However, rapidly dividing cells, such as those found in bone marrow and the gastrointestinal tract, are the most heavily affected tissues. The signs and symptoms that develop in acute radiation sickness occur through four distinct phases.[51]

CLINICAL PHASES OF RADIATION POISONING

1. *Prodromal phase.* Depending on the total amount of radiation absorbed, patients may experience a variety of symptoms including loss of appetite, nausea, vomiting, fatigue, and diarrhea. After high radiation doses, additional symptoms such as prostration, fever, respiratory difficulties, and increased excitability may develop. This is the stage at which most victims seek medical care.

2. *Latent phase.* This is the transitional period in which many of the initial symptoms resolve; it may last for up to 3 weeks, depending on the original radiation dose. This time interval decreases as the initial dose increases.
3. *Illness phase.* The period of time when overt illness develops, often characterized by infection, bleeding, electrolyte imbalance, diarrhea, changes in mental status, and shock.
4. *Recovery or death phase.* This follows the period of overt illness, which may take weeks or months to resolve.

Carefully evaluating the initial presenting signs and symptoms (such as nausea, vomiting, diarrhea, changes in mental status, shock, and lymphocyte count over the first 48 hours) becomes the most reliable indicator of the radiation dose and the patient's ultimate prognosis.[51] In general, longer onset times for initial symptoms correlates with better prognosis. If the initial onset of clinical effects caused by radiation exposure is less than 1 hour, survival is unlikely. Onset times greater than 3 hours indicate a high likelihood of survival. After entering the hospital, the absolute lymphocyte count can be used to assess prognosis. An absolute lymphocyte count less than 1,000 within 48 hours of radiation exposure is an indicator of severe injury.

MECHANISM OF TOXICITY

The most common types of ionizing radiation are particles, β particles, protons, γ-rays, and x-rays. α Particles have high energies and consist of two protons and two neutrons. They travel a few centimeters in air and up to 60 microns into tissue. The high energy and short path result in a dense track of ionization along the tissues with which the particles interact. α Particles do not penetrate the stratum corneum of the skin, and thus they are not an external hazard. However, if α-emitting elements are taken into the body by inhalation, ingestion, or from open wounds, they can produce significant toxicity. β Particles can penetrate the skin and will travel up to a few centimeters into tissue. Exposure to external sources of β particles, which have less energy than α particles, is potentially hazardous, but internal exposure is more injurious. γ-Rays, electromagnetic energy emitted from the nucleus, have a range of many meters in air and many centimeters in tissue and thus, like β particles, can result in both internally and externally injury. X-rays, like γ-rays, are high-energy electromagnetic energy with essentially no mass. X-rays and γ-rays are sometimes referred to as "photons." These waves or rays are very penetrating and can ionize atoms deep within the body. X-rays generally have longer wavelengths and lower frequencies relative to γ-rays and thus have lower energies. The biologic effects of x-rays and γ-rays are better known than any of the other forms of ionizing radiation.

The basic unit for measuring radiation is the rad (radiation absorbed dose). The rad is defined as the deposition of 0.01 joule of energy per kilogram of tissue. Think of a rad as a one-time dose, like an x-ray. To quantify the amount of damage that is suspected from a radiation exposure, rads are converted into rems. The rem (Roentgen Equivalent Man) is adjusted to reflect the type of radiation absorbed and the likelihood of damage. Another way to think of rem is as your cumulative radiation dose. In most cases of one-time "flash" exposure, the rad and rem will be equivalent. There are some other subtle differences between rad and rem, but they are beyond the scope of this chapter.[52] Also, it is important to note that outside of the United States, the international units gray and sievert are used in place of rad and rem, respectively.[52]

Ionizing radiation causes instantaneous chemical changes in the exposed tissues (Fig. 12–4). Free radicals are formed that rapidly interact with cellular membranes, proteins, and genetic material. The body has effective mechanisms to neutralize these radicals after low-dose exposures and repair much of the damage seen with higher doses. However, when the radiation dose exceeds the body's ability to repair itself clinically, significant toxicity occurs. At doses of less than 50 rad, too low to cause acute effects, there is a slightly increased risk of developing a radiation induced cancer many years later. Other problems that may be observed weeks or months after a moderate acute exposure (≈20 rad) include infertility, thyroid dysfunction (hypothyroidism), and cataracts. As a frame of reference, a radiography delivers about 0.01 rad, which is clinically insignificant.

