CHAPTER 193

Weapons of Mass Destruction

Carl H. Schultz | Kristi L. Koenig

PRINCIPLES

Besides managing the injuries and illnesses from common disasters such as earthquakes and airplane crashes, emergency clinicians should also have competence in treating victims generated by terrorist attacks with nuclear, biologic, chemical, or high-energy explosive weapons. Conventional explosives remain the most common weapon used by terrorists; however, the risk from nuclear, biologic, and chemical agents may increase over time. The nomenclature for these weapons is not standardized. The military uses the acronym CBRNE, pronounced "see-burn-ee," referring to *c*hemical, *b*iologic, *r*adiologic, *n*uclear, and *e*xplosive agents. This chapter uses *weapons of mass destruction (WMD)* because of its wide acceptance and familiarity.

The results of an attack with WMD, although admittedly of low probability, are potentially catastrophic. According to a World Health Organization (WHO) estimate, 50 kg of anthrax spores aerosolized above a city of 5 million people would result in 100,000 deaths, with an additional 150,000 people seriously infected. The cost of managing 100,000 cases of anthrax exposure is estimated at between $6.4 and $26.2 billion. These types of estimates have led to authorities establishing emergency preparedness as a priority.

Children are particularly vulnerable to these weapons.[1] They breathe at a faster rate than adults do, increasing their relative exposure to aerosolized agents.[2] Some chemicals, such as sarin, are heavier than air, so they tend to accumulate at the level where children are more likely to inhale them. Children have a greater surface area–to–volume ratio and their skin is thinner. This makes them more susceptible to agents that act on or through the skin. They have smaller fluid reserves and higher metabolic rates. Therefore, they are more vulnerable to dehydration from vomiting and diarrhea and suffer increased toxicity from a given exposure, such as to radioactive iodine (^{131}I).

The use of biologic and chemical agents dates to biblical times, although the threat from radiation and nuclear detonation is relatively new.[3] Assyrians poisoned the wells of their enemies with rye ergot in the 6th century BC. The Mongols catapulted bodies infected with bubonic plague over the walls of Kaffa in the 14th century. The British Army gave American Indians blankets taken from individuals infected with smallpox during Pontiac's Rebellion in 1763. During World War I, the Germans effectively used chlorine and mustard agent against the advancing Allied armies. The Japanese killed hundreds to thousands of Chinese citizens with bubonic plague during World War II by spraying towns with fleas infected with *Yersinia pestis*. Saddam Hussein used a mustard agent against the Iranians during the Iran-Iraq War in the 1980s. Most recently, the Syrian government attacked cities within its own country using chemical nerve agents.

The use of WMD has been predominantly by the military during times of conflict. Toward the end of the twentieth century, however, the use of these agents has taken an ominous turn. Nonaffiliated groups have begun using WMD directed at civilians to achieve political ends. The Bhagwan cult sprayed salad bars in Oregon with *Salmonella* in an attempt to influence an election in 1984. The Aum Shinrikyo used the nerve agent sarin in an unsuccessful 1994 assassination attempt on three judges in Matsumoto, Japan. This same group used sarin again in the 1995 Tokyo subway attack that killed 11 people.[4] The United States experienced multiple anthrax hoaxes during 1997 and 1998, motivated by personal or political agendas. Terrorists initiated an actual anthrax attack using the United States mail in 2001 that resulted in 11 deaths.[5] No one has yet used radiologic or nuclear devices in a successful mass terrorist attack, but at least one attempt has occurred. In addition, several highly radioactive sources have been stolen from American medical facilities, and a Russian dissident, Alexander Litvinenko, was assassinated with a radiologic agent (polonium-210) in 2006.

Many agents are potential candidates for weaponization, and some represent a substantial risk (Box 193.1). Management strategies for patients exposed to WMD are frequently similar to strategies for hazardous materials exposure. However, several features associated with WMD make these events unique (Box 193.2). Additional knowledge and skills are required in the evaluation and treatment of WMD victims. These plans represent only one small part of an overall comprehensive emergency management strategy for all hazards (see Chapter 192). Names of departments, bureaus, and agencies that can assist with planning and response to WMD events are listed in Table 193.1.

SPECIFIC DISORDERS

NUCLEAR AND RADIOLOGIC DEVICES

Principles

Terrorists selecting radiation as a means to inflict casualties are unlikely to use nuclear weapons. These devices are heavily guarded, difficult to move because of their size and weight, and easy to detect. Although Russia acknowledges that 50 to 100 of its 1-kiloton "suitcase" nuclear weapons are missing, the problems of purchasing, moving, and detonating these devices are formidable. Sabotage at nuclear power stations is possible, but given tight security, multiple safety systems, and thick concrete housings surrounding the reactors, the threat is probably low.

Instead, simple radiologic devices, such as those used by hospitals for radiation therapy, are thought to be the source of choice. These sources are plentiful. They do not detonate on their own and give no warning of their presence unless they are dispersed by a conventional explosive (radiologic dispersal device). Thefts of radiotherapy sources have occurred in the United States. Accidental dispersion from a stolen hospital therapy source in Brazil resulted in the screening of 112,000 people for contamination. A total of 249 people were found to be exposed—four of whom ultimately died. Placement of such a device at an information kiosk in a crowded mall during a busy holiday shopping season would silently expose countless persons to significant radiation.

TABLE 193.1

Resources and Contacts for Planning and Response to Events Involving Weapons of Mass Destruction

ORGANIZATION	WEBSITE	TELEPHONE
Radiation Emergency Assistance Center/Training Site (REAC/TS)	orise.orau.gov/reacts/	Daytime: 865-576-3131 Emergency: 865-576-1005
State and local health departments Association of State and Territorial Health Officials (ASTHO) Public Health Resources: State or Territorial Health Departments	 www.astho.org/statepublichealth/ www.cdc.gov/mmwr/international/relres.html	
Centers for Disease Control and Prevention (CDC)	www.cdc.gov	800-CDC-INFO
Federal Bureau of Investigation (FBI)	www.fbi.gov	
Federal Emergency Management Agency (FEMA)	www.fema.gov	800-621-FEMA
U.S. Army Medical Research Institute of Chemical Defense	https://usamricd.apgea.army.mil/	

BOX 193.1

Potential Agents of High Concern for Use as Weapons of Mass Destruction

CHEMICAL
Nerve agents
- Sarin
- Soman
- Tabun
- VX

Mustard agent

BIOLOGIC
Anthrax
Plague
Smallpox
Botulism
Viral hemorrhagic fever
Tularemia

RADIOLOGIC
Simple device
Dispersal device

BOX 193.2

Features of Weapons of Mass Destruction Threat

Fear of unknown or unfamiliar
Lack of training for hospital personnel
Lack of equipment, including personal protective equipment (PPE) and diagnostic aids
Potential for mass casualties
Psychological casualties
Crime scene requiring evidence collection and interaction with law enforcement
Potential for ongoing morbidity and mortality (dynamic situation)

Clinical Features

Ionizing radiation, regardless of its type, causes injury at the cellular level, usually by damaging DNA. Rapidly dividing cells are the most sensitive. Patients have symptoms within hours to days, depending on the dose. Common syndromes associated with radiation exposure include dermal burns, bone marrow failure, and gastrointestinal dysfunction (eg, vomiting and gastrointestinal bleeding) (see Chapter 138). Reviews of medical treatment for radiologic casualties can be found elsewhere.[4]

Management

A basic emergency department (ED) radiation protocol should address decontamination, triage, staff safety, personal protective equipment (PPE), and diagnostic procedures that emphasize radiation monitoring. Victims presenting to the ED will suffer from three types of exposure: irradiation, internal contamination, and external contamination. Irradiated victims have been exposed to a beam of radiation, similar to someone undergoing a chest x-ray examination. They are not radioactive and pose no threat to ED personnel.

