

# Chapter 35

## CHEMICAL, BIOLOGICAL, RADIOLOGICAL, NUCLEAR, AND EXPLOSIVE THREATS

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## INTRODUCTION

The chemical, biological, radiological, nuclear, and explosive (CBRNE) threat to the US military has changed dramatically in recent years due to advancing technological platforms associated with computers, drones, robotics, genetics, and synthetic biology. These changes have created an environment in which individuals, groups, or states can pose an almost invisible threat anywhere around the world. Innovative technologies that empower great good can also be used to inflict great harm. It is reasonable to anticipate that groups that used airplanes like missiles might use toxic industrial chemicals (TICs) like conventional chemical weapons, an emerging infection like a biological weapon, or radioactive isotopes to spread harm or terror, if they could gain access to them. While encountering conventional casualties on the battlefield remains a more likely scenario for today's military medical officer (MMO) due to the increased accessibility of conventional weapons, the MMO must also remain

vigilant for unusual scenarios that might represent the first clue that a CBRNE incident has occurred in a military or civilian population. Because environmental sampling for agent detection and rapid point-of-care testing for agent identification will not be routinely available to most MMOs in the austere environment or most hospital settings, the initial suspicion of a CBRNE attack will rest on clinical recognition of signs and symptoms of poisoning, infection, or injury.

Distinguishing a biological, chemical, or radiological weapons attack from that of an emerging infection or toxic industrial accident will be difficult and outside the normal experience of most MMOs. Regardless, today's MMO must remain alert to the possibility and be prepared to recognize military or civilian CBRNE casualties of warfare or terrorism. This chapter will focus on key principles of CBRNE incident recognition and casualty management, emphasizing relevance to the MMO.

## CHEMICAL WARFARE AGENTS

During the morning rush hour at 8 AM on March 20, 1995, in the heart of Tokyo, five small bags of dilute sarin nerve agent were simultaneously dropped in subway cars and punctured with umbrellas as the cars were converging under a hub of government buildings. It appeared as if someone dropped plastic bags with water on the subway car floors. That morning, the terrorist attack by the Aum Shinrikyo cult sent thousands of terrified Japanese, with varying degrees of nerve agent vapor poisoning, to the local healthcare system within minutes, and brought the city of Tokyo to a standstill. Ultimately, 12 people died, at least 5,500 victims presented for care, and almost one-quarter of the nearest hospital's staff became secondary victims. St Luke's Hospital received 640 victims that day because of news reports that it had the antidote.<sup>1</sup>

Less than a year earlier, in Matsumoto, Japan, the same cult had launched a sarin attack into the open air using an electric heater fan to direct nerve agent vapor toward a targeted apartment. Eight people died and 660 were injured in the first terrorist attack using sarin nerve agent on the general public.

Chemical warfare agents are toxic substances developed for military use to produce death, serious injury, or incapacitation. They may exist as solids, liquids, or gases, but most are stored as liquids and dispersed as a liquid or aerosol. TICs are industrially manufactured chemicals that could be used to produce mass casualties; some were used as chemical agents on the battlefield in World War I. Incapacitating agents

and riot-control agents are chemical agents designed only to produce temporary effects without serious sequelae.

The modern use of chemical warfare agents dates to World War I, when the first chemical agent employed on the battlefield was chlorine gas and the most effective was sulfur mustard. Chemical weapons were not used in World War II. The United States and the former Soviet Union (USSR) both signed the Chemical Weapons Convention and agreed to destroy chemical weapons stockpiles beginning in 1990.<sup>2</sup> More than 31 countries and some terrorist groups possess chemical weapons, and many more are seeking to obtain them.<sup>3</sup> Since the 1980s there have been multiple instances of chemical weapons use on the battlefield, against civilian populations, and in terrorist attacks. The Iraqi military used both nerve agent and mustard against Iran during the 1980–1988 Iran-Iraq war, and widespread use of toxic chemical weapons has been reported in the 2011–present Syrian civil war.<sup>4,5</sup> Because the threat remains high, MMOs have a critical responsibility to competently identify and manage chemical casualties in any setting.

The major categories of lethal traditional chemical warfare agents include: vesicants, nerve agents, lung-damaging (pulmonary) agents, TICs, and cyanide. Nonlethal agent categories include incapacitating agents and riot-control agents. It is important for the MMO to recognize several general features of chemical agents:

1. Each chemical warfare agent category requires similar treatment.
2. An act of chemical warfare or terrorism is likely to involve substances that cannot immediately be identified; real-time testing will be difficult; and the window for effective therapy will likely be narrow.
3. A chemical attack will be more easily recognizable when a group of exposed persons have rapid onset of comparable symptoms.<sup>6</sup>

### General Principles of Chemical Casualty Care

General principles of chemical casualty care for the MMO to consider include identifying chemical threat agents and all exposed patients, protecting medical staff, ensuring proper triage, recognizing the need for decontamination (if liquid contamination is present), managing medical treatment and antidote availability, and ensuring proper patient disposition (evacuation or return to duty). For patients, treatment begins with removal from chemical exposure and decontamination. Persons who suspect they have been exposed should remove and bag their clothing and shower thoroughly with soap and water as soon as possible. Removing contaminated clothing can eliminate 85% to 90% of trapped chemical substances.<sup>6</sup> The MMO must appreciate that the majority of affected patients will be minimally exposed and reach medical facilities through their own efforts, so medical treatment facilities must make advanced preparation to handle ambulatory decontamination and provide psychological support to casualties.

Clinical signs of severe chemical exposure include altered mental status, airway obstruction, respiratory distress, cardiovascular instability, and seizures. Initial supportive treatment for casualties should be focused on airway management, maintaining ventilation and circulatory support, and administering antidote, if available, while simultaneously assessing for burns, trauma, and other injuries. Atropine, pralidoxime, cyanide antidote kits, hydroxocobalamin, diazepam, and Reactive Skin Decontamination Lotion (RSDL) are the most important drugs to stockpile for the treatment of chemical casualties.<sup>7</sup>

### Personal Protective Equipment

The MMO managing contaminated patients with liquid exposure must ensure medical staff wear proper chemical protective clothing until the patient is decontaminated. The M40 Chemical-Biological Field Mask represents the latest generation of protective mask issued by the US military. When properly worn, the

M40 mask will protect from all known chemical, biological, and riot-control agents.<sup>8</sup> The addition of the chemical/biological hood affords additional protection to the head, neck, and shoulders. Filtration is provided by one C2A1 filter canister mounted on either cheek. The new M50 Joint Service General Protective Mask (JSGPM), designed to replace the M40, is the first joint service model. The JSGPM provides improved vision and protection against nuclear, biological, and chemical threats, including designated TICs, with the M61 filter.<sup>9</sup> The chemical protective glove set consists of an outer butyl rubber glove for chemical protection and an inner cotton glove for perspiration absorption. The green or black vinyl over-boots are worn over combat boots and provide protection from chemical and biological agents and radioactive particles (alpha and beta) for a limited time. The Joint Service Lightweight Integrated Suit Technology (JSLIST) Chemical & Biological Protective Garment, a two-piece suit lined with carbon beads, provides 24 hours of protection against known biological and chemical agents and toxins in solid, liquid, or vapor form, and alpha and beta radioactive particles.<sup>9</sup> It should be worn in military environments under threat of nuclear, biological, or chemical attack.

### Vesicants

Vesicants (“blister agents”) are agents that cause chemical burns. To the MMO, sulfur mustard or mustard (NATO designation H or HD) is the most important vesicant and is still considered a major military threat agent. It has been the most frequent chemical weapon used militarily since 1917, and was responsible for most of the chemical casualties in World War I.<sup>10</sup> Mustard is stored and deployed as a persistent liquid agent and constitutes both a liquid and vapor threat to exposed skin and mucous membranes.<sup>11</sup> Accidental exposure from old military ordinance has occurred.<sup>12,13</sup>

Mustard may be detected by multiple military detection devices including chemical agent monitors and detection papers.<sup>11</sup> Routine clinical lab testing for mustard in blood does not exist, but a metabolite, thiodiglycol, may be detected in blister fluid or urine, and advanced analyses of blood samples have verified human exposure to mustard.<sup>10,13</sup>

Properly wearing the full chemical protective mask and ensemble affords full protection against vesicants like mustard. The activated charcoal in the mask filters and over-garment absorbs mustard. The butyl rubber in the chemical protective gloves and boots is impermeable to mustard.<sup>14</sup>

Mustard liquid is absorbed through skin within minutes and rapidly distributed throughout the

body.<sup>10</sup> While the exact mechanism of action of mustard is unknown, its effects are delayed, appearing hours after exposure. Mustard vapor is extremely irritating to the eyes, skin, and airways. Burning or pain may begin anywhere from 2 to 48 hours after exposure. Initial skin injury resembles sunburn, which may progress to blister formation. Blister fluid does not contain mustard and is not a contamination risk.<sup>10</sup> The earliest effects from mustard involving the airway will be burning of the nares, sinus pain, sore throat, and hoarseness. Injury to the upper airways may lead to cough and laryngitis. Damage descends to the lower airways in a dose-dependent fashion.<sup>11</sup> The terminal airways and alveoli are usually not affected, and pulmonary edema is rarely present.<sup>15</sup>