Clinical effects that occur within hours of high-dose exposure are commonly referred to as acute radiation syndrome, which is likely to occur at doses greater than 50 rad. Radiation burns are often seen in those who have been exposed to 300 rad, whereas doses in excess of 450 rad are associated with very high likelihood of mortality. Preexisting illness and trauma compound the effects of radiation. Even simple wounds can exaggerate mortality when complicated by radiation poisoning. Animal studies have demonstrated that moderate doses of radiation (100 rads) increased the mortality in animals from 50% to 65%.[53]

Three different types of radiation exposure can occur: simple irradiation, contamination, or incorporation. Simple irradiation occurs when all or part of the body is exposed to penetrating radiation from an external source. During exposure, this radiation can be absorbed by the body or can pass completely through it. A similar thing occurs during ordinary chest radiography. This type of exposure can occur all at once, like a single radiograph, or on a chronic basis, as with a person who works with radium everyday. Following external exposure, an individual is not radioactive and can be treated like any other patient. Contamination means that radioactive materials are on or in a person's body. Contaminated individuals will have ongoing exposures until they are decontaminated. Effects are often localized to the site of contamination. If the victims have internal contamination, it may be taken up into tissues through a process known as incorporation. In general, radioactive materials are distributed throughout the body based on their chemical properties. Incorporated contaminants are often concentrated into target organs such as bone, liver, thyroid, or kidney.

CAUSATIVE AGENTS

Concentrated Isotopes

Radioactive material can be found in a wide variety of natural and synthetic sources. The majority of exposures to synthetic sources

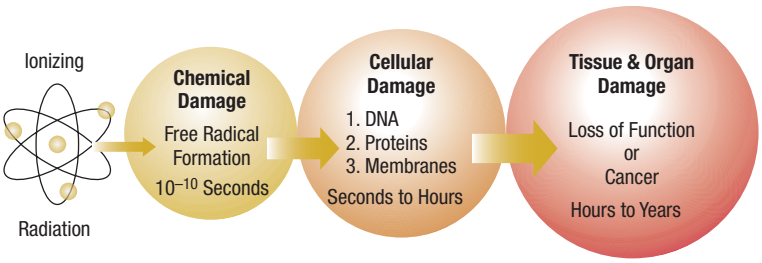


FIGURE 12-4. Ionizing radiation injury.

occur in the healthcare setting as the result of nuclear medicine and radiography procedures. Any exposure to a concentrated source of radioactive material can be potentially harmful, particularly if the dose rate is high or the exposure is prolonged. Several significant cases of radiation poisoning have occurred primarily as the result of improper disposal of products containing radioactive material.[1]

Radiation Dispersal Devices

Radiation dispersal devices are simply weapons designed to spread radioactive material over a large area. The most commonly discussed example of this is the so-called dirty bomb. The dirty bomb is a conventional explosive with radioactive material incorporated into it. Theoretically, the explosion will disperse the radioactive material as shrapnel or smaller contaminating particles. Most experts believe that this type of weapon will not produce acute radiation sickness on a large scale but may require significant victim decontamination and environmental cleanup.[54] In a smaller subset of victims who have traumatic injuries combined with radiation exposure, mortality will be significant.

