Bioterrorism: An Update for Healthcare Professionals

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Faculty

Elizabeth T. Murane, PHN, BSN, MA, received her Bachelor's degree in nursing from Frances Payne Bolton School of Nursing, Case Western Reserve University in Cleveland, Ohio and a master of arts in Nursing Education from Teachers College, Columbia University, New York, New York.

Her nursing experience includes hospital nursing on pediatric, medical, surgical, and long-term units. She lived for 15 years in a village in Eastern Papua New Guinea providing medical and linguistic/literacy services for the villagers. She was a public health nurse for a year with the Brooklyn, New York Health Department and 20 years with the Shasta County Public Health Department in Redding, California. As a public health nurse she established influenza vaccine clinics throughout the community, prepared health education materials on the flu, interacted with the media during influenza season, and participated in surveillance activities.

Carol Shenold, RN, CIC, graduated from St. Paul's Nursing School, Dallas, Texas, achieving her diploma in nursing. Over the past thirty years she has worked in hospital nursing in various states in the areas of obstetrics, orthopedics, intensive care, surgery and general medicine.

Mrs. Shenold served as the Continuum of Care Manager for Vencor Oklahoma City, coordinating quality review, utilization review, Case Management, Infection Control and Quality Management. During that time, the hospital achieved Accreditation with Commendation with the Joint Commission for Accreditation of Hospitals Organization, with a score of 100.

Mrs. Shenold was previously the Infection Control Nurse for Deaconess Hospital, a 300-bed acute care facility in Oklahoma City. She is an active member of the Association for Professionals in Infection Control and Epidemiology (APIC). She now works for the Oklahoma Foundation for Medical Quality.

Faculty Disclosure

Contributing faculty, Elizabeth T. Murane, PHN, BSN, MA, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Contributing faculty, Carol Shenold, RN, CIC, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Division Planner

William Frey, DDS, MS, FICD

Division Planner Disclosure

The division planner has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Audience

This course is designed for dental professionals, all of whom are expected to respond in the case of a bioterrorist event.

A complete Works Cited list begins on page 30.

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Course Objective

The purpose of this course is to address the various components of a bioterrorism, nerve agent, or nuclear attack and the appropriate responses required for dental healthcare providers.

Learning Objectives

Upon completion of this course, you should be able to:

1. Discuss the role of the medical professional in the event of a bioterrorism attack.
2. Reflect on the history of bioterrorism.
3. Outline the CDC categories of possible bioterror agents and diseases.
4. Review the types of dispersion.
5. List some of the bacterial agents, their diagnosis, and treatment procedures, and how they could be used during a bioterrorist attack.
6. Discuss viral agents with the potential for bioterrorist use, including smallpox and viral hemorrhagic fevers.
7. Review biological toxins and how they might be used in biowarfare.
8. Describe the types of nerve agents that have been, or can be, used as weapons.
9. Identify radiation injuries and describe their appropriate treatment.
10. Discuss the detection of and disaster plans for acts of terrorism that involve biological weapons, including considerations for non-English-proficient populations.

EVIDENCE-BASED PRACTICE RECOMMENDATION

Sections marked with this symbol include evidence-based practice recommendations. The level of evidence and/or strength of recommendation, as provided by the evidence-based source, are also included so you may determine the validity or relevance of the information. These sections may be used in conjunction with the course material for better application to your daily practice.

INTRODUCTION

The United States government expects healthcare professionals to be on the front line of defense and treatment in the event of a bioterrorism attack in our country. This includes most medical personnel, but especially physicians, nurses, physician assistants, mental health professionals, and dentists. Increasing awareness and knowledge of possible bioterrorism agents and attacks will increase healthcare professionals' ability to respond properly.

Hospitals and clinics will have the first opportunity to recognize and initiate a response to a bioterrorism-related outbreak. Therefore, overall disaster plans must address the issue. Individual facilities should determine the extent of their bioterrorism readiness, which may range from notification of local emergency networks (i.e., calling 911) and transfer of affected patients to appropriate acute care facilities, to activation of large, comprehensive communication and management networks [1].

This course will attempt to briefly summarize the characteristics, treatment, and prophylaxis of potential bioterror and ionizing radiation agents. The role of the medical professional will be outlined, and the appropriate "do's and don'ts" will be discussed. Reporting procedures and disaster plans will also be reviewed.

UNDERSTANDING AND RESPONDING TO BIOTERRORISM

There are many definitions of bioterrorism. Most are similar to the definition provided by the Centers for Disease Control and Prevention (CDC): "The intentional or threatened use of viruses, bacteria, fungi, toxins from living organisms, or other chemicals, to produce death or disease in humans, animals or plants" [2].

What is the role of the practicing medical professional in the event of a bioterrorism attack and what is the expected response? This may be broken down into three simple steps: Identify, Report, and Refer [3].

IDENTIFY

- Be aware of the signs and symptoms of bioterrorism
- Know the appropriate tests to request
- Have an awareness of possible differential diagnoses

REPORT

- Be able to contact the appropriate agencies
- Initiate the preprogrammed response by public and government agencies

REFER

- Be able to refer victims of possible bioterror to bioterrorism experts or specialists
- Refer any media requests to these individuals as well

The CDC and other public health agencies recommend being extra vigilant with patients, sharing information with them, allaying their fears, and helping them to understand the limits of the bioterror agents. Conversely, these organizations strongly advise against the following:

- Prescribing antibiotics inappropriately
- Stockpiling antibiotics
- Recommending gas masks
- Unnecessarily alarming patients or peers

It is important to remember that no single antibiotic will protect against all potential agents. The duration of protection from antibiotics is short, and indiscriminate use will waste supplies, induce drug resistance, and lead to adverse effects. In addition, any organism used in an attack may have been engineered to be resistant to the usually prescribed antibiotics [3].

BIOTERRORISM IN RECENT HISTORY

The threat of a biological warfare attack on the U.S. has been receiving markedly increased attention as a result of world events, including the September 11, 2001, terrorist attack on New York and Washington, D.C. In years past, medical defense against biological warfare was an area of study for military healthcare providers and did not readily apply to the day-to-day mission of caring for patients in peacetime. However, it has become obvious that the threat of biological attacks against both soldiers and civilians is real and more should be done to educate ourselves about how to prevent and treat biological warfare casualties.

Training efforts intensified following the New York City World Trade Center bombing in 1993. The Tokyo subway sarin nerve agent release and Oklahoma City federal building bombing, both occurring in 1995, stimulated an increase in awareness. In November 1997, Secretary of Defense William Cohen announced that all U.S. military troops would be immunized against anthrax [4]. Additionally, the disclosure that a sophisticated offensive biological warfare program existed in the former Soviet Union and information obtained after the 2001 World Trade Center disaster have reinforced the need for increased training and education.

In December 2001, the Agency for Healthcare Research and Quality (AHRQ) developed a new support system for assessing and improving the U.S. healthcare system's capacity to respond to possible incidents of bioterrorism. It planned to interact more effectively with the private sector, by establishing the Council on Private Sector Initiatives (CPSI) [5]. The CPSI examined the clinical training and ability of front-line medical staff (including primary care providers), emergency departments, and hospitals to detect and respond to a bioterrorist threat. It also focused on research into the use of information and decision support systems to enhance clinical preparedness in the event of a bioterrorist threat. As of 2008, the CPSI was no longer active [5].

The need for education on the subject of bioterrorism is evident. Preparation for such an event must include knowledge of the potential biologic agents with emphasis on their diagnosis, treatment, and management.

TYPES OF AGENTS

The CDC has defined three categories of possible bioterror agents and diseases. Agents are categorized according to their priority as risks to national security [6].

CATEGORY A DISEASES/AGENTS

These are high-priority agents, including organisms that pose a risk to national security because they:

- Can be easily disseminated or transmitted from person to person
- Result in high mortality rates and have the potential for major public health impact
- Might cause public panic and social disruption
- Require special action for public health preparedness

Representative Category A Agents

- Anthrax (*Bacillus anthracis*)
- Botulism (*Clostridium botulinum* toxin)
- Plague (*Yersinia pestis*)
- Smallpox (*variola* major)
- Tularemia (*Francisella tularensis*)
- Viral hemorrhagic fevers

CATEGORY B DISEASES/AGENTS

The second highest priority agents include those that:

- Are moderately easy to disseminate
- Result in moderate morbidity rates and low mortality rates
- Require specific enhancements of CDC's diagnostic capacity and enhanced disease surveillance

Representative Category B Agents

- Brucellosis (*Brucella* species)
- Epsilon toxin of *Clostridium perfringens*
- Food safety threats (e.g., *Salmonella* species, *Escherichia coli* O157:H7, *Shigella*)
- Glanders (*Burkholderia mallei*)
- Melioidosis (*Burkholderia pseudomallei*)
- Psittacosis (*Chlamydia psittaci*)
- Q fever (*Coxiella burnetii*)
- Ricin toxin from *Ricinus communis* (castor beans)
- Staphylococcal enterotoxin B
- Typhus fever (*Rickettsia prowazekii*)
- Viral encephalitis
- Alphaviruses
- Water safety threats (e.g., *Vibrio cholerae*, *Cryptosporidium parvum*)

CATEGORY C DISEASES/AGENTS

The third highest priority agents include emerging pathogens that could be engineered for mass dissemination in the future because of:

- Availability
- Ease of production and dissemination
- Potential for high morbidity and mortality rates and major health impact

Category C agents are generally emerging infectious diseases, such as hantaviruses or Nipah virus.