The MMO must appreciate that no specific antidote for mustard exists; therefore, early decontamination is critical. To be effective in the management of mustard casualties, decontamination must be carried out immediately in the field to prevent injury and further exposure. Unfortunately, patients usually present when pain and lesions develop, hours after exposure. Management may be simple or complex, and the extent and severity of injury is dose-dependent. Although lethality from mustard exposure is low, MMOs must be aware that most casualties will require some form of extended medical care.<sup>10</sup> Dermal injuries may be managed with standard chemical burn care.<sup>11</sup> Early treatment should be focused on keeping the casualty comfortable, maintaining oxygenation, and preventing

infection. Severe eye injuries and vision loss are rare from mustard exposure, and most casualties who lose their vision due to mustard exposure can be safely reassured they will fully recover their eyesight.<sup>10</sup> Significant respiratory effects within 4 hours of exposure signify a severe poisoning and poor prognosis.<sup>11</sup>

### Nerve Agents

The MMO must recognize that the nerve agents GA (tabun), GB (sarin), GD (soman), GF, and VX are the most toxic chemical warfare agents and are considered major military threats. They are hazards in both liquid and vapor states and can cause death within minutes after exposure. The only known battlefield use of nerve agent occurred during the Iran-Iraq War; however, there have been multiple episodes of use against civilian populations, most notably the 1995 Tokyo subway terrorist attack with the nerve agent sarin. Many countries have the technology to manufacture nerve agents, and weapons stockpiles remain major concerns.

Nerve agents are potent organophosphate acetylcholinesterase (AChE) inhibitors, causing cholinergic overstimulation and a clinical syndrome called “cholinergic crisis” (Table 35-1). Most exposures occur via inhalation or through the skin. The attachment of nerve agent to the AChE enzyme is permanent unless removed by medical therapy.<sup>16</sup> The MMO should consider nerve agent poisoning in instances of terrorism when multiple persons suddenly collapse with

**TABLE 35-1**  
**EFFECTS OF NERVE AGENTS IN HUMANS (CHOLINERGIC TOXIDROME)**

Body Part or System	Effect (“DUMBBELLS”)
Skin and sweat glands	<u>D</u> iaporesis
Urinary tract	<u>U</u> rination
Eye	<u>M</u> iosis (unilateral or bilateral), pain in or around the eye; complaints of dim or blurred vision
Nose	Rhinorrhea
Pulmonary tract	<u>B</u> ronchorrhea and <u>B</u> ronchospasm cough; complaints of tight chest, shortness of breath; wheezing on exam
Gastrointestinal tract	<u>E</u> mesis and <u>L</u> oose stools; increase in secretions and motility; nausea, vomiting, diarrhea; complaints of abdominal cramps, pain
Mouth	<u>L</u> acrimation and <u>S</u> alivation
Muscular	Fasciculations (“rippling”), local or generalized; twitching of muscle groups; flaccid paralysis; complaints of twitching, weakness
Cardiovascular	Decrease or increase in heart rate; usually increase in blood pressure
Central nervous system	Acute effects of severe exposure: loss of consciousness, convulsion (or seizures after muscular paralysis), depression of respiratory center to produce apnea

apnea, seizures, or coma. The initial effects of nerve agent, which may begin within seconds, depend on the dose and route of exposure; the severity of clinical effects are dose-dependent. Exposure to a small amount of nerve agent vapor causes effects on the eyes, nose, and airways. Miosis, often accompanied by eye pain, blurred vision, and nausea, is a characteristic finding in nerve agent vapor exposure to the eyes.<sup>16</sup> Rhinorrhea is characteristic of nasal airway vapor exposure, as is chest tightness, bronchoconstriction, and increased secretions. Exposure to a large amount of nerve agent vapor will cause rapidly cascading symptoms in minutes, culminating in loss of consciousness, convulsions, apnea, and muscle flaccidity (Table 35-2).<sup>16</sup>

Standard military chemical agent monitors and chemical agent paper will detect nerve agent.<sup>14</sup> The protective mask and chemical protective ensemble affords full protection. Butyl rubber gloves and boots are impermeable to nerve agents. Pyridostigmine bromide is a safe command-authorized military pretreatment against soman exposure. It is not an antidote and must be taken before exposure.<sup>16</sup>

Medical management includes decontamination for liquid exposure, ventilation, antidotal treatment, and supportive care. Removal of clothing is adequate to prevent exposure to trapped vapor. The need for ventilation will be obvious.<sup>17</sup> Three drugs are used to treat nerve agent exposure: atropine, pralidoxime chloride, and diazepam. The Antidote Treatment Nerve Agent Auto-injector (ATNAA) contains atro-

pine and pralidoxime chloride.<sup>17</sup> Pralidoxime chloride should never be withheld out of concern it may be too late after exposure.<sup>16</sup> Convulsant Antidote, Nerve Agent (CANA) contains diazepam. Benzodiazepines are the only effective anticonvulsants for nerve agent poisoning and should be administered to all patients with severe intoxication.<sup>16</sup> Casualties with severe symptoms should be triaged as *immediate* and receive three ATNAAs and one CANA.<sup>17</sup> Casualties exposed to liquid nerve agent may worsen. Casualties who are walking and talking and no longer being exposed may be triaged as *minimal*.<sup>17</sup> Laboratory testing to confirm nerve agent exposure is based on measuring the level of AChE inhibition, rather than testing for parent nerve agent.<sup>18</sup>

### Lung-Damaging Toxic Industrial Chemicals

On the night of December 2, 1984, during floor cleaning at the Union Carbide pesticide plant in Bhopal, India, water contacted a tank of methyl isocyanate, resulting in an exothermic reaction and explosion. Within an hour, 40 tons of the chemical had vaporized and leaked out into the night air. Heavier than air, the vapor cloud settled along the ground and drifted into the surrounding densely populated slums. Over the next day, the dead and dying arrived by truckloads at local hospitals, and within 48 hours, 8,000 people had died and about 200,000 people were injured in the largest TIC disaster to date.<sup>19</sup>

Today's MMO should recognize that the greatest chemical threat has shifted from structured military offensive capabilities to accidental or intentional release of TICs, such as in the Bhopal disaster.<sup>2,20</sup> Chlorine and phosgene, two of the first chemical weapons used on the battlefield, are commonly used industrial chemicals today. Hundreds of TICs are used in industrial sites, publicly stored, and transported. To the military, lung-damaging TICs released on the battlefield as an aerosol, vapor, or gas are primarily an inhalational threat. When dispersed, they are usually heavier than air and hang close to the ground. TICs that commonly pose a military threat include: phosgene (CG), chlorine (Cl), oxides of nitrogen (NOx), hexachloroethane (HC) smoke, ammonia, and perfluoroisobutylene (PFIB).<sup>20</sup>

The military protective mask and filter will protect against some TICs, but not all. Specific filters or self-contained breathing apparatuses are mandated for certain TICs, such as ammonia. In addition, the protective mask is not effective in environments where TICs displace oxygen, creating a low oxygen environment.<sup>14</sup>

The severity of a TIC exposure is based on multiple factors, including the substance involved and its concentration, the duration of exposure, whether the

TABLE 35-2

#### EFFECTS OF EXPOSURE TO NERVE AGENT VAPOR

Exposure Level	Effects*
Small (local effects)	Miosis, rhinorrhea, slight bronchoconstriction, secretions (slight dyspnea)
Moderate (local effects)	Miosis, rhinorrhea, slight bronchoconstriction, secretions (moderate to marked dyspnea)
Large	Miosis, rhinorrhea, slight bronchoconstriction, secretions (moderate to marked dyspnea), loss of consciousness, convulsions (seizures), generalized fasciculations, flaccid paralysis, apnea, micturition/defecation possible with seizures

\*Onset of effects occurs within seconds to several minutes after exposure.

exposure occurred within a confined space, whether there was loss of consciousness, and whether underlying lung disease is present. Some TICs act preferentially on the central airway compartment (upper airway), some act preferentially on the peripheral airway compartment (lower airway), and some act on both compartments (Figure 35-1). In large doses, TICs affect both central and peripheral airway compartments.

The clinical effects from centrally acting agents such as ammonia are immediate and include irritated upper airways manifested by nasopharynx, oropharynx, and larynx inflammation, resulting in sinus pain, painful swallowing, hoarseness, sensation of choking, stridor, and laryngospasm.<sup>21</sup> The onset of the clinical effects of peripherally acting agents such as phosgene is delayed, usually for hours. Toxicity may include irritation to the lower airways manifested by coughing and shortness of breath, followed by the development of pulmonary edema with production of clear foamy sputum.<sup>21</sup> A shortened latency period portends a more severe exposure and worse prognosis.