Contaminated patients are more challenging, and early involvement of the radiation safety officer is critical. This individual evaluates the degree of the victim's contamination and monitors radioactivity levels throughout the decontamination process. Internally contaminated patients present a therapeutic challenge because they have radioactive material inside their bodies (eg, lungs and gastrointestinal tract) or incorporated into their cells. They should be placed in an isolation room where all secretions and body fluids can be collected. Various medications are available for administration to internally contaminated patients and can limit uptake or facilitate removal of certain radioactive elements. These medications include Prussian blue (Radiogardase) for cesium and thallium ingestions and diethylenetriaminepentaacetic acid (DTPA) for plutonium exposure. Health care providers can receive assistance by calling the Radiation Emergency Assistance Center/Training Site (REAC/TS; http://orise.orau.gov/reacts/) at 865-576-3131 (emergency number: 865-576-1005).

Externally contaminated victims have radioactive material on their skin or clothing and are decontaminated by removal of clothing and washing with soap and water. Washing by protected personnel should continue until monitoring by the radiation safety officer demonstrates the absence of radioactivity. If wounds are present, they are decontaminated first. After the wounds are covered with a sterile, waterproof dressing, the remaining skin is washed. Hospitals should be prepared to decontaminate patients because historical data suggest that up to 80% of patients do not receive this intervention before arrival. Decontamination before hospital entry is crucial because these individuals can expose caregivers to radiation and contaminate the entire hospital through the ventilation system. Removal of clothing and covering

of the head with a surgical cap can reduce contamination by 80% to permit stabilization in the decontamination unit, but complete decontamination should occur before exposure of unprotected staff if the patient's medical condition permits.

Initial triage of radiation casualties is based on their overall pathologic condition, not on exposure.[4] Even patients who have received a lethal dose of radiation do not die immediately as a consequence of the ionizing exposure. Therefore, a patient in acute distress from a myocardial infarction or urosepsis would be triaged ahead of a radiation victim with stable vital signs, regardless of the dose received. If a radiation casualty also suffers a severe injury or illness, immediate intervention is required. Most of the immediate morbidity and mortality associated with a radiologic dispersion device is related to traumatic injuries from the explosion and not to radiation exposure.

In addition to contaminated patients, the radiation safety officer is responsible for monitoring of the exposure of hospital staff. All personnel involved in the care of contaminated patients should wear dosimeters, which measure the amount of radiation received by the wearer. The safety officer tracks the amount of radiation received by each staff member and can remove a health care worker from the area if the exposure is too high. Radiation monitoring is complex, and the radiation safety officer should be involved as early as possible. Hospitals should consider conducting disaster drills that include casualties suffering radiation injuries.

Although many radioactive elements are candidates for use in a terrorist attack, ^{131}I and related isotopes deserve additional discussion because of heightened interest. ^{131}I is found only after a nuclear detonation or in reactor fuel rods. Although it is not impossible, the probability that terrorists could tap either of these sources is very small. The use of ^{131}I in a radiologic dispersal device is unlikely because of its short half-life (8 days). Even if such a device could be made, it is extremely unlikely that the radiologic dispersal device could disperse sufficient radioactive material to pose an acute health hazard. Given these facts, the probability that any significant exposure of the population (especially children) to ^{131}I will occur is equally small. The large number of childhood thyroid cancers that occurred after the accident at the Chernobyl nuclear power plant resulted, to a significant degree, from situations that will not occur in the United States. These include delayed reporting of a breach in the reactor containment vessel preventing timely evacuation of all exposed populations, failure to effectively quarantine contaminated milk and vegetables, and significant iodine deficiency in the exposed population. The risk to children in communities surrounding the Fukushima nuclear power plant is also an issue that will require long-term monitoring. Nonetheless, concern about treatment to prevent thyroid cancer after potential exposure to ^{131}I remains. Current recommendations for treatment with potassium iodide, which blocks uptake of ^{131}I by the thyroid, are listed in Table 193.2. Caveats for use of this table include increasing the amount of potassium iodide for adolescents approaching 70 kg to the adult dose (130 mg) and monitoring thyroid-stimulating hormone and free thyroxine (T_4) levels in neonates when possible. Non-pregnant adults older than 40 years old are unlikely to benefit from this intervention.

TABLE 193.2

Treatment With Potassium Iodide for Radioactive Iodine Exposure

SUBPOPULATION	PREDICTED EXPOSURE (cGy)	POTASSIUM IODIDE DOSE (mg)	NUMBER OF 130-mg TABLETS
Adults >40 years old	>500	130	1
Adults 18 to 40 years old	≥10	130	1
Pregnant and lactating women	≥5	130	1
Children 3 to 18 years old	≥5	65	½
Children 1 month to 3 years old	≥5	32	¼
Neonates, birth to 1 month old	≥5	16	⅛

BOX 193.3

Signs Suggesting Biologic Weapon Deployment

SYNDROMES
Pulmonary symptoms, pneumonia
Rashes
Sepsis syndrome
Influenza symptoms

EPIDEMIOLOGY
Multiple, simultaneous events
Dead animals
Large numbers of patients with high toxicity and death rate

BIOLOGIC WEAPONS

Principles

By convention, biologic weapons are divided into three groups: bacteria, viruses, and toxins. A characteristic shared by these agents is their ability to be dispersed as an aerosol. Because this is the most effective means to expose a large population, aerosol dispersal is the route that terrorists would most likely use to deploy such weapons. Victims, unaware of the exposure to a biologic weapon, present to the ED with nonspecific influenza-like respiratory signs and symptoms. Dermal contact and ingestion are also potential pathways for exposure, and some agents are effective by these routes. People infected in the 2001 United States anthrax attack were inoculated through aerosol and dermal exposures.[5] However, it is logistically more difficult to produce large casualty numbers by nonrespiratory portals of entry, so agents spread primarily by injection or through the gastrointestinal tract are less likely candidates for wide deployment. If the goal is to disrupt the economy or to spread fear among the population, then almost any type of release will suffice, whether or not people actually die.

Clinical Features

Patients exposed to biologic agents usually present with vague symptoms associated with an influenza-like illnesses.[7,8] Unless a biologic attack is announced or suspected, the ED staff may not realize that they are treating victims. It is not always possible to distinguish natural occurrences from engineered outbreaks of diseases. Examples of non-terrorist related occurrences of anthrax include cutaneous disease in intravenous heroin users in Europe, an outbreak of cutaneous anthrax in Bangladesh in 2010 with more than 400 cases, and isolated infections in drum makers after using contaminated animal hides. Because of the challenges in identifying the true etiology of acute events, personnel should be vigilant and at least consider the possibility, especially when warning signs are present (Box 193.3). For example, large numbers

of patients suddenly presenting with "the flu" not during influenza season should cause concern. For these reasons, health surveillance will be paramount in identifying agents and potential sources. The ED should have a working relationship with local and state health departments as well as with local law enforcement and stay apprised of Centers for Disease Control and Prevention (CDC) and Department of Homeland Security guidelines.

Management

Several infectious agents with potential for use as biologic weapons can spread in a hospital environment. Examples include Ebola and smallpox. Hospitals need protocols for PPE and patient isolation to ensure a safe environment. Fortunately, such protocols are similar to those applied to other infectious diseases (Box 193.4) in non-terrorist events (eg, the 2014 Ebola outbreak). For example, implementation of such precautions is credited with halting of the in-hospital spread of the Ebola virus in the 1995 Zaire outbreak. Decontamination is not a priority unless the exposure is acute. Standard precautions are usually sufficient, and special suits (eg, levels A and B) are generally unnecessary.

Whereas the CDC lists six Category A (high threat) agents (anthrax *[Bacillus anthracis]*, botulism [*Clostridium botulinum* toxin], plague *[Yersina pestis]*, smallpox [variola major], tularemia *[Francisella tularensis]*, and viral hemorrhagic fevers [filoviruses (eg, Ebola, Marbug)] and arenaviruses [eg, Lassa, Machupo]), this chapter focuses on three biologic agents—anthrax, plague, and smallpox—that represent the greatest interest.[7,8]

Anthrax

Principles

Bacillus anthracis, a gram-positive spore-forming bacterium, is the causative agent of anthrax ("woolsorter's disease"). The spores are extremely hardy and can survive for years in the environment. The disease is caused by exposure to the spores, not the bacilli in their vegetative state. It is normally a disease of sheep, cattle, and horses and is rarely seen in developed countries because of animal and human vaccination programs. Disease in humans can occur when spores are inhaled, ingested, or inoculated into the skin. The spores germinate into bacilli inside macrophages. The bacteria then produce disease by releasing toxins (eg, protective antigen, edema factor, and lethal factor) that cause edema and cell death.