Nuclear Weapons and Fallout

When a nuclear weapon is detonated, a tremendous amount of energy is released in the forms of pressure, heat, light, and electromagnetic and ionizing radiation. The pressure and heat account for most of this energy and are the major sources of destruction. An initial concentrated burst of ionizing radiation mostly in the form of highly penetrating γ-rays accounts for approximately 5% of the energy released. This initial burst is typically contained within the destructive radius of the explosion and therefore will have little impact on surviving victims (Fig. 12–5). After detonation radioactive particles that are byproducts of the nuclear chain reaction are released in the atmosphere. Fallout refers to the process of these particles returning to earth. Approximately 10% of energy released by the detonation will be in the form of these fallout particles. Fallout is a very heterogeneous group of radioactive materials consisting of over 200 possible isotopes from 36 elements. Different weapon technology and environmental conditions can produce variation in the final composition. A general rule is that for each kiloton of explosive yield in the weapon about 2 ounces of fallout products will be generated. Fallout can also occur as a result of disasters at nuclear power plants, such as the one that happened at the Chernobyl power plant.

Fallout particles range in size from less than 1 micron up to several millimeters. Note that this range encompasses particles that can reach the bronchiole level of the lung and lead to internal deposition. The most concerning radioactive elements in fallout typically include cesium, iodine, plutonium, strontium, technetium, and uranium.[3,51] The greatest risk from fallout occurs in the first 24 hours. This early fallout comprises a little more than half of the total amount, and accounts for an overwhelming portion of the risk to the public. Most of the early fallout comes down in a concentrated plume, feather-shaped area, originating from the detonation site. Fatalities can be very high within this limited area. The expanse of the exposure area is influenced by weather conditions and the fallout spread over this extended area will usually be very dilute and clinically inconsequential.

RISK FACTORS

The amount and type of radiation to which a victim is exposed is a function of four factors: the source material, time spent close to the source, distance from the source, and shielding between the victim and the source. Responders have some control over the aspects of time, distance, and shielding. These parameters can be used to modify radiation dose and limit risk by spending as little time as possible in close proximity to radioactive material. Moving 1 meter from the radiation source will reduce the dose approximately 10-fold. Decontamination procedures will reduce both time and distance. As a general rule anything between you and the source will reduce your exposure. The amount of shielding needed to be effective will depend on the form of radiation that is released. Poorly penetrating radioactive particles can be blocked by common garments, whereas other forms (γ- or x-rays) require very dense substances like lead or thick concrete to fully block them. It is important to remember that contaminated victims pose some risk to healthcare workers but this risk is relatively low if the healthcare workers wear standard gloves, gowns, and masks and interact with the victims for short periods of time.

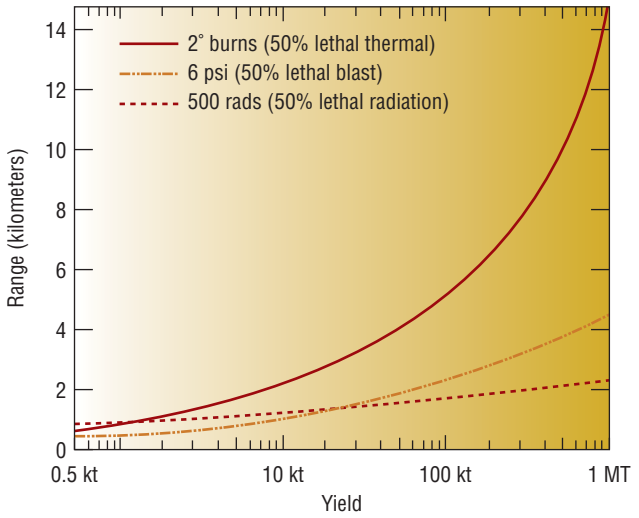


FIGURE 12-5. Destructive ranges for various sizes of nuclear weapons. (kt, Kilotons.) *(From reference 51.)*