Medical management includes terminating exposure, which may include decontamination of any liquid on skin and removal of clothing to prevent further exposure from trapped vapors. There are no commonly available laboratory tests for the specific identification of lung-damaging agents.<sup>21</sup> Rest after exposure is critical. Physical activity in a symptomatic patient may precipitate acute clinical

deterioration.<sup>20</sup> Treatment is supportive; supplemental oxygen is indicated along with bronchodilators for bronchospasm.

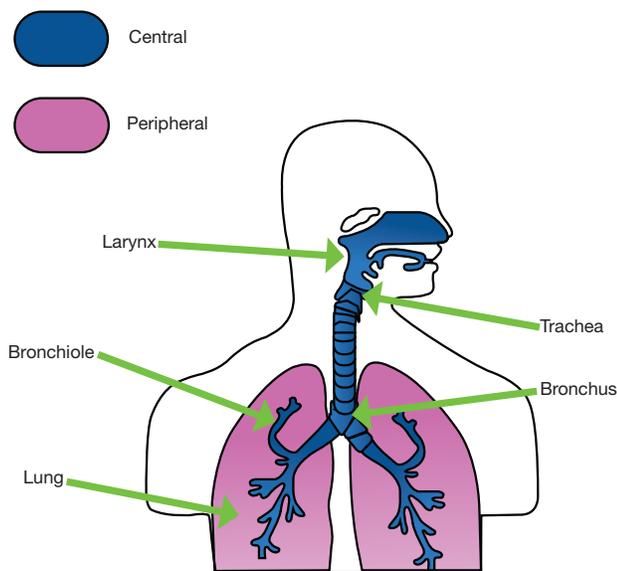
These patients can dramatically deteriorate after an initial latency period. Symptomatic patients require a period of observation with particular attention to airway management and treatment of pulmonary edema. Patients with hoarseness, stridor, upper-airway burns, or altered mental status may require endotracheal intubation. Patients with known exposure will require a period of observation of anywhere from 12 to 48 hours, depending on their presenting symptoms. Patients who remain asymptomatic 8 hours after exposure are unlikely to develop acute lung injury.<sup>21</sup> Patients presenting with shortness of breath can only be returned to duty at 48 hours, if physical exam and objective data are normal.<sup>21</sup>

### Cyanide

There is no military use for cyanide.<sup>22</sup> The primary threat from cyanide for the MMO is its use as a toxic vapor deployed in an enclosed space. Forms of cyanide, such as hydrogen cyanide (AC) and cyanogen chloride (CK), are rapidly acting and highly lethal inhalational agents in high concentration. Cyanides are ubiquitous substances with widespread industrial use. Standard military field detection equipment can detect cyanide, and the chemical protective mask is fully protective against cyanide vapor.<sup>14</sup>

The most important route of cyanide exposure is via inhalation, after which it will be readily absorbed and rapidly distributed throughout the body. Cyanide interferes with oxygen transport and cellular respiration, thereby causing tissue hypoxia, anaerobic metabolism, and severe metabolic acidosis.

Cyanide should be suspected when a laboratory or industrial worker, or a group of individuals, suddenly collapse. The organs most susceptible to cyanide are the central nervous system and the heart. The MMO will find few and nonspecific physical findings, such as anxiety, agitation, vertigo, and feelings of weakness, followed by sudden loss of consciousness, convulsions, and apnea.<sup>23</sup> Classically described findings are severe respiratory distress in an acyanotic individual with “cherry-red” skin.<sup>22</sup> The hallmarks of severe cyanide toxicity are persistent hypotension and acidemia (lactic acidosis) despite adequate arterial oxygenation. Confirmatory lab tests for cyanide are not rapidly available, and while they exist, the turnaround time for test results is generally not rapid enough to support diagnostic use.<sup>22</sup> An MMO can expect to see anion gap metabolic acidosis from severe lactic acidosis in significant cyanide poisoning.<sup>23</sup>



**Figure 35-1.** Airway compartments: central and peripheral. Graphic courtesy of: US Army Medical Research Institute of Chemical Defense.

Dermal decontamination is unnecessary in vapor exposures. Treatment begins with administering 100% oxygen and general supportive care. Severely symptomatic patients should be considered for specific antidotal therapy, either in a two-step process involving infusions of sodium nitrite and sodium thiosulfate, or with a single infusion of hydroxocobalamin (vitamin B12a), if available, to chelate cyanide.<sup>22</sup> While hyperbaric oxygen may be beneficial, it is not readily available, particularly in a mass exposure setting. For the MMO in the deployed setting, most inhalational exposure casualties who survive long enough to reach medical care will need little treatment.

### Incapacitating Agents

Incapacitating agents cause impairments that are temporary and nonlethal. There are two known chemicals of concern: BZ, a synthetic glycolate anticholinergic compound aerosolized as a solid particle, and Agent 15, a compound speculated to be identical or similar to BZ.<sup>24</sup> These agents act as competitive inhibitors of acetylcholine with resulting effects that are generally the opposite of nerve agent poisoning. The United States has developed and stockpiled BZ, and it is reported that Iraq has stockpiled large amounts of Agent 15.<sup>25</sup>

BZ is dispersed as an odorless, non-irritating aerosolized solid.<sup>25</sup> It is primarily a respiratory threat, but it is also a risk via ingestion or absorption through the skin.<sup>24</sup> The characteristic of BZ that makes it incapacitating rather than toxic is its high safety ratio.<sup>24</sup> The high-efficiency particulate air (HEPA) filter of the chemical protective mask prevents exposure to BZ.<sup>14</sup> There is no current detection capability fielded.<sup>24</sup>

BZ intoxication causes classic anticholinergic symptoms that can be divided into peripheral effects, such as mydriasis, blurred vision, dry mouth, and dry skin, and central nervous system effects, such as altered level of consciousness, delusions, hallucinations, slurred speech, disorientation in time and place, and behavioral lability (from quietness to restlessness to combativeness).<sup>25</sup> BZ also produces shared illusions and hallucinations in groups.<sup>24</sup> The onset of symptoms depends on the dose and route of exposure. Symptoms may last 3 to 4 days.<sup>24</sup>

Medical management should focus on decontamination of skin and clothing, confiscation of weapons or similar items from the patient to prevent injuries from erratic behavior, and observation. The MMO should prioritize physical restraint, managing heat stress, control of symptoms with benzodiazepines, and the proper use of physostigmine antidotal therapy.<sup>24</sup> Early return to duty is not realistic for the majority of affected

patients due to the usual time course of intoxication, which could last several days.

### Riot-Control Agents

Riot-control agents are the chemical agents an MMO is most likely to encounter. Also called lacrimators or tear gas, riot-control agents produce temporary discomfort and eye closure, which renders individuals unable to fight.<sup>26</sup> Current military use includes law enforcement for riot control and gas chamber training exercises to evaluate proper use of the protective mask. The primary riot-control agents used in the United States are CN (mace), CS (tear gas), and OC (pepper spray). These agents are crystallized solids dispersed as fine particles via spray, grenade, or foam.<sup>27</sup>

The mechanism of toxicity of riot-control agents is not well characterized, and the main effects consist of temporary pain and burning of exposed mucous membranes and skin. The eye is the organ most sensitive to these agents.<sup>27</sup> Conjunctival burning leads to tearing and blepharospasm producing temporary blindness. Inhalation in the airways causes burning, sneezing, and coughing. The MMO might anticipate more serious pulmonary reactions in individuals with chronic pulmonary diseases.

Usually decontamination will not be needed if exposure was outdoors; however, the skin can be decontaminated with soap and water, and eyes should be decontaminated by flushing with copious amounts of water.<sup>26</sup> Medical providers do not require protection once an exposed patient has been decontaminated. Effects of exposure are usually self-limited and require no specific therapy but can be lethal under high concentration in a confined space. Also, because the effects are self-limiting, most individuals should be able to return to duty.<sup>26</sup>

### Overview of Decontamination

Decontamination, the removal of hazardous chemical, biological, or radiological agents from a person or object, is a critical nonmedical task that is personnel, time, and equipment intensive. Performance while wearing protective equipment is degraded.<sup>28</sup> For suspected contaminated patients, decontamination should occur as quickly as possible after exposure. The goals are to immediately remove the agents from those exposed by non-toxic means, and to maintain an uncontaminated military medical treatment facility (MTF). Decontamination is not critical for people exposed only to vapor,<sup>29</sup> but for patients exposed to liquids, aerosols, or

dry solids, thorough decontamination is required, especially when patients will enter a medical facility where staff are not in protective clothing. Three methods of skin decontamination are preferred by the US military:

1. **RSDL** is a packaged sponge containing liquid potassium solution that deactivates mustard (HD) and nerve agent. It may be used only on intact skin, not on wounds or eyes (only water, normal saline, or eye solutions are recommended for decontaminating the eyes). RSDL is carried by military members for immediate field self-decontamination, but its use does not eliminate the need for thorough decontamination later.<sup>29</sup>
2. **Soap and water** in copious amounts is effective for washing away most agents. It does not destroy biological agents or neutralize radioactive particles. The predominant effects are physical removal and dilution of agents.<sup>29</sup>
3. **Hypochlorite solution, 0.5%** (nine parts water to one part normal 5% bleach), can be wiped on the skin and rinsed with fresh water. The solution will cause a slow chemical decontamination reaction.<sup>29</sup>