Any disease that is contagious would be worrisome in our highly mobile society because people travel every day to many regions of the country and the world. If infected in an attack, a victim might fly from city to city, country to country, before he/she becomes symptomatic, spreading the infecting agent at an alarming rate. However, this course will focus primarily on those agents deemed highest priority (Category A) by the CDC. Information pertaining to chemical agents and radioactive materials will also be provided.

While the wild forms of the various bioterrorism pathogens are frightening and available, the threat of genetically engineered infectious agents is also a consideration. For example, it is known that researchers in Moscow created a recombinant strain of anthrax, raising the possibility that the current vaccine would be ineffective. With the constant advances in bioengineering, it is inevitable that biological weapons will be created that are resistant to current postexposure treatments and vaccines [7].

DISPERSION

Despite the very different properties of bacteria, viruses, and toxins, most biological agents that can be used as weapons share some common characteristics. The most important characteristic is the ability of the agent to be dispersed in aerosols, with a particle size of 1–5 microns. These particles can remain suspended (in certain weather conditions) for hours and, if inhaled, will penetrate the distal bronchioles and terminal alveoli of victims. Particles larger than 5 microns would tend to be filtered out in the upper airway [8].

Many of these agents may also be dispersed by contamination of foodstuffs. One such incident occurred in Oregon in the mid-1980s, when members of the Rajneesh movement attempted to influence the outcome of an election by putting *Salmonella* on the salad bars of ten restaurants. They believed that if the local citizens were inflicted with diarrhea, they would not be able to vote. Hundreds were mildly sick, but if this had been done with volatized anthrax spores, there could have been hundreds of fatalities [9].

BACTERIAL AGENTS

Bacterial agents are among the most probable sources of bioterror and include anthrax, brucellosis, plague, tularemia, and Q fever. They are generally easily accessible and fairly simple to spread. Bacteria can cause diseases in humans and animals by two possible means: by invasion of tissues or by production of toxins that cause a pathologic response. In many cases, pathogenic bacteria possess both properties. Fortunately, this group of agents often responds to specific therapy with antibiotics. The following sections will examine the more common bacterial agents in detail.

ANTHRAX

Background

Anthrax is a zoonotic disease (an animal disease transmitted to humans) that is transmissible to humans through handling or consumption of contaminated animal products. Anthrax spores were actively experimented with as possible weapons by the U.S. in the 1950s and 1960s, before the military program was terminated. At least 17 nations are believed to have had offensive biological weapons programs, but it is unclear how many were working with anthrax. The anthrax bacterium is easy to cultivate, and spore production is readily induced. The spores are highly resistant to sunlight, heat, and disinfectants. These are very desirable properties when choosing a bacterial weapon. In August 1991, Iraq admitted to a United Nations inspection team that it had performed research on the offensive use of *B. anthracis* prior to the Persian Gulf War of 1991 and, in 1995, also admitted to actively producing and testing anthrax as a bioweapon [8; 10].

Anthrax can be produced in either a wet or dried form and stabilized for use as a weapon. It can be delivered as an aerosol cloud either from a line source, such as an aircraft, or as a point source from a spray device. If used as a weapon, an anthrax aerosol would be odorless and invisible following release and would have the potential to travel many kilometers before dissipating. Evidence suggests that following an outdoor aerosol release, persons indoors could be at as high a risk for exposure as those who are outdoors [11].

Three forms of anthrax occur in humans, with manifestations depending on how the organism is contacted. The diseases are distinct; however, infection with one form presents a risk for contracting the others.

Cutaneous Anthrax

Cutaneous anthrax is the most common naturally occurring form, with an estimated 2,000 human cases reported annually [14]. The disease typically follows exposure to anthrax-infected animals. Cutaneous infections occur when the bacterium or spores enter a cut or abrasion on the skin, such as when handling contaminated wool, hides, or leather.

Gastrointestinal (GI) Anthrax

Gastrointestinal (GI) anthrax is not commonly seen; however, outbreaks have occurred in Africa and Asia [14]. GI anthrax follows the ingestion of insufficiently cooked contaminated meat. It is very unlikely that gastrointestinal anthrax would be used as a bioterror agent.

Inhalation Anthrax

Inhalation anthrax is the most deadly form of the disease, but it occurs less frequently as a naturally occurring disease than the cutaneous or GI forms. However, the dissemination of spores could cause widespread disease, and therefore, this is the most likely form of anthrax to be used as a biological weapon. As noted, it has been weaponized by several countries because it is easy to cultivate, the spores are resistant to heat and disinfection, and it can be produced in massive amounts. Prior to the cases in 2001, inhalation anthrax had not been reported in the U.S. since 1976 [11; 14]. This makes even a single case a cause for alarm today.

Diagnosis

The first evidence of a clandestine release of anthrax as a biological weapon would most likely be the sudden appearance of a large number of patients in a localized area, with the acute onset of a flu-like illness. A case fatality rate of 80% or more, with nearly half of all deaths occurring within 24 to 48 hours, is highly likely to be anthrax or pneumonic plague [11; 14].

The initial symptoms are often followed by a short period of improvement [11]. Following this, there is an abrupt development of severe respiratory distress with dyspnea, diaphoresis, stridor, and cyanosis. Shock and death usually occur within 24 to 36 hours after the onset of respiratory distress. In later stages, mortality approaches 90% despite aggressive treatment [11]. Physical findings can be nonspecific. The chest x-ray is usually disease-specific, revealing a widened mediastinum with pleural effusions, typically without infiltrates. Thoracic trauma can have similar signs, but often with infiltrates [12]. A hemorrhagic mediastinitis often develops.

The anthrax skin infection begins as a raised pruritic lesion or papule that resembles an insect bite. Within 1 to 2 days, the lesion develops into a fluid-filled vesicle, which ruptures to form a painless ulcer, 1–3 cm in diameter, with a necrotic area in the center [11]. Pronounced edema is often associated with the lesions because of the release of an edema-producing toxin by *B. anthracis*. The lymph nodes in the area may become involved and enlarged. The incubation period in humans is usually 1 to 7 days but could be prolonged to almost 2 weeks [11]. To describe the lesion in more detail, picture a painless macular eruption that appears within 2 to 5 days, most commonly on an exposed portion of the body. The lesion progresses from a red macule to a pruritic papule, then to a single vesicle or ring of vesicles. This is followed by a depressed ulcer and finally a black necrotic eschar that falls off within 7 to 10 days. There is edema associated with the eschar but usually no permanent scarring of the affected area. The cutaneous form of anthrax progresses to systemic disease in 10% to 20% of the cases, with a fatality rate of up to 20% if untreated [11]. Laboratory tests of blood products are usually normal if the disease is not disseminated. The systemic symptoms of cutaneous anthrax infection include fever, headache, regional lymph node involvement, and myalgia.

Laboratory Analysis

The *B. anthracis* organism can be obtained for culture or gram stain; however, analysis beyond simple cultures should only be performed in a specialized laboratory environment. On gram stain, the organism can be recognized as a large, rod-shaped, gram-positive, spore-forming bacillus. More positive identification requires lysis by gamma phage and direct fluorescent antibody (DFA) analysis or most positively by immunohistochemical staining. There is an enzyme-linked immunosorbent assay (ELISA) test available but generally only at reference laboratories. A negative culture does not rule out cutaneous anthrax, especially if obtained after antibiotics are started.

Treatment

Most *B. anthracis* strains are sensitive to a broad range of antibiotics. Penicillin, ciprofloxacin, or doxycycline is usually recommended for the treatment of anthrax, although penicillin alone is not used [39]. To be effective, treatment should be initiated early. If left untreated, the disease is highly fatal. Immediate prophylaxis with ciprofloxacin 500 mg orally, twice daily is commonly recommended. Treatment should continue for 60 days. If personnel are unvaccinated, a single 0.5 ml dose of vaccine should also be given subcutaneously [8; 14]. Various sources suggest that doxycycline is comparable to ciprofloxacin for prophylaxis if administered at the dose of 100 mg orally twice a day [39].

For inhalation anthrax treatment in adults, intravenous medications are suggested as the initial treatment [39]. The fluoroquinolones may be considered, although they are not yet approved by the U.S. Food and Drug Administration (FDA) for this use. These include levofloxacin, gatifloxacin, and moxifloxacin. Rifampin has been suggested as an adjunct treatment, and the penicillins may be tried if no other antibacterials are available.

In general, the cephalosporins are not useful in treating anthrax because the anthrax organism produces an enzyme that neutralizes them. Supportive therapy for shock, fluid volume deficit, and airway management may also be needed.

EVIDENCE-BASED PRACTICE RECOMMENDATION

According to the Working Group on Civilian Biodefense, a delay of antibiotic treatment for patients with anthrax infection even by hours may substantially lessen chances for survival. Given the difficulty in achieving rapid microbiologic diagnosis of anthrax, the Working Group recommends that all persons in high-risk groups who develop fever or evidence of systemic disease should start receiving therapy for possible anthrax infection as soon as possible while awaiting the results of laboratory studies.

(http://www.guidelines.gov/summary/summary.aspx?doc_id=3220. Last accessed July 14, 2008.)

Level of Evidence: Expert Opinion/Consensus Statement

Treatment for special groups, such as children and pregnant women, must be considered carefully. Fluoroquinolones are not generally recommended because of possible side effects involving the skeletal system. Balancing risks against the concerns about anthrax due to engineered antibiotic-resistant strains, the Working Group on Civilian Biodefense (Working Group) and the CDC recommend that ciprofloxacin be used in pregnant women and in children for therapy and postexposure prophylaxis [11; 39].