TREATMENT

Radioactive Agents

DESIRED OUTCOME AND GENERAL APPROACH TO TREATMENT

Similar to chemical events, appropriate decontamination is essential for management of radioactive contaminants. Because no specific antidote exists to reverse radiation exposure, treatment is primarily supportive with more specialized care directed toward patients with high-dose irradiation and drugs that enhance isotope elimination in those with internal contamination.[51,53] After donning appropriate personal protective equipment (N95 mask, gown, gloves, eye protection, and hair and shoe covers, at a minimum), life-threatening injuries should be addressed as the first priority, even if decontamination has not been performed. After stabilization the victim should be assessed for degree of exposure. Consultation with specialists in burns, hematology, radiation, and infectious disease should be obtained if indicated. In victims with significant exposures, good infection control procedures should be followed to limit secondary infections. Ideally, strict infection control procedures will be followed, including reverse isolation and food sterilization. If surgical interventions are required, they should occur within 48 hours of exposure or be delayed until the immune system has recovered (approximately 2 months).[51,53]

PHARMACOLOGIC THERAPY

6 There are three general approaches to pharmacotherapy for radiation victims: elimination enhancers, mitigators, and protectants.

TABLE 12-3 Specific Therapies for Internal Contamination

Radionuclide	Therapy
Uranium	Enhance elimination (alkalinization of urine w/ bicarbonate)
Tritium	Dilution (force fluids)
Iodine-125 or 131	Blocking (SSKI or potassium iodide) or mobilizing (antithyroid drugs)
Cesium-134 or 137	Blocking (Prussian blue)
Strontium-89 or 90 ingestion	Decrease absorption (aluminum phosphate gel antacids) Blocking (strontium lactate) Displacement (oral phosphate) Mobilization (ammonium chloride or parathyroid extract)
Plutonium and other transuranics	Chelating (Zn or Ca-DTPA; investigational)
Unknown ingestion	Reduce absorption; consider emetics, lavage, charcoal, laxatives

Ca-DTPA, calcium diethylenetriamine pentaacetic acid; SSKI, saturated solution of potassium iodine; Zn, zinc.
Adapted from Tronko MD et al.[50]

Eliminators are drugs that reduce the biologic half-life of internal contamination for specific radioactive elements, radiation mitigators are drugs that accelerate recovery or repair after radiation injury, and protectants are drugs that prevent radiation-induced cellular and molecular damage.[53] Table 12–3 identifies the specific therapies recommended for select radionuclides.

Drug Treatments of First Choice

Elimination Enhancers Potassium iodide is the drug of choice to prevent thyroid uptake of radioactive iodine. It blocks uptake and allows faster elimination but does not reduce or repair radiation effects. It can be administered orally as tablets or in liquid form prepared by diluting saturated solution of potassium iodide (Table 12–4).

It is most effective if administered within 4 hours of exposure and offers essentially no benefit after 12 hours.[51] Potassium iodide therapy in the setting of acute radioiodine exposure is rarely indicated for adults older than age 40 years unless they have been exposed to a massive dose.[55] Children and pregnant women are much more susceptible and therapy should be initiated for essentially any suspected radioiodine exposure. Potassium iodide has been associated with rashes, allergic reactions, and gastrointestinal symptoms. Persons with underlying thyroid disease are at risk for iodine-induced thyroid dysfunction.

Ferric hexacyanoferrate, or Prussian blue, is an insoluble dye that, when administered orally, prevents absorption and enhances fecal excretion of cesium and thallium from the body by means of ion exchange. Although this agent has been used for many years, it was only FDA approved in 2005. Radioactive isotopes of cesium, particularly cesium-137, are a byproduct of nuclear fission reactions and also have many commercial and medical applications. Cesium-137 is considered a likely isotope for small-scale acts of terrorism. Adults and adolescents should receive 3 g of Prussian blue orally three times a day and children 2 to 12 years of age should receive 1 g three times a day for a minimum of 30 days.[53] Treatment may be individualized, depending on the level of internal contamination. The most significant adverse effect associated with Prussian blue is constipation, thus it should be used with caution in patients with severely decreased gastrointestinal motility.