Russia and the United States have developed anthrax into a biologic weapon. The effectiveness of this agent was clearly demonstrated by two events: an accidental release of spores from a biologic weapons facility in the former Soviet Union town of Sverdlovsk in 1979 and the intentional distribution of anthrax spores through the mail along the eastern seaboard of the United States in 2001.[5] After the Sverdlovsk release, at least 66 people died downwind from the compound during the next several weeks, and animal cases of anthrax were reported 30 miles away. The ability of non–state-sponsored terrorist groups to develop anthrax as a weapon is uncertain. The Japanese organization Aum Shinrikyo made several attempts to disperse anthrax throughout Tokyo without success. The individual believed responsible for the United States anthrax attack was not a foreign national. This is consistent with the fact that the strain of anthrax used in the attack (Ames strain) was developed by the United States government.

Inhalational anthrax is the most lethal form of the disease and is caused by inhalation of spores into the lungs. The mortality rate was thought to exceed 90%. However, data from the 2001 anthrax exposure call this figure into question (5 deaths in 11 cases). Although the actual mortality rate is unknown, and would depend on availability of intensive care resources, it is probably in the 50% range. The minimum number of spores required to produce disease is unknown. The original number quoted in the literature—1000 spores—appears high given the experience following the 2001 anthrax event.

Clinical Features

After phagocytosis by macrophages, the spores germinate and are transported to the tracheobronchial lymph nodes, where the bacteria multiply. During the next 2 to 10 days, patients have an influenza-like illness, with malaise, fever, and nonproductive cough. This initial phase can be delayed for more than 1 month in some patients. Within 24 to 48 hours, abrupt deterioration occurs, with overwhelming sepsis, shock, hemorrhagic mediastinitis, dyspnea, and stridor. A chest radiograph obtained at this time may show a widened mediastinum and hilar adenopathy, but typical radiographic findings are not dramatic and could be missed (Fig. 193.1). Computed tomography (CT) scanning of the

BOX 193.4

Recommendations for Prevention of In-Hospital Transmission of Contagious Agents

Isolate patient in single room with adjoining anteroom.
Have handwashing facilities and personal protective equipment (PPE) available in anteroom.
Use negative air pressure if possible.
Use strict barrier precautions: PPE, gowns, gloves, high-efficiency particulate air (HEPA) filter respirators, shoe covers, protective eyewear.
Alert hospital departments that generate aerosols: Laboratory (centrifuges), pathology (autopsies).

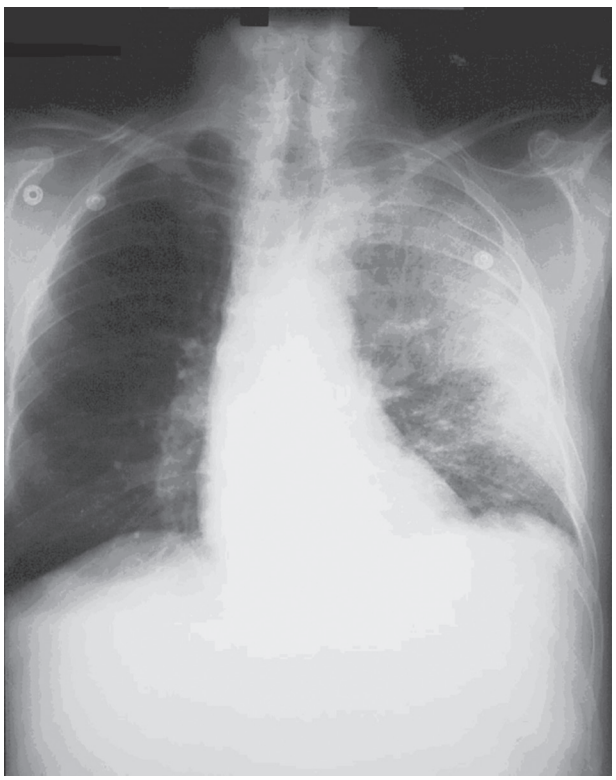

Fig. 193.1. Chest radiograph of anthrax patient showing diffuse left lung consolidation consistent with pneumonia. There is no mediastinal widening. (Courtesy Centers for Disease Control and Prevention [CDC].)

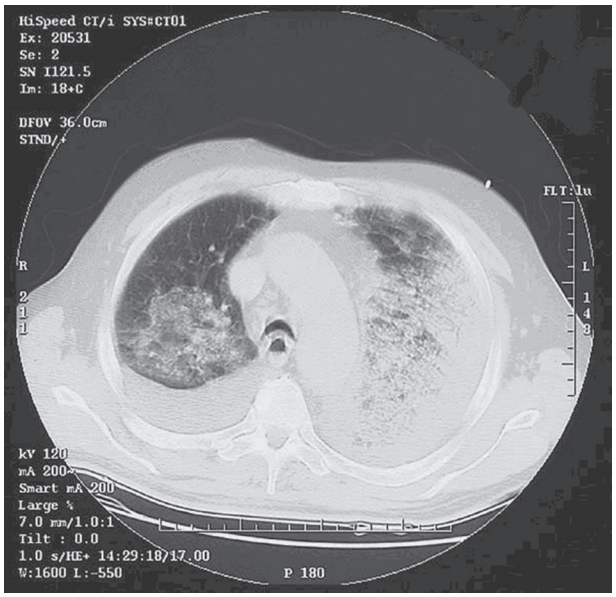

Fig. 193.2. Chest computed tomography (CT) scan of an anthrax patient showing pulmonary consolidation and effusions. (Courtesy Centers for Disease Control and Prevention [CDC].)

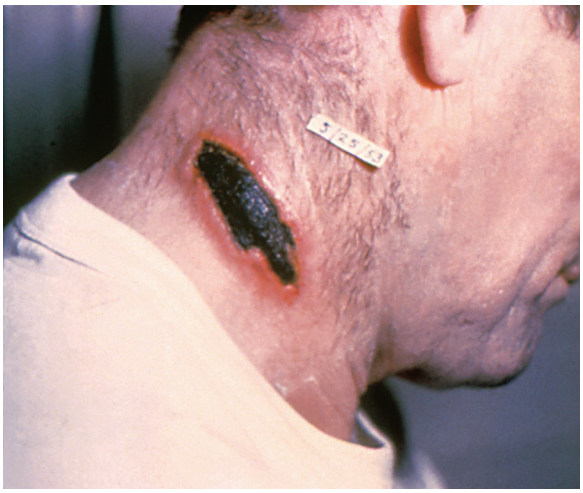

Fig. 193.3. Adult with cutaneous anthrax. (Courtesy Centers for Disease Control and Prevention [CDC].)

chest is more sensitive and should be performed if the disease is suspected. Bloody pleural effusions can also occur, and examination of the lung fields frequently reveals consolidation. This can easily be confused with pneumonia (Fig. 193.2). Death usually results within 3 days, and 50% of patients have hemorrhagic meningitis. Human-to-human transmission has not been reported with inhalational anthrax.

Initial diagnosis is generally made clinically on the basis of an influenza-like or septic illness; a suspicious chest radiograph or CT scan demonstrating hilar adenopathy, infiltrates, or pleural effusions; and a reason to consider anthrax in the first place (eg, current outbreak or warning from authorities). Several clinical algorithms exist that attempt to separate patients with influenza from those with anthrax. As these are based on a handful of anthrax cases, their usefulness remains in doubt. Sputum culture, Gram's stain, and blood cultures are not helpful until late in the course of the disease. Tests to confirm the diagnosis of inhalational anthrax include the polymerase chain reaction for identification of anthrax markers in pleural fluid, serologic detection of immunoglobulin to protective antigen, and immunohistochemical testing of biopsy specimens.