The decontamination process requires controlled removal of the personal protective equipment (PPE) and skin decontamination before treatment in the MTF. Contaminated bandages are removed and wounds are flushed with sterile water. Bandages are replaced if bleeding recurs. Splints are thoroughly rinsed with 0.5% hypochlorite solution.<sup>29</sup> Wounds contaminated with vesicants or nerve agents may present a hazard to providers.<sup>29</sup> The risk from off-gassing from a contaminated wound is not significant, and removal of the foreign material effectively eliminates the hazard, so a

chemical protective mask is not required for surgical personnel.<sup>29</sup> Patients are certified clean from chemical agents after decontamination using M8 paper, the Joint Chemical Agent Detector (JCAD), or the Improved Chemical Agent Monitor (ICAM).<sup>29</sup>

### Patient Decontamination Site

Ideally, decontamination of casualties should be done in the field before evacuation to a medical facility (unfortunately, most victims bypass prehospital care and arrive unannounced at the closest MTF). Decontaminated casualties arriving from a contaminated environment must enter an MTF through a patient decontamination site (PDS).<sup>30</sup> This ensures MTF patients and staff will not become cross-contaminated by arriving contaminated casualties. The principal components of the PDS include:

- an entry control point,
- a triage area,
- an emergency medical treatment (EMT) area,
- a decontamination area, and
- a “hot line” separating the contaminated from clean areas.<sup>30,31</sup>

Medical personnel should be available to perform triage and emergency care in the contaminated “warm” zone before casualties are decontaminated. Casualties needing emergency care are sent to the warm side EMT. Because patient decontamination involves heavy work that can cause overheating, the decontamination team should be supplemented with nonmedical personnel. A safety officer must be appointed to observe PDS workers and manage work/rest cycles. Medical facilities must consider environmental variables such as wind direction and water run-off when establishing a decontamination site.<sup>30,31</sup>

## BIOLOGICAL WARFARE AGENTS

In late March 1979, at a Soviet army biological research facility on the outskirts of Sverdlovsk, USSR, in the foothills of the Ural Mountains, a technician removed a clogged filter in the anthrax drying plant, briefly allowing spores to escape. Approximately 1 g of a powerful weaponized strain, anthrax 836, was released into the cold night air. In a few days all the night shift workers in a plant across the street, in the direct path of the wind, had fallen ill, and within a week almost all were dead. Over the next 6 weeks at least 66 persons died from inhalational anthrax, and farm animals died up to 50 km within a narrow

zone downwind from the factory.<sup>32</sup> The outbreak, a “biological Chernobyl,” demonstrated the power of anthrax as a biological weapon and clearly showed that the USSR was producing offensive biological weapons, in violation of the 1972 Biological Weapons Convention.<sup>33</sup>

Prior to 1969, the United States had an active biological warfare program that included research, development, and stockpiling of offensive biological weapons. Under President Nixon, the United States unilaterally renounced the development and production of biological weapons. From that time forward, US efforts

in biological warfare have been restricted to research and development of vaccines, drugs, and diagnostics as defensive measures against biological weapons.<sup>34</sup> While the United States offensive biological warfare program included open-air testing using simulants thought to be nonpathogenic, the US military has never used biological weapons.<sup>34,35</sup> In contrast to the United States, the USSR (and Russia) had a massive offensive biological weapons program until 1992, and Iraq maintained some offensive biological weapons capacity until 2003.<sup>33,34,36</sup>

There have been two large-scale bioterrorist attacks in the United States: the 1984 Rajneeshee salmonella attack, which resulted in 751 cases of infection, and the 2001 anthrax mailings, which resulted in 22 cases of infection, 5 deaths, and approximately 10,000 suspected exposures to patients who were offered postexposure prophylaxis.<sup>37,38</sup> Published reports suggest that the threat of biological terrorism continues to increase, and the use of biological weapons in both large- and small-scale attacks against US military and civilians continues to be actively explored by nations and terrorist groups.<sup>34,39</sup> In 2001 a team of virologists in Germany and France constructed an Ebola virus from three strands of complimentary DNA using reverse genetics, with technology described by the National Scientific Advisory Board for Biosecurity as “readily accessible, straightforward, and a fundamental tool used in current biological research.”<sup>40,41</sup> However, MMOs should understand that while many biological agents can cause illness in humans, few are capable of affecting public health and medical infrastructures on a large scale, like anthrax and Ebola.

The Centers for Disease Control and Prevention (CDC) has been designated the lead agency for overall national public health planning and response to biological terrorism. It has prioritized high-risk biological agents based on their overall threat to civilians (Table 35-3).<sup>42</sup> This chapter focuses on Category A agents and their relevance to the MMO. MMOs must maintain a high index of suspicion and be prepared to evaluate both symptomatic patients and asymptomatic “suspected exposed” military and civilian patients referred from syndromic surveillance systems.

## Bacterial Agents

### *Anthrax*

Inhalational anthrax in the United States under normal circumstances is so unusual that a single case should prompt an investigation for bioterrorism. Naturally occurring anthrax is primarily a disease of

herbivores. The causative agent of anthrax is a gram-positive sporulating rod, *Bacillus anthracis*, and spores are the usual infective form.<sup>43</sup>

In New York City on September 29, 2001, a 7-month-old infant was noted to have a painless red papule with swelling on his upper arm. During the next 24 hours his arm became increasingly edematous, the papule evolved into a painless macule, and a slight serous drainage began. His pediatrician began antibiotics for presumed cellulitis, but the infant soon required admission for increased swelling and difficulty tolerating oral medication. By hospital day 2 the arm showed massive non-pitting edema with a dark red macule 3 cm in diameter. The working diagnosis was “spider-bite.” The infant continued to deteriorate. On hospital day 13 he was diagnosed with cutaneous anthrax by skin biopsy and blood testing for *B anthracis*. Eventually the infant made a full recovery on appropriate antibiotics. It was later determined that the day before his symptoms began, the infant had spent an hour in his mother’s office at a national news organization, where anthrax spores were subsequently found.<sup>44</sup>

Cutaneous anthrax had never before been diagnosed in an infant in New York. The first case of inhalational anthrax associated with the anthrax mailings was not recognized until October 4. Earlier diagnosis of cutaneous anthrax in this case would have alerted the medical community to the impending danger and prevented further delay in diagnosis of other symptomatic patients.

Anthrax presents as three distinct clinical diseases in humans determined by the route of entry of the spores: inhalational, cutaneous, and gastrointestinal (GI). The most severe of these is inhalational anthrax, which presents as a nonspecific febrile illness after a 1- to 6-day incubation period.<sup>43</sup> The inhalational anthrax syndrome may include nausea, vomiting, nonproductive cough, fever, malaise, headache, and chest discomfort.<sup>45,46</sup> Physical findings are nonspecific early in the course of disease. Evidence of mediastinal widening (hemorrhagic mediastinitis) or pleural effusions may be seen on chest x-ray or computed tomography (CT) scan.<sup>47</sup> Prominent hilar adenopathy is characteristic.<sup>43</sup> The patient will progress to respiratory distress, septic shock, and death unless provided aggressive intensive care.<sup>43</sup> Due to the fulminant course of inhalational anthrax, prompt antibiotics are essential for survival, and monotherapy is not acceptable.<sup>48</sup> More advanced therapies are available under Investigational New Drug (IND) authorization subject to Food and Drug Administration (FDA) regulations.<sup>48</sup>

Direct person-to-person spread does not occur, and standard universal patient precautions are recom-

TABLE 35-3

## CRITICAL BIOLOGICAL AGENT CATEGORIES FOR PUBLIC HEALTH PREPAREDNESS

Biological Agents*	Disease
<b>Category A:</b> moderate to high potential for large-scale dissemination; greatest potential for production of mass casualties and major impact on public health	
<i>Variola major</i>	Smallpox
<i>Bacillus anthracis</i>	Anthrax
<i>Yersinia pestis</i>	Plague
<i>Clostridium botulinum</i> (botulinum toxins)	Botulism
<i>Francisella tularensis</i>	Tularemia
Filoviruses and arenaviruses (eg, Ebola virus, Lassa virus)	Viral hemorrhagic fevers
<b>Category B:</b> some potential for large-scale dissemination; cause less illness and death and expected to have lower public health impact	
<i>Coxiella burnetii</i>	Q fever
<i>Brucella</i> species	Brucellosis
<i>Burkholderia mallei</i>	Glanders
<i>Burkholderia pseudomallei</i>	Melioidosis
Alphaviruses (VEE, EEE, WEE)	Encephalitis
<i>Rickettsia prowazekii</i>	Typhus fever
Toxins (eg, ricin, staphylococcal enterotoxin B)	Toxic syndromes
<i>Chlamydia psittaci</i>	Psittacosis
Food safety threats (eg, <i>Salmonella</i> species, <i>Escherichia coli</i> O157:H7)	
Water safety threats (eg, <i>Vibrio cholerae</i> , <i>Cryptosporidium parvum</i> )	
<b>Category C:</b> could emerge as a future threat; not believed to be a significant public health threat at present	
Emerging threat agents (eg, Nipah virus, Hantavirus, multidrug-resistant tuberculosis, SARS, MERS)	

\*The categories of agents should not be considered definitive and may change as new information is obtained.