Calcium and zinc diethylenetriamine pentaacetic acid (DTPA) are chelating agents used to treat internal contamination with the transuranic elements plutonium, americium, and curium. These agents are similar to chelators that are used to treat lead and other types of heavy metal poisoning. Ca and Zn DTPA react with these elements to form stable ionic complexes, which are then excreted in the urine. The FDA recommends that therapy be initiated with a single 1-g loading dose of Ca-DTPA in adults (14 mg/kg in children younger than age 12 years) administered intravenously as soon as possible after exposure.[53] Ca-DTPA is believed to be teratogenic and should not be administered to pregnant women if Zn-DTPA is available. The recommended maintenance dose is 1 g (14 mg/kg in children) of Zn-DTPA administered intravenously once a day, with a duration of months or years, depending on the level of internal contamination.[53] Ca-DTPA is also effective when administered by nebulizer. Serum levels of trace minerals, including zinc, magnesium, and manganese, should be monitored during therapy as they are susceptible to Ca-DTPA's chelating effects.

Urinary alkalinization can enhance the elimination of uranium and reduce the risk of acute tubular necrosis.[51] Intravenous bicarbonate and potassium are administered to raise the urine pH trapping the uranium in the urine. This is the same procedure that is performed for an aspirin overdose (see Chap. 10). When done correctly elimination rates will increase by approximately 20%.

TABLE 12-4 Recommended Doses of Potassium Iodide (KI) for Different Risk Groups

Ages	Predicted Thyroid Exposure (cGy)	KI dose (mg)
Older than 40 years	≥500	130
18 through 40 years	≥10	
Pregnant or lactating women	≥5	
Children older than age 3 years[a]		65
Older than 1 month through 3 years		32
Birth through 1 month		16

[a]Adolescents approaching adult size (weight >70 kg) should receive the full adult dose (130 mg).
From the U.S. Department of Health and Human Services. Food and Drug Administration, Center for Drug Evaluation and Research, 2001.

Mitigators Ionizing radiation causes dose-dependent declines in circulating blood cells by direct toxic effects on the bone marrow and induction of apoptosis in mature formed elements of the blood. Even if serious damage occurs to most of the hematopoietic system, surviving stem cells can migrate to damaged areas and restore function. The role of bone marrow transplantation for radiation injury is very limited and impractical for a mass casualty situation. However, drugs that promote blood cell formation, such as colony-stimulating factors, are likely to be beneficial for more seriously affected radiation victims.

Colony-stimulating factors are endogenous glycoproteins that induce bone marrow hematopoietic progenitor cells to proliferate and differentiate into specific mature blood cell types. Three recombinant colony-stimulating factors (filgrastim, pegfilgrastim, and sargramostim) are currently approved for use in patients with neutropenia resulting from myelosuppressive chemotherapy. Filgrastim and sargramostim have been used in radiation accident victims and anecdotally appear to hasten recovery of neutrophil counts. Although controlled human trials are lacking, there is good data from nonhuman primate studies demonstrating that these agents shorten the duration of severe neutropenia when administered within 48 hours of severe radiation exposures.[53]

The initiation of cytokine therapy is recommended for victims with potentially life threatening radiation exposures or combination injuries. Therapy with filgrastim at 5 mcg/kg per day or sargramostim at 250 mcg/m^2 per day administered subcutaneously as soon after exposure as possible and continuing therapy until the absolute neutrophil count exceeds 1,000 may be considered.[53] Alternatively, 6 mg of pegfilgrastim can be administered subcutaneously once weekly to adults and adolescents who weigh more than 45 kg.