Vaccine

Vaccination for anthrax can prevent the disease if given prior to contact with the bacillus. However, it can also be used postexposure to help minimize the patient's reaction to the organism. Anthrax vaccine adsorbed (AVA) is the only licensed human anthrax vaccine in the U.S. [14; 40]. The vaccination schedule consists of three injections of 0.5 ml of the vaccine administered subcutaneously in the deltoid region [14]. After the first injection, the follow-up doses are given 2 and 4 weeks later. The vaccine is approved only for healthy, nonpregnant adults. There is an adverse reaction incidence of approximately 6% for local inflammation and 2% to 3% for systemic symptoms [13].

Infection Control

There is no data to suggest patient-to-patient transmission of anthrax; therefore, only standard barrier isolation precautions are recommended for hospitalized patients with all forms of anthrax [8]. There is no need to immunize or provide prophylaxis to patient contacts unless a determination is made that they, like the patient, were exposed to the aerosol at the time of the attack.

Standard disinfectants used for hospital infection control are effective in cleaning surfaces contaminated with infected bodily fluids. In the setting of an announced alleged anthrax release, any person coming in direct physical contact with a substance thought to be anthrax should perform thorough washing with soap and water [11].

Proper burial or cremation of humans and animals that have died because of anthrax infection is essential to prevent further transmission of the disease. Serious consideration must be given to cremation. Embalming of bodies could be associated with special risks [11].

PLAGUE

Background

Plague is a word that brings visions of death and destruction. Indeed, the disease caused by the gram-negative bacillus *Yersinia pestis* has been responsible for millions of deaths throughout history. Of the three main types of plague, bubonic, septicemic, and pneumonic, the most likely source of bioterror would be pneumonic plague [17]. Two other less common forms of the disease, plague meningitis and plague pharyngitis, also occur [37].

Historically, plague represented disaster for Africa, Asia, and Europe [17]. At times, there were not enough people left alive after an outbreak to bury the dead. The cause of plague was unknown, and the outbreaks caused massive panic. It was believed by many that the disease was a form of punishment.

Innocent people blamed for spreading plague found themselves persecuted by panicked masses. Even now, a suspected plague outbreak can incite mass panic [12].

The U.S. worked with *Y. pestis* as a potential biowarfare agent in the 1950s and 1960s, before the biowarfare program was terminated [17]. There is reported evidence that Japan investigated the use of *Y. pestis* as a biological weapon during World War II. They reportedly worked on a plan for attacking enemy troops with the organism by releasing plague-infected fleas [8].

Humans may acquire plague from the bite of infected fleas, contact with contaminated tissue, or inhalation of bacteria-laden droplets. Bubonic plague is the most common form of infection, resulting from the bacteria being taken up by the host macrophages in the lymph nodes [17]. The lymph node becomes inflamed, enlarged, and painful. From the infected lymph node, bacteria may multiply and become bloodborne, occasionally lodging in the lungs. Patients may progress from bubonic or septicemic plague to pneumonic plague if untreated [41].

When plague becomes pneumonic, direct person-to-person transmission via bacterial aerosolization becomes a real threat [41]. Progression of pneumonic plague is rapid and, if untreated, may lead to death in a few days [17]. Pneumonic plague is rare and requires close contact for transmission to occur. Early diagnosis with prompt antibiotic treatment is effective against all forms of plague infection [41].

Few physicians in the U.S. have ever seen a case of pneumonic plague, although *Y. pestis* is distributed worldwide. Techniques for mass production and aerosolization are readily available. The fatality rate of primary pneumonic plague is high, with potential for secondary spread [17]. A biological attack with plague is considered a serious threat. With sporadic cases likely to be missed or not attributed to a deliberate act, any suspected case of plague should be reported immediately by telephone to the local health department. A sudden appearance of many patients presenting with fever, cough, a fulminant course, and high fatality rate should raise suspicion for anthrax or plague. The tentative diagnosis of pneumonic plague is favored if the cough is accompanied by hemoptysis [16].

As noted, less common manifestations of plague include plague meningitis and plague pharyngitis [17]. Plague meningitis, resulting from spread of the bacilli into the meninges, is characterized by fever, nuchal rigidity, photophobia, and headache. Plague that primarily affects the pharynx is caused by inhalation or ingestion of *Y. pestis* and is generally recognized by the associated cervical lymphadenopathy [17].

Diagnosis

The clinical presentation of bubonic plague is differentiated from other syndromes consisting of fever, malaise, headache, and chills by the presence of extremely painful lymph nodes [42]. The nodes involved may be axillary, inguinal, or cervical, with inguinal involvement being the most common. The nodes become fluctuant and tender and may necrose and drain. The bubo is often a discolored, necrotic mass. Advanced cases of the disease may progress to secondary pneumonic or septicemic plague. The typical incubation period for bubonic plague is 1 to 6 days [17]. A history of camping in an endemic area or of contact with infected animals, usually rodents, is a clue to the diagnosis [42].

Primary septicemic plague presents in the same general manner as other gram-negative bacterial septicemias. Like bubonic plague, there is usually a high fever, chills, headache, and malaise. Gastrointestinal disturbance may be present as well. In addition, there may be progression to septic shock with meningitis, coma, and coagulopathy. Secondary pneumonic plague may also develop. Laboratory tests may be required to differentiate it from other causes of gram-negative sepsis. A clue to the diagnosis of septicemic plague is the development of thrombosis in the acral vessels, resulting in gangrene of the fingers and toes [17].

Primary pneumonic plague has an incubation period of 1 to 3 days [43]. Patients present with a very high fever of acute onset, chest pain, myalgia, a cough that may be purulent or bloody, malaise, and headache. The pneumonia may progress rapidly to multiple organ failure and death [17]. Other clinical manifestations may include coagulopathy with acral cyanosis, petechiae, dyspnea, stridor, and finally respiratory failure. A chest x-ray after 2 to 3 days of incubation will reveal a patchy or consolidated bronchopneumonia. Unless appropriate antibiotics are administered within 24 hours of the onset of symptoms, the death rate approaches 100% [8].

Laboratory Analysis

The initial screening for plague is by microscopic analysis of stained samples from appropriate fluids, such as lymph node aspirate, blood, sputum, and/or cerebrospinal fluid. Specimens should be taken prior to initiation of antibiotic therapy [42]. Gram stain can show a characteristic gram-negative rod with a bipolar ("safety pin") appearance that is very suggestive of *Y. pestis* [17]. When Wayson staining is used, the organism shows up as a light blue bacillus with dark blue polar bodies in a pink background. The nonspecific finding of increased leukocytes with a left shift is usually present.

Treatment

The Working Group has developed recommendations for healthcare providers to follow in the event plague is used as a biological weapon [17]. They suggest rapid administration of antibiotics plus supportive care.

The group chose streptomycin as the best choice for adults with primary pneumonic plague [17]. Gentamicin is also suggested. For plague meningitis, they suggest chloramphenicol. Alternative choices include doxycycline, ciprofloxacin, ofloxacin, and levofloxacin. All are highly effective if used within 8 to 18 hours after the onset of pneumonic plague. After a good drug therapy response, reappearance of fever may result from a secondary infection or a suppurative bubo, which may require incision and drainage [16]. The FDA has not yet evaluated the efficacy of quinolones in the treatment of plague in humans, and the third generation cephalosporins do not appear to be effective. Supportive therapy includes maintaining fluid levels with intravenous fluids and monitoring of the patient's hemodynamic status [17].

The Working Group also suggested that persons with close contact to a plague patient should be given antibiotics prophylactically for 7 days following the last known exposure [17]. For prophylaxis, streptomycin is the drug of choice, but gentamicin can be used when streptomycin is not readily available. Tetracyclines and chloramphenicol are alternative choices [17].

Infection Control

For bubonic plague, general care includes hospitalization and use of drainage and secretion precautions for 48 hours after the start of effective therapy. With pneumonic plague, strict droplet and standard precautions against airborne spread are required until 48 hours of appropriate antibiotic therapy have been completed with favorable clinical response [17]. Anyone who was in the household or had face-to-face contact with pneumonic plague-infected patients should be provided chemoprophylaxis [16].

Private rooms are recommended when possible. If not available, patients with similar symptoms and the same presumptive diagnosis (i.e., pneumonic plague) should be in the same room. Maintain spatial separation of at least 3 feet between infected patients and others whenever possible. Avoid placement of patients with droplet precautions in the same room with immunocompromised patients. Special air handling is not necessary, and doors may remain open. Limit movement and transport of patients on droplet precautions to essential medical purposes only. Minimize dispersal of droplets by placing a surgical-type mask on the patient when transport is necessary [17].

Vaccine

Prior to 1999, a licensed, killed, whole-cell vaccine was available in the U.S. for use in those considered to be at risk of exposure to plague [8]. At this time, there is no vaccine available, although research is taking place to develop one that is suitable. Much of this research is occurring outside the U.S. So far, no mass-produced product has been available, and the vaccines that have been used have not been effective against pneumonic plague [17; 18; 19].

TULAREMIA

Background

Tularemia is primarily a disease of rural populations, although occasional urban cases have occurred. The infective organism, *Francisella tularensis*, is a gram-negative intracellular coccobacillus with very marked pathogenic infectivity [20]. Humans can become infected by ingestion of or contact with contaminated water, food, or soil. Transmission can also occur through inhalation of aerosols, handling of infected animal tissues or fluids, and the bites of infective arthropods. Person-to-person transmission has never been reported [20].

Tularemia is one of the most infectious diseases known; as few as ten *F. tularensis* bacteria can cause disease in humans. Consequently, it has been widely exploited as a weapon of bioterror. The Japanese studied it for use between 1932 and 1945, the Soviet Union may have used it on the Eastern Front in Word War II, and the U.S. had it available in weapon form until the use of biological arsenals was eliminated [20]. The most probable dissemination of *F. tularensis* as a weapon would be as an aerosol. In fact, epidemics have occurred after harvests in Northern Europe, where the organism became aerosolized and infected many hundreds of people. The organism is quite hardy and can survive for prolonged periods of time in water, mud, and animal carcasses. Even frozen, *F. tularensis* is highly infectious, and laboratory workers have become infected while inspecting incubation plates [20].