In addition to inhalational anthrax, cutaneous anthrax can occur in any area where large numbers of spores are released, as was the case in the United States in 2001. This form of the disease occurs when spores are introduced into the skin, usually through open wounds or abrasions. The mortality rate is approximately 20% without treatment and 1% with treatment. After an incubation period of 1 to 5 days, a papule develops, progressing to form a large vesicle during the next several days. Severe edema occurs around the lesion and is associated with regional lymphadenitis. The lesions are not tender, and the patient may or may not be febrile (Fig. 193.3). After approximately 1 week, the lesion ruptures, forming a black eschar (thus the name *anthrax,* from the Greek word for "coal"). In the next 2 or 3 weeks, either the eschar sloughs off and the illness is over or the organism disseminates and the patient dies. Antibiotics do not affect the course of local disease but are used to prevent dissemination and death. As with inhalational anthrax, the diagnosis is predominantly clinical. Confirmation is established by culture of the lesion, punch biopsy, or serologic testing. A total of 11 cutaneous anthrax cases occurred in the United States after the 2001 attack.

A few cases of gastrointestinal anthrax and oropharyngeal anthrax are also possible after a terrorist attack. These rare manifestations usually occur with the ingestion of insufficiently cooked, contaminated meat. The mortality rate is approximately 50%. After ingestion, the spores are transported to regional lymphatic tissue, where symptoms develop after a 2- to 5-day incubation period. Patients with oropharyngeal anthrax present with sore throat and neck swelling from cervical and submandibular lymphadenitis. The tonsils are also frequently involved, and symptoms are associated with fever and toxicity. Dysphagia and respiratory distress often follow. Gastrointestinal anthrax begins with nausea, vomiting, and fever associated with mesenteric lymphadenitis. Patients then experience severe abdominal pain, hematemesis, ascites, and bloody diarrhea and may present with an acute abdomen.

Management

Traditional treatment of anthrax infection has been penicillin. However, weapons-grade anthrax is probably resistant to penicillin (although this was not the case with the United States attack). Current treatment recommendations reflect this fact (Box 193.5). These consensus recommendations include fluoroquinolones and tetracycline for all children, regardless of age. Balancing the potential risks of such drugs against the consequences of infection by drug-resistant anthrax strains, the benefits justify the recommendations. Nontoxic victims with cutaneous anthrax can be treated as outpatients with oral ciprofloxacin or doxycycline for 7 to 10 days. Doxycycline is equally effective and may be better tolerated (less diarrheal side effects) than ciprofloxacin. Victims with inhalational, cutaneous, or gastrointestinal disease and toxicity require intravenous therapy with ciprofloxacin or doxycycline plus at least one other antibiotic (eg, linezolid, clindamycin, or an aminoglycoside) that inhibits protein synthesis. If meningitis is present, a third antibiotic is added that can penetrate the central nervous system (meropenem). Patients can be switched to oral antibiotics when toxicity resolves. Other modalities that may be helpful include chest tube drainage of pleural effusions, addition of antibody-based therapies (raxibacumab and anthrax immune globulin), and possibly tracheal intubation and mechanical ventilation.[5] Surprisingly, the latter intervention did not improve

BOX 193.5

Treatment of Anthrax

CUTANEOUS ANTHRAX *WITHOUT* TOXICITY

Adults

Ciprofloxacin, 500 mg PO bid; *or* doxycycline, 100 mg PO bid; *or* amoxicillin, 500 mg PO tid

Children

Ciprofloxacin, 20 to 30 mg/kg/day PO divided bid (maximum 1 g); *or* doxycycline, 4.4 mg/kg/day PO divided bid (maximum 200 mg); *or* amoxicillin, 20 to 40 mg/kg/day PO divided tid (maximum 1500 mg)

All doses are given for 7 to 10 days.

INHALATIONAL, CUTANEOUS, OR GASTROINTESTINAL ANTHRAX *WITH* TOXICITY

For adults and children, consider the antibody-based therapies raxibacumab and anthrax immune globulin in addition to IV antibiotics.

Adults

Ciprofloxacin, 400 mg IV every 12 hours; *or* doxycycline, 100 mg IV every 12 hours; *or* penicillin G, 4 million units IV every 4 hours

For patients without meningitis, add a second drug that inhibits protein synthesis, such as linezolid or clindamycin. For patients with meningitis, add a third drug to this regimen that penetrates the CNS, such as meropenem.

Children

Ciprofloxacin, 20 mg/kg/day IV divided every 12 hours (maximum 800 mg); *or* doxycycline, 4.4 mg/kg/day IV divided every 12 hours (maximum 200 mg); *or* penicillin G, 250,000 to 400,000 units/kg/day IV divided every 4 hours (maximum 24 million units)

For patients without meningitis, add second drug that inhibits protein synthesis, such as linezolid or clindamycin. For patients with meningitis, add a third drug to this regimen that penetrates the CNS, such as meropenem.

All doses are given until toxicity resolves, then switch to oral form. Treat for 60 days or until the patient receives three doses of vaccine.

POSTEXPOSURE PROPHYLAXIS

The same drugs and dosage are prescribed as for cutaneous anthrax without toxicity. Treat for 60 days or until the patient receives three doses of vaccine.

CNS, Central nervous system; *IV,* intravenous; *PO, per os* (by mouth).

mortality. All patients intubated after the United States anthrax attack died.

Treatment is to continue for 60 days or until the patient has received three doses of the anthrax vaccine, given on days 0, 14, and 28. The complete vaccine course requires 18 months. This treatment regimen is also recommended for children and pregnant women. If the anthrax strain proves susceptible, patients can be switched to intravenous penicillin or oral amoxicillin. In vitro studies suggest that ofloxacin or levofloxacin can be substituted for ciprofloxacin.

For postexposure prophylaxis, oral ciprofloxacin (500 mg) or doxycycline (100 mg) twice a day is recommended. Amoxicillin can be substituted if sensitive strains are identified. Antibiotic prophylaxis is to continue for 60 days or until patients have received at least three doses of the vaccine. The vaccine is approved by the U.S. Food and Drug Administration (FDA) for adults but not for children. However, it could become available for use in the pediatric population under the Investigational New Drug process if needed. A review by the Institute of Medicine (IOM) found the vaccine both safe and effective for prophylaxis against inhalational anthrax in adults.

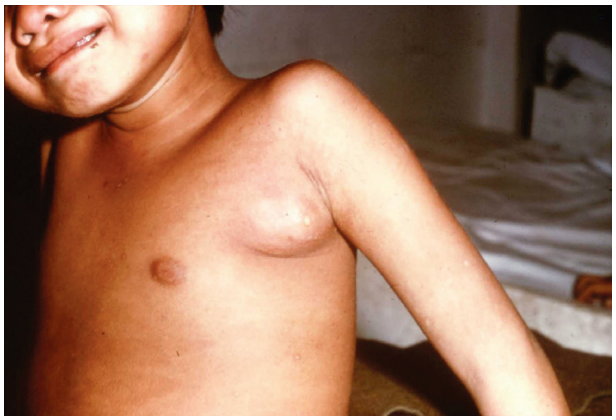

Fig. 193.4. Child with bubonic plague demonstrating axillary bubo. (Courtesy Frederick M. Burkle, Jr., MD, MPH.)

Plague

Principles

Plague has been a human pathogen since antiquity. Many regions of the world, including Asia and India, are currently witnessing the third pandemic of plague, and this affliction is endemic in the western half of the United States. Plague is caused by *Yersinia pestis,* a gram-negative bacillus. It is normally a disease of rodents that is transmitted to humans through the bite of an infected flea or by inhalation. Three forms of the disease exist: pneumonic, bubonic, and septicemic plague. The bacteria do not form spores and die rapidly in the environment. However, they are viable for days in dry sputum, flea feces, and human remains. Dogs are relatively resistant to infection, but cats are highly susceptible and could form a reservoir for maintaining the disease in a human population. Recovery is followed by temporary immunity.