Protectants The available protectant, amifostine, is very interesting in concept but offers limited practical use in response to

TABLE 12-5 Lymphocyte Count for the Assessment of Radiologic Injury

Lymphocyte Count (× 1,000/mm³)	Dose Range (Gy)	Lethality (%)
3.0	0–0.25	–
1.2–2.0	1–2	<5
0.4–1.2	2.0–3.5	<50
0.1–0.4	3.5–5.5	50–99
0–0.1	>5.5	99–100

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radiologic terrorism. Amifostine is approved by the U.S. Food and Drug Administration as a protectant for patients undergoing radiation therapy for head and neck cancers. It is a freely soluble organic thiophosphate cytoprotective agent.[53] Amifostine also appears to enhance the chemical and enzymatic repair of damaged DNA, and animal studies suggest that amifostine administered before irradiation may reduce carcinogenesis and mutagenesis.[53] Data about this drug's efficacy when given after exposure are lacking. Theoretically, amifostine or a similar drug could be used as prophylaxis to reduce the long-term consequences of radiation exposure in first responders entering contaminated areas. Unfortunately, amifostine has significant adverse effects (including severe hypotension, nausea, vomiting, and hypocalcemia) and a short duration of action that render it impractical for prehospital uses.

■ EVALUATION OF THERAPEUTIC OUTCOMES

The need for initial treatment for internally contaminated patients is determined based on the patient's medical condition, history, biologic samples (nasal swabs), and definitive evaluation of internal contamination. Whole-body radiation counting may be needed if internal contamination is suspected. Changes in white blood cells can be used to estimate radiation doses and establish a prognosis (Table 12–5).[51]

THE CLINICIAN'S ROLE IN DISASTER RESPONSE

❼ During a disaster or terrorist attack, demand for healthcare will increase. The individual clinicians need to know, at a minimum, their specified role and how to communicate one level up and down the chain of command. A clinician's specific role in helping to meet this demand will vary depending on the clinician's training, licensure, practice setting, and proximity to the event. Close to the event site the top priorities will be detection of the event, assessing safety hazards, and responding to immediate threats. In this environment resources will initially be scarce and healthcare workers may need to perform tasks outside their normal practice during the first few hours to days, depending on the nature of the event. In the hospital environment there will be a surge of patients, requiring expansion of bed capacity, increasing staffing, and provisioning of additional supplies. The planning issues and opportunities for clinicians to provide assistance at local and national levels are detailed in the following paragraphs. It is critically important that communities and healthcare systems have detailed response plans that are regularly tested in conjunction with outside agencies. Although many different types of threats exist, an "all-hazards" approach to planning will help the healthcare system respond to disasters.

PLANNING

Incident Command

In 2003, the Department of Homeland Security was charged to develop and administer a National Incident Management System. The National Incident Management System provides a consistent nationwide template to enable all government, private-sector, and nongovernmental organizations to work together during domestic incidents. You can find more information about the National Incident Management System and take free online incident command training courses at *http://www.fema.gov/nims/*. Within healthcare, the Hospital Incident Command System was developed to help hospitals create response plans that integrate with National Incident Management System. The Hospital Incident Command System has nine essential positions in the command structure that organize and direct the four sections: Operations, Planning, Logistics, and Finance/Administration (Fig. 12–6). For chemical and radiologic events the Medical/Technical Specialist position is critical and these individuals will provide specific expertise about decontamination needs and agent-specific therapies to the incident command staff and the hazardous materials branch chief, who will direct decontamination operations. Detailed information about Hospital Incident Command System can be found at *http://www.emsa.ca.gov/hics/hics.asp*.