Diagnosis

There are several classification systems for clinical tularemia. One such system categorizes tularemia as either ulceroglandular (occurring in the majority of patients) or typhoidal [44]. Ulceroglandular disease is characterized by lesions on the skin or mucous membranes (including conjunctiva), lymph nodes larger than 1 cm, or both. Typhoidal tularemia describes systemic manifestation of the disease without skin or mucous membrane lesions [20]. In addition to these two types, pneumonic tularemia, caused by inhalation and primarily manifesting as pleuropneumonic disease, also occurs [20]. Pneumonic tularemia is often considered a type of typhoidal tularemia.

Typhoidal Tularemia

As noted, typhoidal tularemia is an acute, nonspecific febrile illness and is not associated with prominent lymphadenopathy or skin lesions [20]. This type of tularemia is caused by inhalation or ingestion of bacilli and may involve significant gastrointestinal symptoms. It is believed that this type would be most prevalent during an act of bioterrorism [44].

The incubation period is usually 3 to 6 days (range 1 to 21 days), although aerosol exposures have been shown to result in incapacitation in the first day [20; 44]. Symptoms may include fever with chills, headache, myalgia, sore throat, anorexia, nausea, vomiting, diarrhea, abdominal pain, and cough [44]. Patients may develop tularemia sepsis, which can be fatal. This syndrome manifests with hypotension, respiratory distress syndrome, renal failure, disseminated intravascular coagulation, and shock [44].

Pneumonic Tularemia

Pneumonic tularemia results from inhalation of infected aerosols or spread of existing untreated disease. Hemorrhagic inflammation of the airways is an early sign [20]. Radiological studies show pleuritis with adhesions and effusions and peribronchial infiltrates; hilar lymphadenopathy is also common [20; 44]. These signs, however, are not always present. Patients may develop acute respiratory distress syndrome and require mechanical ventilation [44].

Ulceroglandular Tularemia

Ulceroglandular tularemia is generally caused by an arthropod bite or handling a contaminated animal carcass [20]. A local papule develops at the inoculation site, with progression to a pustule and ulceration within a few days. The ulcer may be covered by an eschar [20]. Lymphadenopathy develops in 85% of patients [44]. The nodes are usually tender and 0.5–10 cm in diameter [44]. Affected nodes may become fluctuant, rupture, or persist for months to years [44]. In most cases, there is a single ulcer, 0.4–3.0 cm in diameter, with raised borders. Other symptoms include fever, chills, headache, and cough [44].

Ulceroglandular tularemia can also be complicated by oculoglandular disease or oral/pharyngeal involvement. Oropharyngeal tularemia is caused by ingestion of contaminated food, water, or droplets and results in severe throat pain, exudative pharyngitis, stomatitis, or tonsillitis [21; 44]. Oculoglandular tularemia, caused by direct contamination of the eye, is characterized by ulceration on the conjunctiva [20].

Laboratory Analysis

There are several biological variants or subspecies of *F. tularensis*. Type A is considered to be more virulent, while the European variant, *F. tularensis* biovar palaearctica, typically causes a more mild form of the disease [20]. Both types can be identified with DFA analysis, which gives a presumptive diagnosis of tularemia. Direct examination with gram stain may not be helpful because *F. tularensis* is a weakly staining pleomorphic gram-negative coccobacillus, making it difficult to identify [22]. Due to the strong possibility of laboratory workers becoming infected, routine analysis should take place in biosafety level-2 (BSL-2) facilities and handling of identified cultures should be in a BSL-3 lab [20]. *F. tularensis* can be grown in appropriate cultures but may not be identifiable until after 48 hours. Antibody or other serologic tests and/or cultures are necessary for confirmation of the diagnosis. Antibody detection assays include ELISA, tube agglutination, and microagglutination, but significant antibodies may not appear until 10 to 14 days after the onset of the illness [44]. A positive DFA test on a culture can confirm the diagnosis.

Treatment

All forms of tularemia may be treated with streptomycin or, alternatively, gentamicin for 10 days [20]. Gentamicin may be more readily available and easier to administer. Also, because streptomycin has been associated with ototoxicity in fetuses, gentamicin is the drug of choice for pregnant women [44]. In a mass casualty situation, doxycycline or ciprofloxacin are preferred [20]. The use of chloramphenicol is generally discouraged due to the associated serious side effects; however, the Working Group states that it is an alternative, although not FDA approved [20]. Ciprofloxacin is suggested by the Working Group for mass casualty and confined cases, although it also is not FDA approved [20].

Cases of tularemia meningitis require special treatment, as the penetration of streptomycin or gentamicin into the cerebrospinal fluid is suboptimal. Combination therapy with chloramphenicol plus streptomycin or possibly a third-generation cephalosporin plus streptomycin is the recommended treatment for meningeal infections [44].

Infection Control

Because tularemia is not believed to be transmissible from person to person, respiratory isolation rooms are not required [44]. In general, standard precautions are sufficient [20]. Ulcers, when present, should be covered and contact isolation maintained, as *F. tularensis* remains present in such lesions for more than a month [44]. All postmortem procedures likely to cause aerosols should be performed using respiratory precautions or avoided altogether [12; 20; 44]. It must be reinforced that significant personal safety precautions be taken when handling tissues or other samples possibly containing *F. tularensis* because it is the second most common cause of laboratory-associated infections in the United States [22; 47].

Vaccine

A live, attenuated tularemia vaccine was available as an investigational new drug, but it was not approved by the FDA [20]. An attenuated vaccine has been used in the former Soviet Union to immunize tens of millions of people [45]. Research is being conducted to find a suitable vaccine that can be used widely in the United States [46]. The live vaccine strain has proven effective in preventing laboratory-acquired tularemia, although its effectiveness in preventing pneumonic tularemia is limited. The degree of protection depends upon the magnitude of the challenge dose [8; 20].

VIRUSES

SMALLPOX

Background

The use of smallpox as a biological weapon has a long history. In U.S. history, contaminated blankets were given to the American Indians to assist in their conquest during the French and Indian war [23]. In 1520, the Aztecs captured one of Cortes' men who was infected with smallpox. The resulting epidemic aided the Spaniards in defeating the Aztecs.

Variola virus, the smallpox causative organism, can be used as a biological weapon in aerosol form or deposited onto surfaces. Because smallpox vaccination of the general population in the U.S. was discontinued in the 1980s, the use of the smallpox virus as a weapon constitutes a large threat, especially because certain countries may be harboring stockpiles of the virus. The virus, which is quite stable in the environment, is usually spread by the respiratory route. It is also spread easily through direct contact.

Diagnosis

Variola virus belongs to the family Poxviridae, subfamily Chordopoxvirinae, and genus Orthopoxvirus. It is a single, linear, double-stranded DNA molecule of 140–375 kb pairs. It replicates in cell cytoplasm. Electron micrographs show that variola viruses are shaped like bricks. This brick shape distinguishes variola from varicella zoster, the virus that causes chickenpox and shingles [24].

Smallpox is transmitted from one person to another by droplets. Droplets containing the variola virus can be transmitted through face-to-face contact while talking, singing, coughing, or sneezing. It is also transmitted by saliva through sharing food or drink and kissing on the mouth. These activities contribute to a more vulnerable population than in the days before eradication.

COURSE OF SMALLPOX (VARIOLA)

Exposure INCUBATION 7 to 17 days
(not contagious)

Days 0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28

Prodromal 1 to 4 days

Lesions CONTAGIOUS scab off
from throat lesions to when all scabs have fallen off

Incubation (noncontagious): 7 to 17 days
Prodromal (fever, headache, prostration, chills): 1–4 days
Lesions (contagious): approximately 14 days

Source: [24] *Figure 1*

The virus is not shed during the incubation period, which can be from 7 to 17 days but most commonly is 10 to 14 days ***(Figure 1)***. During the incubation period, the virus enters the respiratory tract, seeds the mucous membranes, passes quickly to the lymph nodes, and multiplies in the reticuloendothelial system [24]. It is believed that only a few virions (virus particles) are sufficient to cause infection [25].

The prodromal phase, which follows the incubation period, lasts from 1 to 4 days, begins abruptly, and is characterized by:

- Fever — at least 38.5–40.5 degrees C (101–105 degrees F)

And at least one of the following [26; 27]:

- Prostration
- Severe (splitting) headache (90%)
- Backache (90%)
- Chills (60%)
- Vomiting (50%)
- Delirium (15%)
- Abdominal colic (13%)
- Diarrhea (10%)
- Convulsions (7%)

At the end of prodromal phase (about 24 hours before the skin rash erupts), minute red spots (the enanthem) appear on the tongue and soft palate. The patient may complain of a sore throat, as lesions may also be present lower in the respiratory tract. When the lesions in the mouth and pharynx open and release the virus, the patient is contagious. Patients are most contagious for the first week but can still transmit the disease until all the epidermal scabs from the skin lesions have fallen off, usually in approximately 21 to 28 days.

The smallpox rash erupts at the end of the prodrome. A few lesions usually appear first on the face, especially on the forehead. These are called the "herald spots." Occasionally, the rash is first seen on the forearms. Lesions tend to appear on the proximal portions of the extremities and the trunk, and then on the distal portions of the extremities. However, the rash usually progresses so quickly that it is apparent on all parts of the body within 24 hours and the patient does not notice how the rash progressed. Normally, more lesions appear over the next one or two days, possibly followed by a few fresh lesions later. Generally, the rash is distributed in a "centrifugal" pattern. The rash is most dense on the face and denser on the extremities than on the trunk. It is more prominent distally than proximally and on the extensor rather than on the flexor surfaces. There may also be lesions on the palms and soles [26].