EEE: Eastern equine encephalomyelitis; MERS: Middle East respiratory syndrome; SARS: severe acute respiratory syndrome; VEE: Venezuelan equine encephalomyelitis; WEE: Western equine encephalomyelitis

Reproduced with permission from: Rotz LD, Khan AS, Lillibridge SR, et al. Public health assessment of potential biological terrorism agents. *Emerg Infect Dis.* 2002;8(2):225-226.

mended. Anthrax is detectable in early stages via blood culture or polymerase chain reaction (PCR) and later stages via Gram stain of blood, cerebral spinal fluid (CSF), or pleural fluid.<sup>43</sup> *B anthracis* culture requires biosafety level (BSL) 2 lab precautions.

Biothrax (Anthrax Vaccine Adsorbed [AVA]; Emergent BioSolutions, Gaithersburg, MD) is a safe vaccine licensed for the prevention of anthrax.<sup>43</sup> It is included in the Strategic National Stockpile and indicated for postexposure prophylaxis (PEP).<sup>48</sup> Antibiotics and AVA are indicated for PEP; all patients exposed to anthrax should receive prophylactic antibiotic treatment for 60 days.<sup>48</sup> Anthrax is thought to be the most likely biological agent to be used in future bioterror-

ism attacks.<sup>45</sup> Anthrax spores were weaponized by the United States, the USSR, and Iraq, among other countries.<sup>49,50</sup> During the Persian Gulf War, US military members carried ciprofloxacin to be used prophylactically in the event of an anthrax attack on US forces.<sup>43</sup>

### Plague

*Yersinia pestis* is a gram-negative bacterium that causes plague, a naturally occurring disease spread from rodents through direct contact or contact with infected fleas. Plague is endemic to the US southwest, but naturally occurring pneumonic plague is rare. Three pandemics of plague occurred in the 6th, 14th,

and 19th centuries, killing millions of people.<sup>51</sup> The highly contagious nature of plague via person-to-person transmission makes it an attractive high-threat biological terrorist weapon, and it was weaponized by the United States and USSR.<sup>52</sup>

Plague appears in three forms in humans: pneumonic, septicemic, and bubonic. Pneumonic plague would be the disease form expected after aerosol dissemination and presents as a severe respiratory illness of sudden onset 1 to 6 days after exposure.<sup>52</sup> Classic symptoms include high fever, headache, and cough with hemoptysis.<sup>52</sup> Death results from respiratory failure, circulatory collapse, and bleeding diathesis.<sup>51</sup> Plague should be suspected by the MMO if a large number of previously healthy individuals present with severe pneumonia with hemoptysis. The MMO can establish a presumptive diagnosis by identifying gram-negative coccobacilli in sputum. A definitive diagnosis requires culturing the organism, which usually takes 48 to 72 hours. PCR and direct fluorescent antibody tests may be available in certain reference labs.<sup>53</sup>

Early treatment with antibiotics is required for survival, ideally within 1 day of symptoms, although naturally occurring antibiotic-resistant strains exist.<sup>53</sup> Patient management requires respiratory droplet precautions because pneumonic plague is easily spread person-to-person via aerosol, yet this has not occurred in the United States since 1925.<sup>51</sup> All individuals who come within 2 m of a patient with pneumonic plague should receive PEP with antibiotics.<sup>53</sup> No vaccine has been available since 1998, and the previously available vaccine was not effective against pneumonic plague.<sup>51,53</sup>

### **Tularemia**

*Francisella tularensis*, the causative agent of tularemia, is a small, naturally occurring, hardy, and extremely virulent gram-negative coccobacillus. *F. tularensis* can be stabilized and aerosolized to make an effective offensive weapon, and it has been associated with multiple environmental biosurveillance alerts in the United States since 2001.<sup>54</sup> As a result, the MMO could see “suspected exposed” patients referred via bioterrorism aerosol surveillance programs.<sup>54</sup>

Tularemia is acquired primarily through contact with rabbits, ticks, or fleabites. It was weaponized by the United States and the USSR and has a very low infectious dose; exposure to approximately 10 organisms will cause disease.<sup>55</sup> A high index of suspicion is needed to make an early diagnosis of tularemia. After aerosol inhalation and an incubation period of 3 to 6 days, the disease manifests as abrupt onset of

fever, headache, malaise, myalgia, and prostration, followed by pleura-pneumonia.<sup>56</sup> *F. tularensis* is difficult to culture with standard lab media, and isolation of the organism requires a BSL-3 level containment lab.<sup>57</sup>

The initial treatment is with intravenous antibiotics. There has been no known human-to-human transmission of tularemia, so only standard precautions are required.<sup>55</sup> Since there is no licensed vaccine available, PEP is managed with antibiotics and should be continued for 14 days.<sup>57</sup>

### **Viral Agents**

Viruses, as intracellular parasites requiring host cells for replication, cannot be cultivated in synthetic nutrient materials. The MMO should recognize that some viruses are well suited as bioweapons.

#### ***Smallpox (Variola)***

Smallpox, caused by the variola virus, was declared eradicated by the World Health Organization in 1980. The United States ended routine civilian vaccination in 1972 and routine smallpox military vaccination in 1989.<sup>58</sup> Two repositories for the smallpox virus exist in the United States and Russia; however, the extent of clandestine stockpiles as a biological weapon is unknown, and the possibility of its reemergence exists. Smallpox was easily cultured, very stable, and successfully weaponized.<sup>59</sup> Large stockpiles of this agent existed in the USSR, where it was viewed as a strategic weapon of opportunity. Since routine civilian immunization ended, there is now a large immunologically naïve population.<sup>33,58</sup>

The initial diagnosis of smallpox is clinical. The MMO must differentiate smallpox from other papulovesicular lesion-producing diseases. The clinical manifestations of smallpox appear in a series of distinct phases that are uniquely characteristic, and its rash may be confused with chickenpox. Lesions appear first on the face and hands, then spread to the extremities, and finally the trunk. Classically, lesions remain synchronous in their stage of development throughout the body during each clinical phase. Microscopy cannot distinguish between the orthopox viruses, but PCR may distinguish variola.<sup>58</sup> The MMO may fail to recognize patients with immunocompromise who develop different, non-classic forms of disease, and human monkeypox may look indistinguishable from smallpox.<sup>58</sup>

To the MMO, any case of smallpox should be considered a public health emergency. There is no FDA-approved chemotherapy, but antiviral drugs for use against smallpox are under investigation.<sup>60</sup> Individuals

with successful smallpox vaccination within 3 years that resulted in a confirmed clinical take (progression from papule to vesicle to pustule to scab at the inoculation site) are considered immune to smallpox; however, routine revaccination of all potentially exposed individuals would be prudent in the face of significant exposure risk.<sup>60</sup>

Immediate vaccination or revaccination with smallpox (live vaccinia virus) vaccine (ACAM 2000), ideally within 4 days for all exposed personnel, will likely ameliorate or prevent disease.<sup>60</sup> There are no absolute contraindications to postexposure vaccination for high-risk exposures, and vaccinia immune globulin (VIG) is indicated for rare life-threatening complications from vaccinia vaccine, such as eczema vaccinatum and postvaccinial encephalitis.<sup>58,59</sup>

The MMO must recognize that smallpox is highly infectious; transmission occurs person-to-person by respiratory droplets and is enhanced by coughing.<sup>58-61</sup> Infection can also occur from contact with infected clothing or bedding. Patients are infectious from onset of rash until all scabs separate. Infectious patients require isolation with contact, airborne, and droplet precautions.<sup>60</sup> All asymptomatic contacts must be quarantined for 17 days.<sup>60</sup>

PCR testing for smallpox is available under BSL-4 conditions at national laboratories (US Army Medical Research Institute for Infectious Diseases and the CDC) via the Laboratory Response Network. A PCR test that detects all orthopoxviruses may be available via the military area medical laboratory.<sup>60</sup>

### *Viral Hemorrhagic Fever*

On September 25, 2014, a 45-year-old man from Liberia, who had arrived in the US 5 days earlier, went to a Dallas, Texas, emergency department with fever (100.1° F), abdominal pain, and headache. He was treated for possible sinusitis and discharged. He returned to the same emergency department via ambulance on September 28 with fever (101.4° F), abdominal pain, and severe diarrhea. He tested positive for Ebola virus on September 30, the first imported Ebola virus infection diagnosed in the United States. Despite intensive care, the patient died 8 days later. Although PPE and appropriate precautions were used, two nurses caring for the patient subsequently contracted Ebola virus disease (EVD) and required prolonged intensive care; both survived. Multiple community contacts of all patients were either voluntarily quarantined or actively monitored for 21 days, and 12 persons in this group developed fever or other symptoms compatible with EVD, but no other person contracted EVD.<sup>62</sup>