Clinical Features

Primary pneumonic plague results when bacilli are inhaled into the lungs. The mortality rate approaches 100% if it is not treated early. Pneumonic plague will be the most frequently encountered form of the disease because terrorists are likely to use aerosolization as the method of dispersal. After an incubation period of 2 or 3 days, victims have sudden onset of fever, chills, and an influenza-like illness. This is followed within 24 hours by a fulminant pneumonia associated with hemoptysis, systemic toxicity, respiratory failure, circulatory collapse, and death. The pneumonia is classically lobar, but any x-ray pattern is possible, including acute respiratory distress syndrome. Six percent to 10% of victims have plague meningitis. Coagulation abnormalities and hepatocellular injury occur. The coagulopathy is characterized by ecchymoses, disseminated intravascular coagulation, and acral gangrene ("black death"). The gangrene is caused by bacterial production of the coagulase enzyme in areas of the body where the temperature drops below 98.6° F (37° C). This induces blood to clot in fingers, toes, and the nose, with resultant infarction and gangrene. If the victims survive, long-term rehabilitation is required. Pneumonic plague is transmissible human to human.

Bubonic plague occurs when organisms are inoculated into the skin, usually from a flea bite. During the 2- or 3-day incubation period, the bacilli migrate to regional lymph nodes, where they multiply and cause inflammation and necrosis of lymphatic tissue, resulting in large, tender nodes, or buboes. Typically, buboes develop in the groin, axilla, or cervical region and are so painful that the patient will refrain from moving the affected area (Fig. 193.4). Individuals experience fever, chills, and weakness. In approximately 25% of patients, vesicles or ulcerations occur at the

site of the flea bite. The buboes are usually nonfluctuant but rarely can suppurate. Organisms can be aspirated from the nodes for diagnosis, but incision and drainage are not recommended because the lymphadenitis resolves with antibiotic treatment, and practitioners could become infected if they are exposed during the procedure.

During the next week or more, the bacteria disseminate in approximately 50% of patients with bubonic plague. These victims have septicemic plague or secondary pneumonic plague and die if they are untreated. Those with septicemic plague experience endotoxemia, shock, disseminated intravascular coagulation, and coma. If bacteremia does not occur, most victims recover. A small percentage of those infected by fleas have septicemic plague without detectable buboes. Direct human-to-human transmission does not occur with bubonic or septicemic plague. However, both of these conditions can lead to secondary pneumonic plague, which is communicable. Therefore, initial isolation (for the first 48 hours) is recommended for all patients with plague.

Differential Diagnosis

The preliminary diagnosis of plague is clinical. Few diseases other than plague cause fulminant gram-negative pneumonia associated with hemoptysis in previously healthy individuals. Other diseases cause lymphadenopathy and the differential diagnosis for such conditions includes cat-scratch disease, tularemia, and staphylococcal or streptococcal infections. However, the extremely tender nature of the lymphadenopathy and the toxicity of the patient strongly suggest plague. Once the disease is suspected, Gram's stain and culture of sputum, blood, cerebrospinal fluid, or lymph node aspirate are helpful. State health departments or the CDC can test specimens for the presence of the capsular antigen by direct fluorescent antibody staining. Polymerase chain reaction also holds promise. Because all laboratory tests require several days to complete, initial management decisions are based on clinical findings.

BOX 193.6

Treatment of Plague

PARENTERAL THERAPY

Adults
Streptomycin,* 1 g IM bid
Gentamicin, 5 mg/kg once daily IM or IV
Doxycycline, 100 mg IV bid
Ciprofloxacin, 400 mg IV bid
Chloramphenicol, 25 mg/kg IV qid

Children
Streptomycin,* 15 mg/kg IM bid (maximum 2 g/day)
Gentamicin, 2.5 mg/kg IM or IV tid
Doxycycline, 2.2 mg/kg IV bid (maximum 200 mg/day)
Ciprofloxacin, 15 mg/kg IV bid (maximum 800 mg/day)
Chloramphenicol, 25 mg/kg IV qid

Pregnant Women
Same as above but exclude streptomycin and chloramphenicol

ORAL THERAPY

Adults
Doxycycline, 100 mg bid
Ciprofloxacin, 500 mg bid
Chloramphenicol, 25 mg/kg qid

Children
Doxycycline, 2.2 mg/kg bid (maximum 200 mg/day)
Ciprofloxacin, 20 mg/kg bid (maximum 1 g/day)
Chloramphenicol, 25 mg/kg qid

Pregnant Women
Same as above but exclude chloramphenicol

*Although streptomycin is recommended as first-line treatment, it may not be readily available.
IM, Intramuscular; *IV,* intravenous.

Management

Antibiotic treatment is essentially identical for all three types of plague (Box 193.6). The same caveats for the use of fluoroquinolones and tetracycline in children with anthrax apply to plague. In the case of pneumonic and septicemic plague, treatment should be started within 24 hours of symptoms for outcome to be improved. Antibiotics are given for a minimum of 10 days. As patients improve, oral antibiotics are substituted for intravenous therapy to complete the course. Respiratory isolation of patients with pneumonic plague is necessary for 4 days after beginning of antibiotics to guarantee sterilization of sputum. Patients with septicemic and bubonic plague require isolation for 48 hours. If they do not have pneumonia or draining lesions during this time, isolation can be discontinued. Nonseptic patients with mild bubonic plague can be treated at home with oral doxycycline or tetracycline for 10 days.

The mainstay of prophylaxis against plague remains oral antibiotics. A vaccine exists but has no value in an acute outbreak. It is effective only against bubonic disease and takes several months to impart immunity. The drugs for prophylaxis are tetracycline, doxycycline, ciprofloxacin, chloramphenicol, and possibly trimethoprim-sulfamethoxazole for children.

Smallpox

Principles

Smallpox was eradicated in 1980. The only known repositories of the variola virus, the etiologic agent of smallpox, are in the United States and Russia. However, Russia was successful in weaponizing the virus, which may have been sold or smuggled out of the country. The effectiveness of Russia's weaponized strain was demonstrated in 1971 when an individual became infected while traveling on a ship 15 km downwind from a Soviet bioweapons test site (Vozrozhdeniye Island in the Aral Sea). Furthermore, in July 2014, several vials of smallpox were discovered in an unused storage room at the National Institutes of Health in Bethesda, MD, raising serious concerns about the security of the virus. In addition, most of the world's population is no longer fully immune to infection because vaccination against smallpox ceased approximately 40 years ago in nonmilitary personnel. Given its high infectivity and lethality, this makes smallpox an excellent biologic weapon.

The variola virus is spread as an aerosol. It can survive for 24 hours, and possibly 48 hours, in the environment. The occurrence of smallpox in hospital employees whose only exposure was handling of laundry from infected people is testimony to its viability. Approximately 30% of exposed people become ill. One infected person has the potential to infect up to 20 other individuals. People are infectious from the time the rash first appears until the scabs fall off (1 or 2 weeks). Anyone exposed to smallpox should be closely monitored by public health authorities for 17 days to rule out infection.

Clinical Features

The disease is manifested clinically in several forms. Variola major and variola minor represent 90% of the cases. Variola major is the

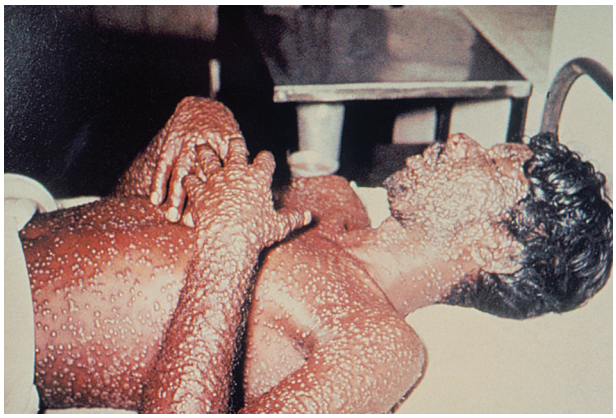

Fig. 193.5. Man with smallpox. (From the Centers for Disease Control and Prevention [CDC] Public Health Image Library.)

classic form, a more severe illness with a mortality rate of 30%. Variola minor is a milder form, with less toxicity, fewer pox, and a mortality rate of 1%. Two other forms of the disease, hemorrhagic and malignant (or flat) smallpox, are seen in 10% of cases; the mortality rate is greater than 90%. Patients with hemorrhagic smallpox have symptoms earlier and become toxic quickly. Instead of pox, their rash is characterized by petechiae and hemorrhage. Death occurs in 5 or 6 days. Those with malignant smallpox have a similar course, but their rash is characterized by soft, flattened lesions that do not progress to pustules. If they survive, the lesions resolve without forming scabs.