Classic smallpox lesions are round, well-circumscribed vesicles that are deep-seated and firm. As they continue to develop, the lesions become umbilicated, having a central "naval-like" depression. The more confluent the lesions, the poorer the prognosis. Another distinguishing feature of the smallpox rash is that the lesions on any specific area of the body are all in the same state of development, meaning that they are all simultaneously vesicles, pustules, or umbilicated lesions. In contrast, the rash of chickenpox starts as a vesicle on top of erythema. Chickenpox lesions arrive in "crops," so in any one area of the body there will be a variety of vesicles, pustules, and crusts (scabs). The palms and soles are rarely involved, and patients are rarely toxic or moribund [27].

There are many possible secondary complications in smallpox. Most are due to viral activity in an unusual site or secondary bacterial infections. Smallpox can affect several systems. The skin lesions can become infected with bacteria, but the broad-spectrum antibiotics available today and good hygiene will prevent many of these secondary infections. Mild conjunctivitis at the time of the skin eruptions is part of the disease; however, corneal ulceration and keratitis may occur, causing blindness. Mostly, corneal lesions occur in patients with confluent or semiconfluent rashes. The joints may be involved, causing arthritis in approximately 1.7% of survivors [48]. The elbow is the most commonly affected joint. Respiratory complications may develop around day 8, and pulmonary edema is fairly common in hemorrhagic and flat-type smallpox [48]. However, cough is a rare symptom in smallpox. Encephalitis occurs in 1 in 500 cases, usually appearing between day 6 and 10 [48]. If the patient recovers, the recovery is slow but usually complete. The sequelae in persons who recover from smallpox, in order of frequency, are facial pockmarks, blindness (due to corneal scarring), and limb deformities (due to osteomyelitis and arthritis) [26].

Laboratory Analysis

Laboratory analysis for the distinct diagnosis of smallpox is not always easy because the pox viruses can only be rapidly distinguished from one another by polymerase chain reaction (PCR) assay or electron microscopy (EM) [28]. For EM, skin samples (scrapings from papules, vesicular fluid, pus, or scabs) may be collected. This can provide rapid identification of the pox viruses, including smallpox, cowpox, and monkeypox. Skin samples may also be used for agar gel immunoprecipitation, immunofluorescence, or PCR assay. In the event of known exposures, early postexposure (0 to 24 hours) nasal swabs and induced respiratory secretions may be collected for viral culture, fluorescent antibody assay, and PCR assay. After 2 days, blood may be collected for viral culture. Serological tests may be useful for confirmation or early presumptive diagnosis [28].

Treatment

There is still no known treatment for smallpox [48]. Therefore, the development of smallpox vaccine has been a significant medical achievement. Because there have been no natural cases of smallpox since 1977, the antivirals currently available have never officially been tested on smallpox.

Because no curative treatment is available, management of smallpox patients is limited to supportive care. This consists of [48]:

- Skin care
- Monitoring for and treatment of complications
- Monitoring and maintaining fluid and electrolyte balance
- Isolation of the patient to prevent transmission of variola virus to nonimmune persons

Infection Control

Smallpox patients should be considered infectious until scabs separate, usually about three weeks from the time of infection. Patients should be handled using standard precautions, and isolation with droplet and airborne precautions should be exercised for infected individuals and all contacts for a minimum of 16 to 17 days following exposure. In cases of mass casualties, isolation in the home or other non-hospital facilities should be considered where possible, as the risk for transmission is high and few hospitals will have enough negative pressure rooms for proper isolation. Immediate vaccination, if available, should be given to all medical personnel. Outside of the hospital setting, patients and household contacts should wear an N95 mask. Caregivers should wear disposable gowns and gloves as well. Bed linens, clothing, and other exposed articles must be sterilized or incinerated [28].

EVIDENCE-BASED PRACTICE RECOMMENDATION

The Centers for Disease Control and Prevention recommend that in addition to isolation of infectious smallpox patients, careful surveillance of contacts during their potential incubation period is required. Transmission of smallpox virus rarely occurs before the appearance of the rash that develops 2 to 4 days after the prodromal fever. If a vaccinated or unvaccinated contact experiences a fever >101 degrees F (38 degrees C) during the 17-day period after his or her last exposure to a smallpox patient, the contact should be isolated immediately to prevent contact with nonvaccinated or nonimmune persons until smallpox can be ruled out by clinical or laboratory examination.

(http://www.guidelines.gov/summary/summary.aspx?doc_id=2850. Last accessed July 14, 2008.)

Level of Evidence: Expert Opinion/Consensus Statement

Vaccine

Two smallpox vaccines are available as of 2008: Dryvax and ACAM2000 [29]. Until 2007, the only available vaccine was Dryvax, which was created in the early 1980s from calf lymph obtained from the New York City Board of Health. In August 2007, a second-generation smallpox vaccine, ACAM2000, was approved by the FDA [49]. The new vaccine is derived from a clone of Dryvax, purified, and produced using cell culture technology rather than by using live animal models [50]. The biological profile is similar to Dryvax, so equivalent efficacy and tolerability are expected.

It should be noted that although these vaccination are called "smallpox vaccinations," they do not contain any smallpox virus and cannot transmit the disease. However, the vaccines can transmit vaccinia and can produce life-threatening adverse events in rare cases [30]. The FDA has approved "black box" warnings to be included with the smallpox vaccines due to the possibility of encephalitis, myopericarditis, ocular complications, and skin and systemic infections (i.e., progressive vaccinia, generalized vaccinia, severe vaccinial skin infections, and erythema multiforme major) [13].

The CDC has identified the following high-risk groups for priority vaccination in the case of a smallpox outbreak [48]:

- Face-to-face close contacts (≤6.5 feet or 2 meters) or household contacts to smallpox patients after the onset of the smallpox patient's fever
- Persons exposed to the initial release of the virus (if the release was discovered during the first generation of cases and vaccination may still provide benefit)
- Household members (without contraindications to vaccination) of contacts to smallpox patients
- Persons involved in the direct medical care, public health evaluation, or transportation of confirmed or suspected smallpox patients
- Laboratory personnel involved in the collection and/or processing of clinical specimens from suspected or confirmed smallpox patients
- Other persons who have a high likelihood of exposure to infectious materials (e.g., personnel responsible for hospital laundry, waste disposal, and disinfection)
- Personnel involved in contact tracing and vaccination; quarantine/isolation or enforcement; or law-enforcement interviews of suspected smallpox patients

VIRAL HEMORRHAGIC FEVERS

Background

The viral hemorrhagic fevers (VHFs) are a group of diseases that can be transmitted to humans from animal reservoirs or arthropod vectors. There are four families of RNA viruses that are known to cause the infections: Arenaviridae, Bunyaviridae, Filoviridae, and Flaviviridae [31]. The diseases produced by these organisms vary according to the type, but in general, they present as very contagious hemorrhagic fevers with almost no known cure. Person-to-person transmission has been well documented for almost all of the VHFs, with the exception of the flaviviruses and Rift Valley fever [31].

The associated reservoirs and vectors are known for all of the virus types except the filoviruses ***(Table 1)***. In addition to natural disease potential, many of the VHF agents are potential biological warfare threats. These viruses are highly infectious by aerosol, and they are associated with high morbidity and, in some cases, high mortality. They have been shown to replicate sufficiently well in cell culture to permit use as a weapon [31]. Some of these agents are known to have been weaponized by Russia and the United States. The filovirus types, which include Ebola and Marburg viruses, as well as some of the arenavirus types, specifically Machupo and Junin, were stockpiled by the former Soviet Union and Russia until 1992 [31]. Yellow fever, a flavivirus, and Rift Valley fever, a bunyavirus, were developed as weapons by the U.S. prior

VIRAL HEMORRHAGIC FEVERS (VHFs) OF BIOWARFARE INTEREST					
Virus Type	**Name of VHR and Species**	**Region**	**Vector**	**Incubation Period (days)**	**Treatment**
Arenavirus	Argentine Fever (Junin virus)	Americas	Rodent	7-14	Ribavirin* and Supportive
	Bolivian Fever (Machupo virus)	Americas	Rodent	7-14	Ribavirin* and Supportive
	Brazilian Fever (Sabia virus)	Americas	Rodent	7-14	Ribavirin* and Supportive
	Venezuelan Fever (Guanarito virus)	Americas	Rodent	7-14	Ribavirin* and Supportive
	Lassa Fever	West Africa	Rodent	5-16	Ribavirin* and Supportive
Bunyavirus	Congo-Crimean	Africa, Asia, Middle East, Eastern Europe	Tick	3-12	Ribavirin* and Supportive
	Rift Valley	Africa, Middle East	Mosquito	2-6	Ribavirin* and Supportive
Filovirus	Ebola	Africa	Unknown	2-21	Supportive
	Marburg	Africa	Unknown	2-14	Supportive
Flavivirus	Kyanasur Forest Disease	India	Tick	2-9	Supportive
	Omsk	Central Asia	Tick	2-9	Supportive
	Yellow Fever	Africa, Americas	Mosquito	3-6	Supportive
*Intravenous ribavirin is available as an investigational new drug (IND) in the United States.					
Source: [31]					*Table 1*

to the program termination in 1969. More recently, the Japanese cult group, Aum Shinrikyo, attempted to obtain Ebola, a filovirus, for use as a bioweapon [31]. Hantavirus and dengue fever are sometimes included in this group, but they are more common as naturally occurring diseases in the U.S. and are not considered major bioterror threats. VHFs are frightening to the public and frustrating to the medical profession. The ease of contagion, lack of curative drugs, and vague initial presentation warrant their inclusion in this discussion.