Viral hemorrhagic fever (VHF) is an acute febrile syndrome from a diverse group of tick-, rodent-, and mosquito-borne viral illnesses naturally occurring in specific geographic locations. These diseases are unified by their potential to present as a severe febrile illness with a bleeding diathesis and high mortality rate. The MMO should recognize two VHF viruses, yellow fever and dengue, that have great significance in the history of military medicine.<sup>63</sup> While the VHFs have not been weaponized, they are recognized as having significant potential for aerosol dissemination and weaponization, and the Aum Shinrikyo group attempted to obtain Ebola virus samples from West Africa for development in their bioterrorism program.<sup>33,63-65</sup> Aerosol dissemination does not occur naturally.<sup>63,64</sup>

The clinical presentation of VHF includes various combinations of fever, malaise, myalgia, headache, vomiting, and diarrhea. The initial constellation of symptoms makes VHF difficult to distinguish from other acute febrile illnesses. VHF should be considered by the MMO in any patient presenting with severe acute febrile illness and abnormal bleeding.<sup>66</sup> Differentiating the VHFs is difficult, and making a definitive diagnosis of VHF requires a reference laboratory with BSL-4 advanced bio-containment capability. Rapid enzyme immunoassays and PCR testing exist but may not be readily available for specific VHFs. Lab specimens must be appropriately collected, handled, double-bagged, decontaminated, and shipped to the BSL-4 lab.<sup>66</sup>

Treatment includes intensive supportive care with vigorous fluid resuscitation under strict contact precautions and negative-pressure isolation. Management of the hemorrhagic component mirrors other patient coagulopathies. Intramuscular injections and aspirin and other anticoagulants should be avoided. Airborne precautions must be instituted for procedures that create aerosols. Antiviral therapy may be available on an investigational new drug basis.<sup>64</sup> VHF patients harbor extensive infectious viral load in blood, body fluids, and body secretions,<sup>63,64,66</sup> and MMOs must be aware that caring for these patients has proven to be highly risky and labor and staff intensive. Staff treating VHF patients should wear double gloves, impermeable gowns with leg and shoe coverings, eye protection and HEPA (N95) masks or positive pressure air-purifying respirators.<sup>66</sup> Medical staff will experience significant risk from contaminated PPE, in particular during the doffing process, and all waste should be carefully handled and incinerated or autoclaved.

After a presumed bio-warfare attack with unknown VHF agent, the MMO should consider intravenous antiviral drugs for any exposed individual with fever

higher than 101° F, until the agent is identified.<sup>66</sup> Yellow fever is the only VHF for which a licensed vaccine is available. Experimental vaccines exist for other VHFs, but are not readily available.<sup>66</sup> Close personal contacts of VHF patients, including medical personnel, should be closely monitored for fever and other symptoms during the established incubation period.

### Biological Toxins

Toxins are harmful substances produced by living organisms. By nature they lack volatility (there is no vapor hazard), do not persist in the environment, are not dermally active, and pose no risk for person-to-person spread.<sup>67</sup> Biological toxins have military utility as aerosolized weapons based on the magnitude of their toxicity.<sup>67</sup>

#### *Botulinum*

By weight, botulinum toxins are the most toxic substance known. It has been estimated that 1 g of aerosolized botulinum toxin could kill more than a million people.<sup>68</sup> Botulinum toxins are a group of seven related neurotoxins produced by the spore-forming bacillus *Clostridium botulinum*, which is present in the soil.<sup>67</sup> Botulinum toxin inhibits neurotransmission by preventing acetylcholine release at the nerve terminal.<sup>67</sup> Neurotoxins produced by *C botulinum* are readily denatured in the environment.<sup>67</sup> There are three forms of naturally occurring botulism: foodborne botulism, wound botulism, and intestinal botulism (infant and adult).

The intentional use of botulinum toxin can be either an inhalational or foodborne threat, and industrial-scale fermentation could produce large amounts of toxin.<sup>67</sup> A large aerosol release would easily overwhelm healthcare capabilities. Botulinum toxin has been weaponized by the United States, USSR, Iraq, and terrorist organizations.<sup>67-70</sup> Aum Shinrikyo attempted to dispense botulinum toxin in Tokyo in the mid-1990s.<sup>65</sup> In an outbreak related to an intentional aerosolized release, the MMO should expect patients presenting as afebrile, alert, and oriented, with descending paralysis manifested by cranial nerve palsies, including ptosis, diplopia, blurred vision, dysphagia, and dysphonia, followed by symmetrical descending

flaccid paralysis.<sup>67,68</sup> Respiratory failure, which may occur abruptly, is the most common cause of death. Symptoms may progress over hours or days depending on the exposure dose. Sensory symptoms do not occur and botulinum toxin does not cross the blood-brain barrier, so altered sensorium should not occur.<sup>71</sup>

Botulism is a clinical diagnosis because laboratory testing can be inconclusive. Mouse neutralization (bio-assay) is the most sensitive test and can take up to 4 days; an enzyme-linked immunosorbent assay (ELISA) test also exists.<sup>71</sup> Early administration of antitoxin is critical; antitoxin must never be withheld from the patient, even if treatment is delayed.<sup>71</sup> Postexposure prophylaxis with antitoxin administration, while not recommended, should be considered under extraordinary circumstances after a high-risk exposure.<sup>67,71</sup>

#### *Ricin*

Ricin is a potent cytotoxin derived from the mash of the castor bean. Its mechanism of toxicity is via inhibition of protein synthesis.<sup>72</sup> Ricin has military significance because of the ease with which it can be extracted from the castor bean. It is ideal for small-scale bioterrorism attacks and has been successfully used in several notorious political assassinations.<sup>72,73</sup>

Ricin's clinical presentation depends on the dose and route of exposure. It is primarily a threat via aerosol inhalation and ingestion.<sup>72</sup> The MMO should suspect ricin in a large number of geographically clustered cases of acute lung injury, because inhalation causes severe, progressive lung inflammation leading to respiratory failure over days.<sup>74</sup> Ingestion will cause severe GI inflammation and multiorgan failure.<sup>74</sup> The diagnosis of ricin poisoning will be challenging for the MMO because multiple pulmonary pathogens could present similarly to aerosolized ricin. Specific tests exist but are not readily available.<sup>73,74</sup>

There is no antitoxin to ricin. Treatment for ricin poisoning is supportive, regardless of the route of exposure. Patients should be thoroughly decontaminated with soap and water.<sup>72-74</sup> Ricin-induced lung injury will not respond to antibiotics, and ricin ingestion is managed by lavage and cathartics.<sup>73,74</sup> Ricin toxicity is not contagious, and protective masks are effective. While vaccines are under investigation, none currently exist.<sup>74</sup>

## RADIOLOGICAL AND NUCLEAR EXPOSURES

In 2011, an earthquake with a subsequent tsunami struck Japan, resulting in flooding of the nuclear reactor plant in Fukushima. The subsequent loss of power caused the reactor to overheat, followed by meltdowns

and evacuations from the surrounding area. The event was categorized as level 7 on the International Nuclear and Radiologic Event Scale, and is estimated to involve 10% of the exposure that occurred at

Chernobyl, Russia, in 1986.<sup>75</sup> The Chernobyl accident is the largest nuclear disaster in history, causing 30 immediate deaths and the evacuation of over 300,000 people. Reports of health issues related to radiation exposure continue.<sup>76</sup>

Three types of devices pose a risk of radiation exposure to military personnel: (1) a radiation exposure device (RED); (2) a radiological dispersion device (RDD); and (3) an improvised nuclear device (IND). An RED has a radioactive source within a container or sealed source for the purpose of exposing those nearby to high doses of radiation. Various military and civilian/industrial supplies and equipment contain radioactive material that could be used to create an RED or RDD to employ as a weapon or cause exposure due to improper storage or handling. RDDs are intentionally engineered to disperse radiation but without a nuclear blast. Dispersal may be through a plume or contamination of the food and water chain.

INDs, designed to deliver a nuclear detonation at either full or partial yield, are the most catastrophic of these devices. INDs expose individuals to a high level of external radiation, blast and thermal injury, and subsequent radiation exposure through inhalation of particulate matter and ingestion of contaminated materials. The primary effect of an IND is the blast effect. The medical management of blast injury from both nuclear and non-nuclear explosive devices is discussed in detail later in this chapter. Unique to INDs is an intense thermal wave of energy known as the nuclear flash. Individuals in the immediate vicinity will be incinerated. Surviving individuals will suffer burns on the side exposed to the blast or from secondary fires ignited by the thermal wave. The other principal output from a nuclear blast is radiation, in both primary and secondary exposures.

## Radiation Effects

Radiation effects can be divided into two categories, acute external exposure and internal contamination. Both an RDD and an IND can cause an immediate release of radiological material leading to acute radiation syndrome (ARS). Acute external exposure usually involves beta and gamma particles. Internal contamination can occur via inhalation, ingestion, or absorption from a contaminated wound. Internal contamination can be due to any isotopes, of which there are over 8,000. Radioactive decay from isotopes creates ionizing radiation whose properties can vary (Table 35-4). Internal contamination is unique from external exposure and ARS because isotope identification is crucial in medical management.