The infection begins when the virus is inhaled. After migrating to regional lymph nodes, the virus replicates for 3 or 4 days and then asymptomatically spreads to the spleen, bone marrow, other lymphoid tissue, and liver. A second viremia occurs 8 to 12 days later and is associated with fever, prostration, and headache. Mental status changes can occur. During this phase, which lasts 2 or 3 days, the virus localizes to the skin and pharyngeal mucosa. A maculopapular rash soon appears, which becomes vesicular and finally pustular. In contrast to chickenpox, the rash first appears on the face and forearms, later spreading to the legs and trunk. All the lesions in any one area of the body are at the same stage (Fig. 193.5). During the next 8 to 14 days, the pustules crust over and separate from the skin, leaving pitted scars.

A clinical algorithm developed by the CDC can assist in assessing the probability that an individual has smallpox.[7] It relies on three major and five minor criteria. The major criteria are a febrile prodrome, classic smallpox lesions, and lesions in the same stage of development. The minor criteria are centrifugal distribution of pustules; first lesions on the oral mucosa, face, or forearms; toxic appearance; slow evolution of lesions; and pustules on the palms and soles. A patient with all three major criteria is at high risk and should be isolated and reported to public health authorities and law enforcement agencies as soon as possible. Patients with the febrile prodrome and either four minor criteria or one other major criterion are at moderate risk. Emergency clinicians should consult with infectious disease and dermatology specialists and order tests to confirm varicella. If smallpox cannot be ruled out after these interventions, the patient should be treated as high risk. If a patient does not have the febrile prodrome or has the prodrome but no other major criteria and has fewer than four minor criteria, the individual is at low risk for smallpox. These patients can be managed as clinically indicated.

Differential Diagnosis

As with anthrax and plague, the initial diagnosis of smallpox is clinical. Other illnesses resembling smallpox include chickenpox, herpes simplex, and monkeypox. Unlike with variola, the rash associated with chickenpox (varicella) is seen first on the trunk and then spreads to the extremities and face. In addition, the pustules are in different stages of evolution in any one area of the body. If the first case seen is hemorrhagic or malignant smallpox, the diagnosis will probably be missed until more typical cases present.

Diagnostic Testing

For confirmation of the diagnosis, vesicular fluid or scabs are sent for electron microscopic examination or tissue culture. Polymerase chain reaction techniques are also useful for rapid viral identification, with sensitivities and specificities in the 98% range.

Management

No effective therapy exists for victims infected with smallpox who become symptomatic. However, potential antiviral agents, such as tecovirimat and cidofovir, show promise. In mice exposed to a lethal cowpox challenge, administration of an oral lipid prodrug of cidofovir in modest doses once a day for 5 days produced 100% survival. Vaccinia immune globulin (VIG) has no role in the treatment of active disease. Some practitioners suggest that most smallpox patients should be isolated at home or other nonhospital facilities because the virus spreads easily in a hospital environment and the disease is currently untreatable.

The best strategy for containment of the disease is vaccination of the susceptible population. Vaccination of an immunocompetent individual within 3 days of exposure will prevent or significantly ameliorate illness. Vaccination up to 7 days after exposure may prevent death. Complications from vaccination with vaccinia virus occur and can be fatal. Groups at risk for these adverse consequences include pregnant women and people with eczema, human immunodeficiency virus (HIV) infection, and immunosuppressive conditions (eg, malignant disease, chronic steroid use, and hereditary immunodeficiencies). Given the seriousness of the disease, the current recommendation is to vaccinate these individuals if there is risk of exposure and simultaneously administer 0.3 mL/kg of VIG intramuscularly. For people who have complications from the vaccine (eg, progressive vaccinia, ocular autoinoculation, and eczema vaccinatum), the dose of VIG is 0.6 mL/kg intramuscularly and is divided during 24 to 36 hours. Ribavirin can be administered but is considered experimental. VIG is not indicated for vaccinia-associated encephalitis.

The smallpox vaccine supply situation has improved dramatically in the United States. The CDC has replaced the traditional smallpox vaccine (Dryvax) with a next generation product, ACAM2000, in sufficient quantity to immunize the United States population. A British company developed the second-generation vaccine from the same vaccinia virus used in Dryvax but grown in cell cultures. As a consequence, its use can still produce the same adverse reactions as Dryvax. To improve the vaccine's safety profile, work has commenced on production of an improved vaccine based on a different vaccinia strain. Two new candidate vaccines, LC16 and Modified Vaccinia Ankara, show promise. Preliminary studies demonstrate safety and immunogenicity in populations for whom the traditional vaccine is contraindicated. The virus used in the modified vaccinia Ankara vaccine is so attenuated that it does not replicate in a human host. This may make it safe for administration to immunocompromised individuals.

CHEMICAL WEAPONS

Unlike victims of biologic weapons, casualties exposed to chemical agents manifest symptoms quickly, from acutely to a few hours after chemical contact.[3] Therefore, surveillance and recognition

BOX 193.7

Emergency Department Preparedness for Chemical Weapons of Mass Destruction

Community-based hospital planning
Personnel trained in recognition, mass casualty triage, and treatment
Decontamination facility with protocols (eg, runoff water, warm water)
Personal protective equipment (PPE) readily accessible and compliant with regulations
Rapid access to antidotes, cyanide kits, and anticonvulsants
Hospital incident management system in place
Knowledge of how to access experts quickly

are less problematic. The challenge is decontamination and treatment.

Terrorism with chemical weapons produces casualties similar to those seen in hazardous materials incidents, and medical management is comparable. However, the unique features of such events, including the volume of patients and the risk of hospital contamination, necessitate additional preparation. For example, the Tokyo subway attack with use of sarin in 1995 resulted in 11 deaths and more than 5000 patients converging on local EDs. Although the majority of these patients had subclinical exposure or psychological symptoms alone, the health care system was severely stressed. Secondary contamination by direct contact or vaporization occurred in ambulances and at the hospitals.

Health care facilities should have protocols in place to deal with the eventuality of chemically contaminated patients (Box 193.7). Current recommendations for levels of PPE and types of decontamination facilities necessary in a hospital setting have been advanced, but evidence-based recommendations remain inconclusive. Collection of waste water from the decontamination process in a containment vessel is ideal but not required if this would impede necessary and appropriate actions to protect human life (https://nepis.epa.gov/Exe/ZyNET.exe/P1002ZKP.txt).

The four basic classes of chemical compounds are nerve agents, vesicants (blistering), cyanides (previously referred to as *blood agents*), and pulmonary intoxicants (previously referred to as *choking agents*). Although all have potential for use as weapons, the nerve agents and vesicants are thought to represent the greatest threat.

Nerve Agents (Sarin, Tabun, Soman, and VX)

Principles

Nerve agents are organophosphates. They inhibit the enzyme acetylcholinesterase, blocking the degradation of acetylcholine at the postsynaptic membrane. Acetylcholine accumulates, resulting in overstimulation of muscarinic and nicotinic receptors.

Clinical Features

Symptoms are receptor dependent. Stimulation of muscarinic receptors produces miosis, salivation, rhinorrhea, lacrimation, bronchorrhea, bronchospasm, vomiting, and defecation. The major life threat associated with this syndrome is ventilatory compromise from profound bronchorrhea and bronchoconstriction. Stimulation of nicotinic receptors produces muscle fasciculations, flaccid paralysis, tachycardia, and hypertension. Unlike with typical organophosphates, exposure to nerve agents has not been associated with urination. In addition, bradycardia is rare, and miosis does not respond to systemic therapy.