Diagnosis

There is a variety of clinical presentations of VHFs, and not all patients show the classic signs and symptoms of the diseases. However, common initial clinical manifestations include fever, hypotension, bradycardia, tachypnea, conjunctivitis, and pharyngitis [31]. The overall incubation period can range from 2 to 21 days, which is followed by pronounced headache, high fever, nausea, abdominal pain, and diarrhea [31]. Hepatic involvement is common, but clinical jaundice is usually only seen in Rift Valley fever and yellow fever. The filovirus, flavivirus, and bunyavirus diseases usually have an abrupt onset, while the arenavirus diseases demonstrate a more gradual and insidious pattern of signs and symptoms [31].

The diseases progress to advanced stages, in which hemorrhagic diathesis is evident and includes petechiae, mucous membrane and conjunctival hemorrhage, hematuria, hematemesis, and bloody diarrhea [31]. Central nervous system dysfunction may occur, with convulsions, delirium, and coma. Eventually, there may be evidence of intravascular coagulation and circulatory collapse, followed by death [31].

A high index of suspicion is required because of the similarity of the initial presentation to so many other diseases, especially if the usual risk factors are not evident (as would be the case in a biological warfare attack).

Laboratory Analysis

Only the most secure laboratories are able to process any tissues, blood, or secreta that may be obtained for clinical analysis [31]. Of course, any suspected cases must be immediately reported to the appropriate public health and other government agencies [51].

The methods of detection include antigen-capture ELISA, PCR, and viral isolation. The most useful methods are reverse transcriptase PCR analysis and antibody detection [31]. The ELISA test usually does not become positive until late in the disease. Convalescent serum showing a four-fold rise in IgG titer or the presence of IgM can help make a presumptive diagnosis.

Treatment

General principles of supportive care apply to the hemodynamic, hematologic, pulmonary, and neurologic manifestations of VHF regardless of the specific etiologic agent. Patients are either moribund or recovering by the second week of illness, but only intensive care will save the most severely ill. Fluid resuscitation and invasive hemodynamic monitoring should be used, but extra precautions should be taken with needles due to the risk for nosocomial transmission of viral agents. Due to the bleeding associated with VHFs, intramuscular injections, aspirin, and anticoagulants should be avoided [8].

There is no available cure for the VHFs. In fact, there are no medications approved by the FDA that can be used to treat these diseases [31]. Ribavirin, a nucleoside analog, has shown some benefit in treating patients with arenavirus and bunyavirus infections; however, it requires an investigational new drug (IND) application and availability is limited [31]. It has not been an effective agent, in vivo or in vitro, against the filoviruses or flaviviruses. The Working Group has additional recommendations available in the event of a contained or mass casualty situation [31].

Infection Control

The Working Group has made some very stringent recommendations about personal safety for those who must come in contact with victims of VHFs. They stress that these diseases can be very easily transmitted and suggest the following protective measures [31]:

- Strict adherence to hand hygiene
- Double gloves
- Impermeable gowns
- N95 masks or air purifying respirators
- Negative isolation rooms with 6 to 12 air changes per hour
- Leg and shoe coverings
- Face shields
- Goggles
- Restricted access for all except necessary personnel
- All VHF patients housed together
- Dedicated medical equipment that stays with the patient
- Environmental disinfection with appropriate materials

The CDC recommends that patients who have died as a result of a VHF should be handled as little as possible [51]. Remains should not be embalmed, and burial should take place as soon as possible.

Vaccine

There are no licensed vaccines for any of the VHFs, with the exception of yellow fever. The yellow fever vaccine, 17D, was developed when outbreaks caused widespread disease among workers and military forces in endemic areas. The vaccine is a live attenuated preparation that is very effective when administered to travelers and those in endemic areas [31]. It is not available in large amounts and would not be useful in preventing disease in multiple areas or in large populations. It would also not be useful in a postexposure scenario because yellow fever has an incubation period significantly shorter than the time it takes for the inoculated person to develop the neutralizing antibodies [31].

TOXINS

BOTULINUM TOXIN

Background

Botulinum toxins gained widespread recognition as a result of the introduction of botulinum Type A (Botox) into the field of cosmetology. The toxins have been important medically for many years due to the serious and often fatal consequences of ingesting improperly canned or bottled foods. Botulinum toxins are proteins produced by the anaerobic bacterium *Clostridium botulinum* and consist of 7 separate but related neurotoxins, denoted A through G. All of the strains produce similar effects when ingested or inhaled. They are among the most toxic compounds known, with an estimated toxic dose of only 0.001 µg/kg of body weight. These neurotoxins act by binding at the presynaptic nerve terminals and at the cholinergic autonomic sites. They also block acetylcholine transmission, causing skeletal muscle weakness and paralysis as well as bulbar palsies [32; 33]. If effectively dispersed in aerosol form, 1 gram of botulinum toxin has the potential to kill more than 1 million people [53].

Human disease is caused by strains A, B, E, and rarely F and G. The type A strain is the most virulent and is the type most commonly found in the U.S., primarily in the eastern part of the country [33]. The disease can also be caused by wounds infected with *C. botulinum*, known as "wound botulism." An intestinal form has been reported in infants when the organism is ingested and germinates in the gastrointestinal tract. There is no transmission of botulism from person to person. The airborne transmission of botulism does not occur naturally, but if produced as a weapon or by accident in a laboratory, its effects would be catastrophic. From a study of three human cases of accidental inhalation botulism, it is postulated that inhaled *C. botulinum* will cause a similar symptom complex as the foodborne disease [52].

Diagnosis

The typical incubation period for botulism is 12 to 72 hours but may range from 2 hours to 8 days, depending on the dose. The early signs and symptoms of the disease are diplopia, blurred vision, dry mouth, ptosis, and photophobia [33]. This is followed by skeletal muscle weakness and paralysis, which is typified by a descending, symmetrical pattern, ending in respiratory difficulty and eventually respiratory failure [53]. Interestingly, the patient usually remains alert and afebrile, although there may be dysarthria, dysphagia, and dysphonia. The pupils may be dilated and fixed, the gag reflex may be absent, and deep tendon reflexes are diminished or absent. The patient may develop hypotension, cyanosis, and evidence of carbon dioxide retention. In foodborne botulism, all of these findings have been evident in patients within 24 hours of the ingestion of the tainted item [33]. In the few documented cases of inhalation botulism, patients displayed dysphagia, dizziness, unsteady gait, and ocular paralysis [53].

EVIDENCE-BASED PRACTICE RECOMMENDATION

According to the Working Group on Civilian Biodefense, any outbreak of botulism should bring to mind the possibility of bioterrorism, but certain features would be particularly suggestive. These features include multiple simultaneous outbreaks with no common source or an outbreak with a large number of cases of acute flaccid paralysis with prominent bulbar palsies, an unusual botulinum toxin type (i.e., type C, D, F, or G, or type E toxin not acquired from an aquatic food), or a common geographic factor among cases (e.g., airport, work location) but without a common dietary exposure (i.e., features suggestive of an aerosol attack).

(http://www.guidelines.gov/summary/summary.aspx?doc_id=3619. Last accessed July 14, 2008.)

Level of Evidence: Expert Opinion/Consensus Statement

Laboratory Analysis

Some cases of botulism might be confused with disorders such as Guillain-Barré syndrome or myasthenia gravis (MG). It has been suggested that the edrophonium (Tensilon) test may be used to differentiate botulism from MG, but because it may be transiently positive in botulism, its actual usefulness is in doubt. The Tensilon test requires that the patient have a sign, such as ptosis, which can be reversed with an intravenous injection of a cholinesterase agent like edrophonium. In many cases, the distinctive paralysis associated with botulism is the defining characteristic [53].

Only very limited information can be obtained from laboratory tests. Survivors usually do not develop an antibody response to the toxin due to the subimmunogenic amount of material required to produce major symptoms. In addition, cultures are not helpful in cases of inhalation botulism. As opposed to ingested botulinum toxin, inhaled toxin may not be identified in serum or stool. However, an ELISA test might possibly detect the toxin on nasal mucous membranes within 24 hours after inhalation [33].

The current recommended test for confirmation of botulism is the mouse neutralization bioassay [33]. This assay can detect as little as 0.03 ng of botulinum toxin within 1 to 4 days of exposure.

Treatment

For patients with symptoms of botulism, the prompt administration of botulinum antitoxin and supportive care can markedly reduce the mortality rate. Supportive care may include ventilatory assistance for several weeks or even months and feeding by enteral tube or parenteral nutrition [33; 53].

There are good antitoxins available; however, they only halt the progression of future symptoms and do not reverse the existing clinical presentation [53]. A licensed bivalent antitoxin for types A and B and a trivalent preparation for types A, B, and E are available. The antitoxins are of equine origin, which means that skin testing must be performed to help prevent serum sickness or anaphylaxis in susceptible individuals [33]. The military has worked on an antitoxin useful for types A through G, but this preparation is not available for public use [53]. It should also be noted that antitoxin would need to be administered prior to the development of significant symptoms in the general public to be effective in the event of an aerosolized botulinum biowarfare attack. In cases of exposure to large amounts of the toxin, patients' serum should be retested after antitoxin administration to ensure adequate treatment [53].

Infection Control

Botulism poisoning is not an infection. It is not transmitted from person to person, and only standard precautions are required to control its spread. As botulism poisoning is not transmittable, patients do not need to be isolated. A 10% bleach solution is approved by the Occupational Safety and Health Administration (OSHA) for decontamination purposes to kill the botulinum spores [33].