## External Exposure

ARS is the result of high-level (> 0.7 Gy) exposure to ionizing radiation. Exhibit 35-1 lists conditions that can result in ARS. A characteristic constellation of clinical events results from radiation damage to cells that occurs within seconds of exposure. The organ systems and cell lines with the highest turnover are the most sensitive to radiation exposure. ARS follows a predictable course through four phases: prodromal, latent, well-defined illness, and finally recovery or death. The transition time between phases depends on the dose of radiation received. The prodromal phase, which can last minutes to days, is characterized by nausea, vomiting, diarrhea, mild fever, and transient skin erythema. The patient then may appear well for a few hours, or even a few weeks, during the latent phase, which is characterized by silent cell and tissue destruction. This destruction is later manifested clinically as one or more of the syndromes described below.

**TABLE 35-4**  
**PROPERTIES AND EFFECTS OF IONIZING RADIATION**

Type	Source	Properties	Clinical Concern
Alpha particles	Charged particles from heavy nuclei	Travel short distance, shielded by clothes/skin	Wound absorption
Beta particles	Electrons from fallout or certain isotopes	Travel short distance in tissue	Can cause radiation burns, damaging if internalized
Gamma rays	Photons from nuclear detonation, fallout, or nuclear decay	High energy and pass through matter easily	Whole body effects from both external exposure and internalization
Neutrons	Uncharged particles emitted from fission	High energy and pass through matter easily	Same effects as gamma rays with more significant damage

**EXHIBIT 35-1****CONDITIONS REQUIRED FOR ACUTE RADIATION SYNDROME**

- Dose must be large (>0.7 Gy).
- Dose must be external.
- The radiation must be penetrating (x-rays, gamma rays, neutrons).
- The entire body must be exposed.
- The dose must be delivered in a short time.

Adapted from: Centers for Disease Control and Prevention. Acute radiation syndrome: a fact sheet for physicians. <https://emergency.cdc.gov/radiation/arsphysicianfactsheet.asp>. Updated August 23, 2017. Accessed July 4, 2018.

Death can occur within days for extremely high doses but may not occur for weeks to months. Recovery can take up to 2 years.

There are three classic ARS syndromes: (1) hematopoietic, (2) GI, and (3) neurovascular. The hematopoietic syndrome, also known as the bone marrow syndrome, occurs with doses above 0.7 Gy. Hematopoietic progenitors are unable to divide, resulting in bone marrow failure and lymphopenia or pancytopenia. Destruction of cell lines leads to infection, bleeding, and poor wound healing. Survival depends on dose, concomitant injuries, and access to supportive care. The mean lethal dose required to kill 50% of humans within 60 days, LD<sub>50/60</sub> is about 3.5 to 4 Gy. Providing medical therapy including antibiotics, transfusions, and cell line stimulation can improve survival at higher exposure doses.

The GI syndrome occurs in conjunction with the hematopoietic syndrome at doses higher than 6 Gy. This level of radiation causes damage to the small intestine, targeted at intestinal crypt cells that have a high turnover rate. This syndrome has the typical flu-like prodromal phase, and diarrhea is often characteristic. The overt clinical phase involves malaise, anorexia, severe diarrhea, and fever. The diarrhea can lead to dehydration and electrolyte imbalance. Loss of GI integrity can lead to malabsorption and nutritional disorders. Bacteria can translocate across the damaged epithelial lining of the intestinal wall and lead to gram-negative sepsis. More severely affected patients can present in renal failure or cardiovascular collapse. While aggressive supportive care can extend the survival period, death usually occurs from sepsis and multiorgan failure.

The most severe and rapidly fatal of the syndromes, due to doses higher than 12 Gy, is the neurovascular

syndrome. High radiation exposure will result in an immediate burning sensation, followed by nausea and vomiting, fever, hypotension, and neurologic dysfunction such as ataxia and confusion. Symptoms are rapidly progressive and severe; death typically occurs in 24 to 48 hours. Recovery is not expected in patients with this syndrome.

Knowing that the clinical syndromes are dose dependent, markers to estimate radiation dose early in the evaluation of exposed patients can be very useful. Radiation dose can be estimated using the medical history, serial blood counts, and the time to emesis. Medical history should include the circumstances of suspected exposure, taking note of location relative to the incident, sheltering, and any other pertinent exposure details, in addition to clinical symptoms. Serial blood counts are one of the most readily available and useful methods to characterize exposure. An initial complete blood count followed by serial measurements three times a day for 2 to 3 days will facilitate determination of the slope of lymphocyte decline. A drop in lymphocyte count by more than 50% in the first 24 hours indicates a potentially lethal exposure. Time to emesis can be used in the absence of laboratory support or as an adjunct to lymphocyte count. Emesis within 1 to 2 hours of exposure carries a poor prognosis.

The chromosome-aberration cytogenetic bioassay (specifically lymphocyte dicentrics) is considered the gold standard in estimating dose. However, samples must be obtained within 24 hours of exposure, and results may not be available for 2 to 3 days, so time to emesis and lymphocyte counts remain the most useful tools in the initial assessment period. It is helpful to remember that if an individual has not vomited within 8 to 10 hours of exposure, it is unlikely he or she was exposed to a dose over 1 Gy.<sup>77,78</sup> The Armed Forces Radiobiology Research Institute Biodosimetry Assessment Tool is a software package that can help providers assess exposure and guide therapy. The tool has a complimentary package for first responders called the First Responders Radiologic Assessment Triage. These useful tools can facilitate optimization of a standardized framework for the response to nuclear or radiological catastrophe.<sup>79</sup>

### **Triage and Treatment of Radiation-Injured Patients**

Radiation-injured patients are emergently treated for life, limb, or eyesight injuries regardless of contamination. A radiological detonation produces casualties with a combination of blast injury, thermal injury, and various wounds—all requiring medical

attention. Triage of patients with combined injury should follow trauma protocols. If the only injuries are radiation injuries, then triage should consist of assessment of dose rate, prodromal symptoms, and specimen collection for biodosimetry. Contaminated patients pose little threat to healthcare personnel, and treatment of emergent conditions should not be delayed due to concerns of contamination. Decontamination is a time-consuming and resource-intensive process, so patients should be stabilized prior to decontamination. Fortunately, removing clothing, bandages, and personal effects removes 90% of contamination, so exposure for trauma management begins the decontamination process. Further decontamination involves washing the skin with soap and water (preferred over 0.5% hypochlorite solution) without irritating the skin. Standard hospital PPE (gown, cap, double gloves, and shoe covers) is adequate when decontaminating patients. If possible, irrigation effluent should be collected and disposed of deliberately.

Decontamination should be confirmed with radiation detection, indication, and computation (RADIAC) counters such as the AN/VDR-2 and the AN/PDR-77; refer to Table 35-5 for decontamination standards. To minimize local tissue injury and systemic contamination, particulate matter with alpha or beta emitters should be removed from wounds, and then the wound should be thoroughly irrigated. However, aggressive surgical debridement to eliminate particulate matter is not recommended and may cause more damage to tissue than would be posed by the radiation risk. Similarly, burns should be irrigated and cleaned while leaving blisters intact and minimizing damage to the skin. Once wounds and burns have been cleaned, they should be reexamined with a RADIAC counter.

After life-threatening injuries have been addressed and decontamination is complete, attention can be

given to treatment of ARS. Therapy is determined by signs and symptoms, and laboratory parameters help guide treatment. Antibiotic agents and possibly antifungals and antivirals can be used in neutropenic patients to prevent infection. Fluoroquinolones with streptococcal coverage are most appropriate in the radiation-poisoned patient. When the patient is not neutropenic, antimicrobial therapy should be targeted to the specific infection. Supportive care such as anti-emetics, fluid therapy, electrolyte replacement, and analgesics can provide significant relief. Vomiting is common and, as described above, can be a prognostic indicator. While prophylaxis is not indicated, anti-emetics should be given once vomiting has begun. Serotonin receptor antagonists have well-documented efficacy for nausea and vomiting in radiation-treated patients, and thus should be useful in the setting of radiation poisoning. Fluid resuscitation should address losses due to trauma, burns, and GI symptoms. Patients with early onset multiorgan failure should be managed as expectant with the goal of providing comfort care coupled with psychological support.

For patients with low to moderate exposure and manifestation of the hematopoietic syndrome, attention should be given to support of cell lines. For exposures greater than 3 Gy, hematopoietic colony stimulating factors (CSFs) are recommended. For pediatric, geriatric, or polytrauma patients, the threshold for therapy should be lower. Therapy should be started as soon as biodosimetry or clinical signs and symptoms suggest this threshold exposure level. More severe exposures, over 7 Gy, may require transfusion therapy and even stem cell transplantation in addition to prolonged therapy with CSFs. Survival from acute effects in partial body exposures over 10 Gy is possible with hematopoietic support and early use of CSFs. Adjunctive therapies become necessary as ARS develops over days to weeks.