Nerve agents also cause direct central nervous system toxicity that is manifested as seizures, coma, and apnea. In survivors, residual central nervous system effects are manifested as psychological changes that can last 4 to 6 weeks. These manifestations are caused by chemical effects, not stress.

BOX 193.8

Type and Degree of Nerve Agent Exposure

VAPOR EXPOSURE (SARIN)
Mild: Rhinorrhea and miosis
Moderate: Mild symptoms plus increased secretions, wheezing or dyspnea, muscle weakness or fasciculations, or gastrointestinal effects
Severe: Apnea, seizures, loss of consciousness, flaccid paralysis, or major involvement of two organ systems

LIQUID EXPOSURE (VX)
Mild: Localized sweating and fasciculations where a drop touches the skin; no miosis; may be delayed for 18 hours
Moderate: Gastrointestinal effects; miosis uncommon; may be delayed for 18 hours
Severe: Apnea, seizures, loss of consciousness, flaccid paralysis, or major involvement of two organ systems; occurs in less than 30 minutes at or above median lethal dose (LD_{50})

A preliminary diagnosis of nerve agent exposure is based on clinical findings. Important features include muscle fasciculations and miosis, which are sufficient to justify treatment pending further evaluation. Diagnosis is confirmed by measurement of red blood cell cholinesterase levels. This test may not be readily available, and results are difficult to interpret without a baseline level as significant variation exists within normal populations. Therefore, treatment is to begin before test results are known.

Terrorists are most likely to use the nerve agents sarin (designated GB) and VX. Sarin exists as a liquid at room temperature but represents primarily a vapor threat because of its high volatility. Symptoms occur within seconds after inhalation of vapor and peak at 5 minutes. There are no delayed effects; patients remaining asymptomatic 1 hour after possible chemical contact have not received a clinically significant exposure. They can be sent home. VX is a thick liquid with low volatility. It represents a liquid threat only. In general, victims have symptoms after skin exposure. The median lethal dose (LD_{50}) for VX is 10 mg, a droplet slightly larger than a pinhead. Death from doses of this size occurs in less than 30 minutes. Delayed symptoms occur, so individuals should be observed for 18 hours before potential intoxication can be ruled out.

Management

Decontamination of victims exposed to sarin vapor requires removal of clothing. People contaminated with VX or liquid sarin should have their clothing removed and then be decontaminated by using showers. When the level of exposure or the involved agent is uncertain, full decontamination is prudent. Responders caring for patients in the presence of liquid sarin exposure may require level A or B protective suits.

The treatment of nerve agent victims depends on the form (liquid or vapor) and level of exposure (mild, moderate, or severe) (Box 193.8). Three drugs are the mainstay of treatment: atropine for the muscarinic effects (improves ventilation), pralidoxime chloride (2-PAM) for the nicotinic effects (reverses paralysis), and diazepam for the prevention and treatment of seizures (Box 193.9). The dose of atropine is titrated to the drying of respiratory secretions and not to heart rate or pupil size. 2-PAM is most effective if it is administered within 4 to 6 hours of sarin exposure. After this period, the drug's impact wanes because of "aging,"

BOX 193.9

Treatment of Nerve Agent Exposure*

VAPOR

Mild: *Observe for 1 hour,* then release; no treatment
Moderate: One or two Mark I kits IM; *or* atropine, 2 to 4 mg IV, may repeat every 5 to 10 minutes as needed; *and* 2-PAM, 1 g IV during 30 minutes, may repeat every hour as needed
Severe: Three Mark I kits IM and one diazepam autoinjector IM; *or* atropine, 6 mg IV, may repeat 2-mg boluses IV every 5 to 10 minutes; *and* 2-PAM, 1 g IV during 30 minutes, repeat every hour for total of 3 g; *and* midazolam or diazepam, 5 mg IV, or midazolam 10 mg IM, may repeat as needed

LIQUID

Mild: One Mark I kit IM; *or* atropine, 2 mg IV; *and* 2-PAM, 1 g IV during 30 minutes
Moderate: Same as for vapor
Severe: Same as for vapor

PEDIATRIC DOSES

Atropine, 0.02 mg/kg IV
2-PAM, 20 to 40 mg/kg IV during 20 to 30 minutes
Midazolam, 0.15 mg/kg IV; *or* diazepam, 0.2 to 0.3 mg/kg IV

*Give atropine before attempting intubation. Otherwise, airway resistance will inhibit ventilation. Continue atropine until secretions are dry (usually 20 mg). In hypoxic patients, IV atropine has been reported to cause ventricular fibrillation, so consider use of IM atropine.
IM, Intramuscular; *IV,* intravenous.

defined as the permanent attachment of sarin to the acetylcholinesterase enzyme. Hypertension can occur during 2-PAM administration and is controlled by intravenous phentolamine, 5 mg for adults and 1 mg in repeated doses for children. In 2009, investigators published data that question the efficacy of oximes in the treatment of commercial insecticide exposure. In one study, the use of oximes did not improve clinically important outcomes.[9] Whether these results apply to nerve agents remains uncertain. Midazolam may be a more effective benzodiazepine for control and prevention of seizures, and it may replace diazepam as the drug of choice for treatment of severe nerve agent toxicity in future guidelines.[10,11]

An autoinjector kit (Mark I) approved by the FDA consists of two cartridges, one containing atropine (2 mg) and the other 2-PAM (600 mg). Mark I kits are available as part of civilian pharmaceutical caches strategically located throughout the United States. A newer version with both drugs combined in a single autoinjector (Antidote Treatment Nerve Agent Auto-Injector referred to as *DuoDote*) will gradually replace the Mark I kits. An autoinjector containing 10 mg of diazepam is an additional option if intravenous access is not possible. Doses should be adjusted for pediatric and geriatric patients. Atropine autoinjectors are manufactured in three doses (2 mg, 1 mg, and 0.5 mg) for these groups. Use of the Mark I kits to treat children and the elderly can be problematic because of difficulty in adjusting the dose. An alternative solution is to inject the medication into a sterile vial. The drug can then be re-aspirated in an appropriate amount for the patient's weight or age and administered.

Vesicants (Mustard)

Principles

Vesicants (blistering agents) are chemical warfare agents that induce blister formation on contact with skin. Terrorists could use several of these compounds, but sulfur mustard is considered the most likely. Mustard is a liquid at room temperature but has both liquid and vapor toxicity. Injury from mustard exposure occurs in 1 or 2 minutes, but symptoms do not develop for 4 to 8 hours.

Clinical Features

The exact mechanism is unknown, but the agent damages DNA, causing eventual cell death. These effects are similar to radiation exposure and often described as "radiomimetic." Mustard has both local and systemic toxicity. Local effects occur from direct exposure to the skin, eyes, and airway. Systemic effects result from the impact of absorbed mustard on the bone marrow.

Management

Treatment is supportive and includes decontamination (to prevent secondary contamination) and airway maintenance. No specific antidote for mustard is currently available. A topical iodine preparation showed promise in initial trials but did not demonstrate efficacy in larger studies.

Eye damage from mustard exposure varies from conjunctivitis to corneal ulcer and perforation; however, only 1% of patients have permanent eye damage. Ninety percent of ocular injuries will heal within 2 weeks to 2 months of exposure without sequelae. Severe pain is frequently associated with mustard injury and causes significant blepharospasm. Irrigation is beneficial if it is performed within minutes of exposure but ineffective once symptoms occur. Standard treatment includes mydriatics, topical antibiotics, oral analgesics, and petroleum jelly applied to the lids to prevent adhesions. Commercially available topical antibiotic/glucocorticoid ophthalmologic ointments have demonstrated efficacy when applied early in animal models. Application of this drug combination in the first few hours to days of exposure appears to reduce inflammation and subsequent injury. Continued use of topical steroids should occur under the supervision of an ophthalmologist.