Strategic National Stockpile/CHEMPACK Program

The Centers for Disease Control and Prevention maintains a Strategic National Stockpile (SNS) of medicine and medical supplies to protect the American public if there is a public health emergency (terrorist attack, flu outbreak, earthquake, etc.) severe enough to potentially deplete local supplies. The SNS contains antibiotics, chemical antidotes, antitoxins, life-support medications, IV admin-

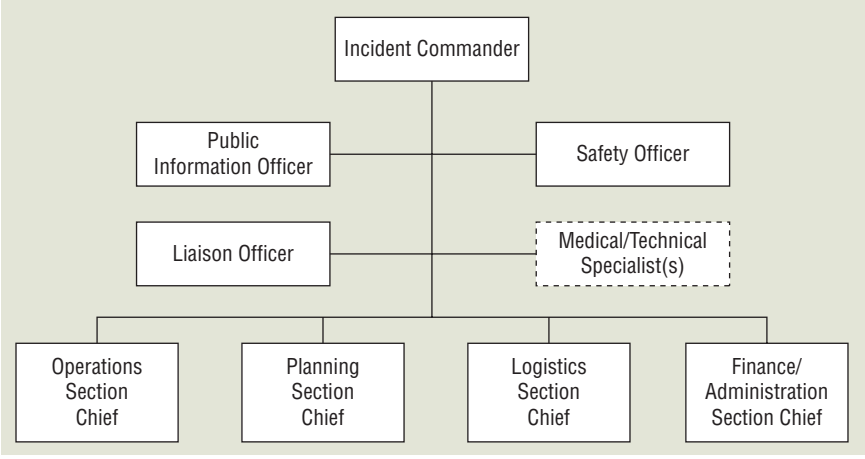

FIGURE 12-6. Hospital Incident Command Structure. *(From State of California Emergency Medical Services Authority, Incident Management Team Chart, 2006.)*

istration sets, airway maintenance supplies, and medical/surgical items. The exact contents are frequently evaluated and updated based on needs assessments.

Once federal and local authorities agree that the SNS is needed, medicines will be delivered to any state in the United States. The first line of support lies within the immediate response 12-hour Push Packages. These are caches of pharmaceuticals, antidotes, and medical supplies designed to provide rapid delivery of a broad spectrum of assets for an ill-defined threat in the early hours of an event. These Push Packages are positioned in strategically located, secure warehouses ready for immediate deployment to a designated site within 12 hours of the federal decision to deploy SNS assets. Each state has plans to receive and distribute SNS medicine and medical supplies to local communities as quickly as possible. The SNS is organized for flexible response. If the incident requires additional pharmaceuticals and/or medical supplies, follow-on vendor-managed inventory supplies will be shipped so as to arrive within 24 to 36 hours. If the chemical or radiologic agent is well defined, vendor-managed inventory can be tailored to provide pharmaceuticals, supplies, and/or products specific to the suspected or confirmed agent(s). In this case, the vendor-managed inventory could act as the first option for immediate response from the SNS Program.

To augment local response plans for nerve agent attacks, part of the SNS has been allocated to state and local governments to be predeployed within the community or region. These assets are called CHEMPACK and contain supplies that are expected to be needed for nerve agent exposure.

Surge Capacity

In addition to an effective command system mass casualty incidents also require careful planning to ensure capacity for the anticipated large number of victims. Most communities' healthcare systems are operating at or near maximum capacity and have very limited ability to absorb a large influx of patients requiring decontamination and/or treatment. Surveys and large-scale exercises indicate that many hospitals are not prepared to deal with extensive chemical or radiologic exposures.[6,56,57] Developing plans for managing decontamination needs and expanding treatment facilities is critical. There are several models for setting up offsite facilities with varying levels of treatment capability. The goal of these models is to prevent less critically injured victims from overwhelming hospitals. Potential sites include civic centers, school gyms, vacant hotels or shopping centers, and improvised outdoor facilities. One of the most difficult aspects of such facilities is getting supplies and personnel to staff them. Surge capacity planning must address shelter, food, and personal needs for staff as well as patients.