In addition to medical therapy, it is important to recognize the psychological injuries that may occur as a result of nuclear or radiological injury. It is likely that the fear and anxiety associated with exposure outweighs the actual medical effects. Attention should be given to the immediate psychological response, combat stress effects, and long-term sequela of such a psychological stress such as posttraumatic stress disorder. A responsive, competent, compassionate, and confident medical response will do much to alleviate immediate anxiety and fear. Information flow should be accurate and timely. Anticipating the need for mental health support will help ensure resources are available to mitigate adverse psychological outcomes.<sup>77,78</sup>

**TABLE 35-5**  
**DETECTION LIMITS\*FOR DECONTAMINATION**

Type of Radiation	Limit
Alpha particles	< 1,000 disintegrations/minute
Beta particle	< 1 mR/h
Gamma rays	< 2 × local background level

\*Upper limit of radiation that must be reached to consider an individual thoroughly decontaminated. If an individual is above these levels, decontamination efforts should be continued until detectable radiation is below these limits.

## Internal Exposure

Ingestion, inhalation, or contamination of wounds with radioactive material are mechanisms of internal exposure. Isotope identification is crucial in the determination of medical management. An in-depth discussion of specific isotope management is beyond the scope of this chapter; however, some general principles apply to the care of these patients, based on reducing ongoing exposure. Available methods of reducing internal contamination include dilution, chelation, and chemically altering the isotope. Absorption in the GI tract can be reduced by lavage or cathartics; pulmonary load can be reduced by bronchoalveolar lavage; and contamination in wounds can be excised. Further treatment should be directed at decorporation of the isotope. Treatment for some of the more common isotopes is listed in Table 35-6.<sup>78</sup>

Internal radiation exposure and ARS with associated physical and psychological injuries form a complex medical picture that requires optimization of decision-making and resource management to maximize

**TABLE 35-6**

### TREATMENT OPTIONS FOR SELECTED RADIOISOTOPES

Radionuclides of:	Treatment
Plutonium 239	Zn-DTPA or Ca-DTPA
Yttrium 90	Zn-DTPA or Ca-DTPA
Uranium	Sodium bicarbonate
Cesium 137	Prussian blue
Strontium	Calcium or aluminum phosphate
Radiiododines	Potassium iodide

Zn-DTPA: zinc diethylenetriamene pentaacetate

Ca-DTPA: calcium diethylenetriamene pentaacetate

medical outcomes. Survival can be greatly affected by wise therapy and supportive care, underscoring the importance of understanding the evaluation, triage, and medical management of radiological exposure.<sup>77,78</sup>

## EXPLOSIVE (BLAST) INJURIES

Blast injury can involve a complex array of injuries with various wounding mechanisms. Care of the blast victim can be especially challenging because the provider may be faced with several life-threatening injuries that must be addressed simultaneously. The magnitude of blast effects is influenced by several factors. For example, pressure generated in water moves more quickly and dissipates more slowly than pressure waves in air, so underwater blasts may lead to more injury. As distance from the blast increases, injury risk decreases, and shielding can provide significant protection. On the other hand, being in a confined space, or being close to a surface that reflects the propagating pressure wave, may result in magnification of the blast effects.

### Mechanisms of Blast Injury

Explosions cause injury by several mechanisms. The initial gas expansion causes a blast wave with high winds that can cause displacement of people or objects. This is followed by a pressure differential created by the blast wave, and then a negative pressure phase occurs before air pressures return to normal. Heat generation, fragmentation, and collapse of infrastructure can all contribute to injury. Blast injuries are thus characterized as primary, secondary, tertiary, and quaternary injury. Although this is a simplified taxonomy, it can be useful to theoretically organize the anticipated effects.

Primary blast injury is a result of the blast overpressure and the forces it exerts upon the body. The pressure differential created by alternating overpressure and underpressure leads to both local tissue and systemic effects. Air-filled organ systems such as the GI, pulmonary, and auditory systems are the most sensitive, but blast effect can also cause musculoskeletal tissue damage, central nervous system injury, and even visual and cardiovascular effects. Injury is not isolated to local tissue effects. Cardiovascular collapse may occur as the result of pressure effects on the vagus nerve and dysfunctional vasoconstriction in response to diminished cardiac output.

Flying debris displaced as a result of the blast wave and winds causes secondary injury in the form of both penetrating and blunt trauma. Secondary injury is seen more commonly than severe primary injury, and these injuries can be devastating. Tertiary injury occurs with structural collapse or when forces displace a person who then sustains blunt trauma such as fractures or a closed head injury. While tertiary injury may have a high mortality rate at the site of the explosion, it only represents a small portion of overall deaths. Lastly, the term quaternary injury captures all the other miscellaneous injuries that may occur as a result of explosions, such as burns, asphyxia, toxic (including chemical and radiological) exposures, and psychological sequelae. Evaluation and management of secondary, tertiary,

and quaternary injuries follows routine trauma management principles, so the following discussion will be limited to primary blast injury.<sup>80,81</sup>

### Evaluation and Management of Primary Blast Injury

Due to their large amount of air-filled tissue, the lungs are susceptible to primary blast injury. The pressure differential causes disruption of lung tissue with damage to the alveolar-capillary interface. Blast lung may be complicated by pneumothorax, hemothorax, pulmonary contusion, pulmonary hemorrhage, pulmonary emboli, mediastinal air, and subcutaneous air, all of which contribute to difficulty in oxygenation due to ventilation/perfusion mismatch. A chest x-ray done as part of routine trauma management will help identify pulmonary injuries. However, radiographic findings may be delayed, so observation for 4 to 6 hours may be necessary in symptomatic patients. A CT may also be useful because some injuries may be missed on chest x-ray. Bilateral pulmonary infiltrates are commonly noted. Pneumothorax or hemothorax can be treated with tube thoracostomy. Severe injury resulting in impaired ventilation and oxygenation may require mechanical ventilation. Minimizing peak inspiratory pressures and allowing permissive hypercapnia may help minimize the risk of air emboli. To avoid volume overload, fluid use should be judicious. Similarly, cardiovascular collapse (described above) is best treated with inotrope support instead of aggressive fluid administration.

Much like the lungs, the GI tract is susceptible to injury due to air-filled viscus. Bowel injuries including contusion, ischemia with the risk for necrosis, or perforation are uncommon but possible results of blast waves. Body armor may help prevent secondary injury but cannot fully protect against pressure effects on the bowel. Bowel injury may be delayed in presentation; therefore, a high index of suspicion should drive evaluation. CT can be useful to evaluate for injuries, but it

lacks sensitivity for contusions and mesenteric injury. Thus, serial exams are an important part of ensuring such injuries, or delayed development of hematoma or perforation, are not missed. Perforation, necrosis, and even severe ischemia are indications for laparotomy and likely resection.

The tympanic membrane (TM) is highly susceptible to blast injury, and the absence of TM injury makes it less likely there is significant injury to the lungs, GI tract, or CNS in otherwise asymptomatic patients. Sensorineuronal deafness and tinnitus can occur in addition to TM rupture. The blast wave may cause displacement of the ossicles or damage to sensory structures. Small, isolated TM ruptures will likely heal without surgical treatment, but larger perforations and other injuries should be referred for surgical evaluation. Patients with TM rupture should be evaluated closely for concussive brain injury.

While traumatic brain injury (TBI) is more commonly associated with secondary and tertiary mechanisms, it can be caused by primary blast injury. Cerebral concussive syndromes are common and may result from oxidative injury and neuronal cell death caused by the blast. Standardized assessment tools such as the Military Acute Concussion Evaluation (MACE) can help collect baseline and follow-up comparisons to risk-stratify patients and guide referral for further evaluation and therapy. Fortunately, most patients are categorized as mild TBI and recover quickly with conservative care.

Myriad other injuries have been described as a result of blast injury, including ocular injuries such as globe rupture, conjunctival hemorrhage, and hyphema, and cardiac injuries such as myocardial wall contusion, hemorrhage, and atrial rupture. Clearly, explosions can cause a complex array of blast effects that present clinical challenges. Understanding blast effects in an effort to make sound diagnostic and therapeutic decisions is important for the MMO. The evolution of modern warfare has underscored the importance of expertise in caring for victims of explosion.

### CONCLUSION

The MMO must remain vigilant against a host of CBRNE threats while forward deployed as well as in garrison. Today's unpredictable environment includes the risk of either traditional CBRNE attacks or for asymmetric engagements with novel methods such as the use of industrial chemicals as weapons. A substantial knowledge base and constant surveillance are required to quickly identify and respond to these possible events. Clinical practice guidelines

(CPGs) relevant to the care of the CBRNE patient in the DoD environment can be found at [http://jts.amedd.army.mil/index.cfm/PI\\_CPGs/cpgs](http://jts.amedd.army.mil/index.cfm/PI_CPGs/cpgs). The MMO should be familiar with the various CBRNE threats and means to mitigate such threats, possess the knowledge to recognize an exposure when it occurs, be able to conduct appropriate decontamination, and be familiar with management of CBRNE casualties.

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