RICIN

Background

In 2003, ricin was discovered at a postal facility in South Carolina, and in 2004, letters containing the toxin were sent to two members of the U.S. Senate [54; 56]. In 2008, ricin that was subsequently linked to a possible bioterrorism plot was found in a hotel room in Nevada [55]. This potent agent is considered a low-level risk for use in biowarfare; however, it is obvious that it can, and has been, used as a weapon of terror. Some reports have indicated that quantities of ricin were found in the caves evacuated by the Al Qaeda in Afghanistan [56].

Ricin is a protein toxin extracted from the bean of the castor plant, *Ricinus communis*, either by direct isolation of the toxin or as a byproduct of the production of castor oil from the castor bean [7]. The mechanism of action is an inhibition of protein synthesis, specifically RNA ribosomal damage that leads to cell necrosis [7].

For use as a biological weapon, ricin can be made into an aerosol for widespread airborne dissemination. In addition, it can also be used in powder or liquid form to contaminate water or food, or it can be injected or penetrated through the skin to induce a parenteral exposure [7; 22]. Ricin is on the CDC's B list of agents as a potential bioterrorism weapon [6]. Although it is relatively easy to make in small quantities, it is considered a moderate threat because it is generally unsuitable for producing mass casualties.

Diagnosis

The gastrointestinal signs and symptoms of ricin poisoning include abdominal pain, vomiting, gastrointestinal hemorrhage with bloody diarrhea, fluid and electrolyte depletion, hypotension, and eventually hepatic, splenic, pancreatic, and renal necrosis [22]. The incubation period depends on the amount ingested and is usually 4 to 6 hours, although some cases have been seen with symptoms beginning within 15 minutes [7]. As noted, the initial dose can be as low as 1 mg, but this is not commonly seen. Death can occur in 3 to 5 days from organ failure and hypovolemic shock [22].

The signs and symptoms of aerosol exposure to ricin include rapid onset of chest pain, fever, dyspnea, and weakness [22]. A cough is usually present, as well as conjunctival irritation, optic nerve damage, diaphoresis, arthralgias, and the signs and symptoms seen with oral ingestion of ricin. Pulmonary edema, acute respiratory distress syndrome, and death can occur if the dose inhaled was sufficient to produce these major problems [22].

Parenteral exposure would not be expected as a means of bioterror attack. The presentation would be expected to be similar to sepsis, with fever, headache, dizziness, nausea, anorexia, hypotension, and abdominal pain [7]. There may also be tissue necrosis at the injection site [7].

The laboratory diagnosis includes analysis of nasal or throat swabs for toxin within 24 hours of exposure or toxin assay for antibody response in a serum sample obtained within 1 to 2 days after exposure and IgM and IgG increases 6 days after exposure [22].

Management

There is no specific treatment or antidote for ricin poisoning [22]. Supportive treatment, including pulmonary care and fluid replacement, is required. A single dose of charcoal may be considered for patients who are not vomiting, although the efficacy is unknown [7]. Patients who have been exposed to aerosolized ricin may require oxygen, bronchodilators, endotracheal intubation, and supplemental positive end-expiratory pressure [7]. Some patients may require long-term hemodialysis or, in severe cases, renal transplant [15]. Close scrutiny of all affected patients must be continued for several days [22].

Vaccine

In 2004, the FDA approved the University of Texas Southwestern Medical Center to begin safety trials in humans of an experimental ricin vaccine. The vaccine, RiVax, is a genetically engineered protein that has been found safe and capable of eliciting ricin-neutralizing antibodies in first-phase human trials [15]. A nasal formulation of RiVax is also in development. In addition, it has been reported that scientists at the United States Army Medical Research Institute have created a vaccine, RTA 1-33/44-198, that has shown promise in studies in mice [15]. As of 2008, neither vaccine was approved by the FDA to prevent ricin poisoning.

Infection Control

There is no person-to-person transmission of ricin, and secondary transmission of aerosols from victims of ricin poisoning is not documented [22]. If ricin is released as an aerosol, careful decontamination will be necessary to prevent cross contamination. Ricin-infected patients' clothing and personal effects should be removed and disposed of according to safety regulations. If possible, this should take place prior to arrival at a healthcare facility [15]. Exposed skin can be decontaminated with soap and water and a 0.1% sodium hypochlorite solution, which inactivates the ricin toxin [22]. Eyes may be irrigated with a saline solution.

CHEMICAL AGENTS

Chemical warfare agents have the potential of being effective weapons for a terrorist attack. They are generally available or easy to manufacture, can be transported and delivered by many means, and their effects can be immediate or delayed. They are also familiar, as they were first widely used in warfare during World War I [22].

The categories of chemical agents include nerve agents, such as sarin and tabun, and irritants and vesicants, including mustard gas, lewisite, and industrial chemicals. Also included are cyanide and less harmful agents, such as mace and pepper spray. This section will focus on the diagnosis and treatment of patients exposed to nerve agents.

NERVE AGENTS

Background

Nerve agents are the most toxic weapons in the military chemical warfare arsenal. The most common are sarin (GB), tabun (GA), soman (GD), and VX liquid. Any of these compounds can cause seizures, apnea, loss of consciousness, and death [22]. They are all in the class of organophosphates and have physiological effects similar to those seen when household insecticides are sprayed on an insect [22].

The mechanism of action for all nerve agents is the binding and inhibiting of the enzyme cholinesterase, causing a major increase in the amount of acetylcholine at synaptic clefts and receptor sites. This produces an overstimulation of the muscarinic, central nervous system, and nicotinic postsynaptic receptors, resulting in physiologic responses ranging from increased salivation to paralysis [34]. There may also be an antagonism of the neurotransmitter gamma-aminobutyric acid (GABA), adding to the central nervous system effects. This entire spectrum of signs and symptoms was found in the victims of the sarin attacks by the Aum Shinrikyo cult in 1994 and 1995 [22].

Diagnosis

Victims of a nerve agent attack may present with [22]:

- Miosis (pinpoint pupils)
- Hyperactivity of the genitourinary and gastrointestinal tracts, with involuntary urination, defecation, vomiting, and diarrhea
- Bronchoconstriction
- Increased glandular secretions such as thick bronchial mucus
- Rhinorrhea
- Lacrimation
- Salivation
- Increased sweating

The nicotinic effects present as muscle fasciculations and cramping, twitching, weakness, and finally paralysis. The combination of miosis, fasciculations, and respiratory distress is a signal that organophosphate poisoning is present [22].

Other signs and symptoms may include cardiac dysfunction, which can be a tachyarrhythmia, ventricular fibrillation, or bradyarrhythmia and hypotension. The central nervous system effects from small doses of nerve agents include nervousness, irritability, minor memory disturbances, and psychological manifestations that may persist for weeks. Larger doses result in seizures, loss of consciousness, apnea, paralysis, and death [22].

The type of exposure, whether from a liquid or vapor, can result in a different pattern of signs and symptoms. For example, VX, which is usually a liquid, can cause fasciculations at the contact site from a small droplet of the agent [22]. Larger doses, however, produce the more generalized somatic effects witnessed with the inhaled nerve gases. After contact with a liquid agent, the onset of symptoms may be delayed from 10 minutes to 18 hours, depending on the dose [22].

Although the primary diagnosis of a nerve agent attack is made on clinical grounds, the CDC has established a laboratory network to analyze blood and urine samples to detect the presence of chemical warfare agents [22].

It should be noted that in 2005, the CDC's designation of laboratories was changed, which affected the Laboratory Response Network for chemical terrorism. The new designation is opposite to that used previously, with Level 1 labs now being the most secure and having the most specific analytical equipment. Level 3 labs are the most numerous and are able to perform basic tests [35].

Treatment

The initial care of a victim of either a vapor or liquid nerve agent attack includes rapid decontamination. At a minimum, this includes removal of all clothing, jewelry, and any other possibly contaminated items. Soap and water can be used to wash the skin and hair of the patients who are suspected of being victims of a liquid nerve agent [22]. Special care should also be given to self protection.

Supportive treatment must include the establishment of a patent airway with the probable need for assisted ventilation. Most patients will die if no antidote is administered and aggressive airway maintenance is not initiated [22].

Atropine, pralidoxime chloride (2-PAMCL), and diazepam are the current favored drugs for treatment of nerve agent victims [22]. Atropine blocks the effects of acetylcholine at the muscarinic sites. The drug 2-PAMCL breaks the bond between the nerve agent and acetyl cholinesterase, allowing the enzyme to become available to break down acetylcholine [22]. Diazepam has been suggested as the best medication to use for seizures associated with nerve agent attacks. It has also been suggested that diazepam be used in all victims whether they are convulsing or not. These drugs are available in kits, many of which include "autoinject" syringes. The military has used a kit called the MARK 1, which includes atropine and 2-PAMCL in autoinjectors [22].

Containment

Because the nerve agents are not biological organisms, there is no vaccine or infection control to discuss. However, there are important steps that must be taken to prevent injury to medical personnel who will be taking care of the victims of an attack and to limit cross contamination. Obviously, the first consideration is to avoid contact with the noxious materials by using proper technique when handling the patients [22]. This includes wearing rubber gloves and other protective clothing if dealing with a possible liquid agent. The removal of all possibly contaminated items prior to attempting to provide care will help in protecting the medical personnel at the scene, in the transport vehicle, and at the hospital.

RADIOACTIVE MATERIALS

Although injury from nuclear radiation does not involve harm caused by a chemical or a biological organism, the topic is included in this course because its damaging effects are due to a biological process. In addition, the threat of the use of radioactive materials as possible weapons of terror makes a discussion of ionizing radiation beneficial for all healthcare professionals.