The hallmark of mustard injury is skin blisters resembling second-degree burns. Within 4 to 8 hours of exposure, erythema and burning occur, followed by vesicle and bulla formation. Most vapor injuries do not involve the entire dermis, so wounds will not require skin grafting. If liquid exposure occurs to skin, full-thickness burns may result. The patient should be decontaminated by removal of clothing and washing with water or a dilute bleach (1:10 hypochlorite) solution. More concentrated bleach solutions are contraindicated, because they can cause skin damage. Decontamination immediately after exposure, ideally at the scene, prevents further injury to the patient, but delayed decontamination is indicated to protect staff. Treatment is supportive and includes standard burn wound management, analgesia, and tetanus prophylaxis. An important exception is fluid resuscitation. Fluid losses from mustard injury are much less than those associated with thermal burns. Therefore, standard burn formulas for fluid administration do not apply, and caution should be used to avoid overhydration.

The degree of airway injury after mustard exposure is dose dependent. Mild exposure causes irritation of the nose, sinuses, and pharynx and can be treated with cool, humidified mist. Moderate exposure extends to the larynx and upper trachea and may require treatment with oxygen, continuous positive airway pressure, or even intubation. Severe exposure involves the lungs, producing hemorrhagic necrosis of the bronchioles. Pulmonary edema is rare. Intubation is usually required, and patients may benefit from positive end-expiratory pressure and inline bronchodilators. Steroids are of questionable benefit, and antibiotics should be given only for established infection. Recent trials of inhaled tissue plasminogen activator in a rat model of sulfur mustard pulmonary injury show promise.[12]

Systemic toxicity from mustard is caused by bone marrow suppression. Absorbed mustard kills stem cells, causing the white blood cell count to decline after 3 to 5 days. Survival is rare if the white blood cell count falls below 200, which generally occurs when more than 50% of the total body surface area is involved from exposure to liquid agent. Death after mustard exposure usually results from secondary infection and respiratory failure.

Cyanides (Blood Agents)

Principles

Cyanide molecules, most typically hydrogen cyanide or cyanogen chloride, bind to cytochromes within mitochondria and inhibit cellular oxygen use.

Clinical Features

Low-dose exposures result in tachypnea, headache, dizziness, vomiting, and anxiety. Symptoms subside when the patient is removed from the source. At higher doses, the symptoms progress to seizures, respiratory arrest, and asystole within minutes of exposure.

Management

Victims should be removed from the area, have their clothing discarded, and receive oxygen. If no improvement occurs, the cyanide antidote is given. This has traditionally been the sequential administration of amyl nitrate, sodium nitrite, and sodium thiosulfate. However, the FDA has approved intravenous hydroxocobalamin for treatment of cyanide exposure. The initial dose is 5 g and can be repeated if necessary.[13-15]

Pulmonary Intoxicants (Phosgene and Chlorine)

Pulmonary or choking agents cause an inflammatory reaction when they come into direct contact with the eyes and upper airway. They can be life-threatening if inhaled. No specific antidote exists. Treatment is mainly supportive and consists of removal of the patient from the source, decontamination, airway maintenance, bronchodilator administration, and eye irrigation.

KEY CONCEPTS

- Emergency department (ED) preparedness for a radiation incident should address decontamination (an external freestanding decontamination unit is best), triage, staff safety, personal protective equipment (PPE), and diagnostic procedures that emphasize radiation monitoring. It is important that emergency personnel know their radiation safety officer.
- Management of acute life-threatening conditions takes priority over radiation-associated issues.
- Aerosol dispersal is a likely route that terrorists may use to deploy biologic weapons, so victims will present primarily with respiratory complaints.
- In addition to "flulike" symptoms, anthrax typically causes mediastinal widening, pulmonary consolidation, and pleural effusions best seen on chest computed tomography (CT) scans.
- Smallpox can spread in a hospital environment; thus patients thought to have smallpox should be admitted to locations separated from the rest of the hospital.
- Decontamination is a key activity in the management of patients exposed to chemical agents, and hospitals should provide this intervention.
- Nerve agents are organophosphates, and patients exposed to these agents are treated with large doses of atropine (repeated frequently), pralidoxime, and benzodiazepines.

The references for this chapter can be found online by accessing the accompanying Expert Consult website.

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CHAPTER 193: QUESTIONS & ANSWERS

193.1. Three patients arrive at triage simultaneously: One has received a 4 Gray work-related irradiation exposure from a food sterilizer but no other injury, one is experiencing an acute ST elevation myocardial infarction (MI), and one likely has urosepsis but with a stable blood pressure and heart rate of 105 beats/min. Which of these patients should receive your attention first?

A. Activate the cardiac catheterization team.
B. Decontaminate the irradiated victim before placing him in a room.
C. Initiate intravenous (IV) fluid bolus and prepare for intubation of the radiation-exposed patient.
D. Place a central venous catheter in the urosepsis patient.
E. Place the irradiated victim in an isolation room.

Answer: A. Even patients who have received a lethal radiation dose do not die quickly as a consequence of the ionizing exposure. Patients should still be triaged according to severity of the medical conditions and/or vital sign derangements. Here, the patient with the MI is most acute and should be treated first by activating the cardiac catheterization team. The radiation-exposed patient was not contaminated, just irradiated. As such, decontamination and isolation are not necessary. Although the victim has received the $LD_{50/60}$ dose of ionizing radiation, no significant injury will result just after exposure, so this patient does not take priority over the MI patient at this point and intubation is not indicated. The septic patient is not critically ill and should not be treated ahead of the MI patient.

193.2. Which of the following statements best describes issues in management of anthrax infection?

A. Antibiotics do not change the mortality of cutaneous disease.
B. Cutaneous anthrax lesions are nontender.
C. Doxycycline or ciprofloxacin is the single-agent treatment for symptomatic inhalational anthrax.
D. Intubation/mechanical ventilation clearly improves mortality from inhalational anthrax.
E. Sputum culture and Gram's stain obtained early in the disease help differentiate inhalational anthrax.

Answer: B. Cutaneous anthrax causes a severe, although nontender, peripheral vesicle and then eschar with regional adenopathy. Antibiotics lower the mortality from cutaneous anthrax twentyfold. For inhalational, gastrointestinal, and cutaneous anthrax with toxicity, intravenous (IV) treatment is with ciprofloxacin or doxycycline plus at least two other agents. Regarding inhalational anthrax, mechanical ventilation may not improve mortality, and sputum cultures and Gram's stains are not helpful until late in the disease.

193.3. Several children ages 5 to 8 years old have definitely been exposed to anthrax spores. Health department officials have brought these children to the emergency department (ED). They are all ambulatory with normal vital signs and without symptoms. Which of the following is the most appropriate management?

A. Admission for parenteral penicillin G
B. Doxycycline for 5 days
C. Observation
D. Outpatient ciprofloxacin for 60 days or until the children have received three doses of vaccine
E. Penicillin VK for 7 to 10 days

Answer: D. See Box 193.5. For children without toxicity, ciprofloxacin, doxycycline, or amoxicillin orally is indicated for a minimum of 60 days or until the child has received three doses of vaccine. The vaccine has not been approved for children but may be indicated to reduce the long-term exposure to antibiotics. Note that weaponized anthrax may be penicillin resistant.

193.4. An individual is exposed to sarin vapor. She presents complaining of difficulty with vision, salivation, vomiting, and the urge to defecate. The most appropriate treatment for this patient is which of the following?

A. 5 mg diazepam intravenous (IV)
B. 6 mg atropine IV and 1 g 2-PAM IV every hour for a total dose of 3 g
C. 10 mg diazepam intramuscular (IM) via auto-injector
D. Observation for 6 hours and then discharge if she does not develop new symptoms
E. One or two Mark 1 kits IM

Answer: E. The victim described would be characterized as a moderate exposure to sarin vapor. As such, treatment is indicated with one or two Mark 1 auto-injectors IM. Observation would not be appropriate. Diazepam is not indicated for moderate exposures. If an IV is established, the initial treatment is atropine 2 to 4 mg IV and 2-PAM 1 g IV.