OPPORTUNITIES TO ASSIST

When disasters occur, clinicians who are not directly affiliated with hospitals often want to assist in the response but are frustrated because they are not plugged into the system. There are several ways to offer assistance during a disaster. It is best to have a preexisting relationship with aid organizations or response teams. This way one can be credentialed in advance and be ready to respond to an emergency. Participation with these organizations offers one training opportunities and will facilitate the activation of the response operation. One of the best known and most widely available response organizations is the American Red Cross, a volunteer organization that functions independently of the government but works closely with government agencies, such as the Federal Emergency Management Agency (FEMA), during times of major crises. Numerous other volunteer organizations, charities, and faith-based organizations also provide services at the local, state, and national level.

There are several response organizations that are supported in part by state and federal governments. At the local level, the Community Emergency Response Team program educates people about disaster preparedness for hazards that may impact their area and trains them in basic disaster response skills, such as fire safety, light search and rescue, team organization, and disaster medical operations. Community Emergency Response Team members can assist others in their neighborhood or workplace following an event when professional responders are not immediately available to help. Community Emergency Response Team members also are encouraged to support emergency response agencies by taking a more active role in emergency preparedness projects in their community.

In 2002 the Medical Reserve Corps initiative was established to help communities prepare medical responses for disasters. Medical Reserve Corps units are community-based and locally organized, and use local healthcare professionals who want to donate their time and expertise to prepare for and respond to emergencies and promote healthy living throughout the year. Medical Reserve Corps volunteers supplement existing emergency and public health resources and include medical and public health professionals such as physicians, nurses, pharmacists, dentists, veterinarians, and epidemiologists. Medical Reserve Corps units are given, by the U.S. Surgeon General, specific areas of responsibility that strengthen the public health infrastructure of their communities.

The U.S. Department of Health and Human Services, through the National Disaster Medical System fosters the development of Disaster Medical Assistance Teams (DMATs). A DMAT is a group of professional and paraprofessional medical personnel (supported by a cadre of logistical and administrative staff) designed to provide medical care during a disaster. DMATs are principally a community resource available to support local, regional, and state requirements. However, as a national resource, they can be federalized. Each team has a sponsoring organization, such as a major medical center, public health or safety agency, nonprofit, public, or private organization that signs a Memorandum of Agreement with the Department of Health and Human Services. The DMAT sponsor organizes the team and recruits members, arranges training, and coordinates the dispatch of the team. DMATs deploy to disaster sites with sufficient supplies and equipment to sustain themselves for a period of 72 hours while providing medical care at a fixed or temporary medical care site. In mass casualty incidents, their responsibilities may include triaging patients, providing high-quality medical care despite the adverse and austere environment often found at a disaster site, and preparing patients for evacuation. In other types of situations, DMATs may provide primary medical care and/or may serve to augment overloaded local healthcare staffs. Under the rare circumstance that disaster victims are evacuated to a different locale to receive definitive medical care, DMATs may be activated to support patient reception and disposition of patients to hospitals. DMATs are designed to be a rapid-response element to supplement local medical care until other federal or contract resources can be mobilized, or the situation is resolved. DMAT members are required to maintain appropriate certifications and licensures within their discipline. When members are activated as federal employees, licensures and certifications are recognized by all states. Additionally, DMAT members are paid while serving as part-time federal employees and have the protection of the Federal Tort Claims Act in which the federal government becomes the defendant in the event of a malpractice claim. More information about the National Disaster Medical System and contact information for regional DMAT teams can be found at *http://www.oep-ndms.dhhs.gov/index.html*.

CONCLUSIONS

Mass casualty incidents caused by chemical or radiologic exposure may be caused by terrorist activity or industrial catastrophes. Famil-

iarization with the major threat categories and treatment needs will help the individual practitioner to take appropriate safety precautions and properly treat victims. In either case, demand for healthcare resources will increase. Besides basic care, these events will require victim decontamination and, depending on the agent involved, the use of antidotal therapies. Proactive planning and participation in community wide drills will improve response capability.

ABBREVIATION

metHb: methemoglobin

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