TYPES OF POSSIBLE TERRORIST ATTACK

There are thought to be five primary ways in which nuclear materials might be used by terrorists. They include [22]:

- **Simple radiological device (SRD)**. Radioactive material is spread around a public place without the use of explosives. This could be with sealed sources or loose material. The effects would be more psychological than physiological unless extremely high radiation doses could be produced.

- **Radiological dispersal device (RDD)**. Explosives are utilized to spread contamination over a greater area. The bomb portion could injure, or possibly kill, those in the immediate vicinity, while the radioactive material affects those in the surrounding area. The high explosives rip the weapon apart and spread radioactive plutonium, an alpha emitter, around the accident site. This type of incident would occur if a nuclear weapon ("atomic bomb") was accidentally dropped or otherwise inadvertently destroyed. It is almost impossible for the weapon to "go nuclear" when dropped from a plane by mistake.
- **Nuclear reactor sabotage (NRS)**. This is an unlikely scenario in the U.S. and most parts of the world. Many fail-safe protections would need to be bypassed and high security areas breached by a terrorist. The nuclear accident in Chernobyl, for example, required several safety systems to be bypassed and occurred in a building that did not have appropriate containment. All reactors in the U.S., as in essentially all the world at this time, are in containment shells that are designed to prevent the escape of any significant amount of radioactivity from the facility.
- **Improvised nuclear device (IND)**. This is a nuclear device created with the intent of harm. The level of sophistication required to produce such a device is so high that this is thought to be an unlikely scenario. Although a terrorist could obtain the components of such a weapon, the ability to get it to function properly would almost certainly be lacking. Most likely, an attempt to utilize an improvised nuclear device would result in a situation more like a radiological dispersal device.
- **Nuclear weapon**. This scenario incites the most fear, especially if terrorists could obtain one or more of the devices. It is felt that the existing supply of weapons, in the countries which possess them, are secure from theft. However, there have been many smaller, tactical nuclear weapons produced in the past that are not accounted for. This type of weapon could produce mass casualties, including killing those closest to the explosion, burning others, and producing radiation sickness in those in the immediate proximity who were not fatally injured by the blast.

DIAGNOSIS

Diagnosing injuries from ionizing radiation, in most cases, requires the history of radiation exposure. There can be instances when a victim is unaware of the cause and presents with a suggestive constellation of signs and symptoms. In addition, there may be some things that point to radiation injury, such as skin erythema or lesions, without the history of thermal burns. Unexplained epilation or a sudden drop in leukocytes or platelets could suggest radiation exposure as the etiology [22]. An examination of the blood, urine, or feces can be performed to determine the presence of any radioactive materials that may have entered the body.

TREATMENT

Radiation injuries, traumatic injuries, and burns can occur simultaneously in a nuclear terrorist attack that includes the use of explosives. Because high doses of ionizing radiation can impair healing, a victim who receives high levels of whole body radiation will usually have a greater degree of total injury, delayed recovery, and probability of death. A patient who has received more than 200 rems must have all major traumatic injuries treated within 48 hours. (Of note, a rem is equal to a rad for gamma rays.) This includes reducing fractures, suturing wounds, treating burns, and performing any required stabilizing surgery. If these interventions cannot be performed within the first 2 days, any major surgical procedures should be delayed an additional 2 to 3 months [22].

The immediate treatment for victims of radiological events includes prompt decontamination. This must be performed prior to the patient entering a care facility to prevent the facility from becoming contaminated. The procedure is similar to decontamination techniques used for the chemical weapons of terror, including the removal of clothing, copious washing of the body and wounds, and putting all contaminated items into a closed container.

Patients who received less than 100 rems will usually not need treatment. Supportive treatment for those with doses suspected to be more than 100 rems includes fluid and electrolyte replacement with antiemetics as needed. For those with doses in the range of 200 to 800 rems, there will probably be a significant drop in leukocyte count requiring protection against infection with antibiotics, antifungals, hyperalimentation, and possible blood replacement [22]. Patients with doses greater than 1200 rems are unlikely to survive. (The LD50, the acute penetrating dose to kill half of those exposed, is approximately 400 to 500 rems [22].)

Radioactive materials are considered "incorporated" when they enter the body and become lodged in the cells [22]. There are procedures available to diminish the radiation dose of those who have internal contamination or incorporated radionuclides. The mechanisms of action of the materials used to "decorporate" include binding, displacing, or in some way enhancing the elimination of the radioactive material from the body. Increasing fluid intake, or in some cases forcing fluids, may be sufficient treatment for a selected group of patients.

PERSONAL PROTECTION

There are no vaccines to prevent the harmful effects of large doses of ionizing radiation. Therefore, reducing exposure to the source of the radiation is the best preventive measure. This can be accomplished by reducing the amount of time in the vicinity of the source, increasing the distance from the source, and using shielding [22].

The radiation dose from a localized radiation source decreases by the square of the distance from it. For example, doubling the distance from the source will result in a dose rate one-fourth of the original dose. Going three times the distance will result in a dose rate of one-ninth the original dose rate.

Reducing the amount of time spent in the radiation field will obviously reduce the dose received. Appropriate shielding will also reduce the absorbed radiation dose. Heavy metals, such as lead, have typically been used to shield from x-rays, gamma rays, and other penetrating radiation. However, neutrons are best shielded by materials with high hydrogen content, such as waxes, concrete, or even water.

The same procedures of decontamination used for patients apply to healthcare professionals. To review, remove all potentially contaminated clothing and equipment and shower thoroughly with soap and water.

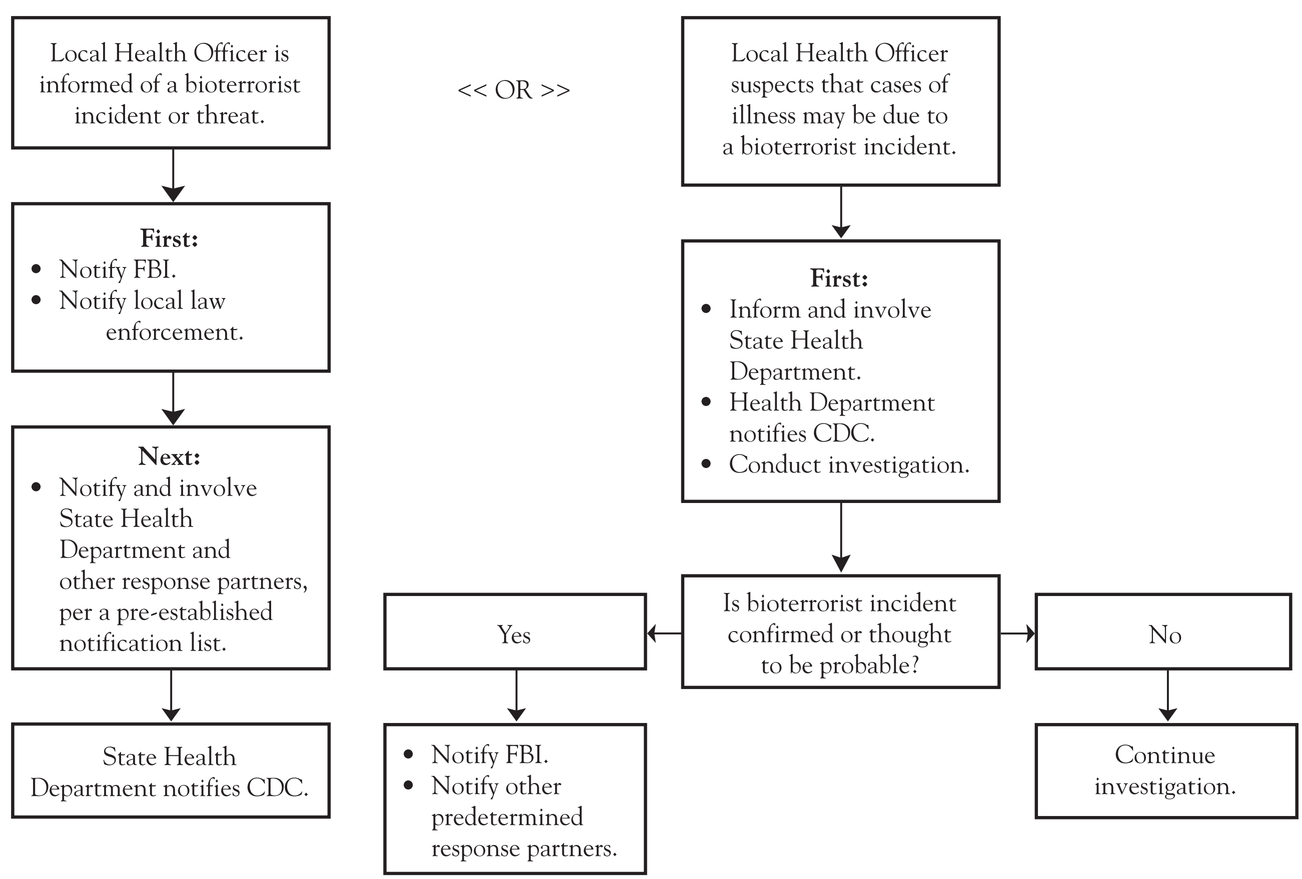
DETECTING AND MANAGING A BIOLOGICAL ATTACK

A thorough epidemiological investigation of a disease outbreak, whether natural or artificial, will assist healthcare professionals in identifying the pathogen and instituting appropriate medical interventions. The CDC realized this as early as 1951, when the Epidemic Intelligence Service was created to train epidemiologists in case a biological warfare attack took place against the U.S. during the Cold War [32]. Documenting who is affected, possible routes of exposure, signs and symptoms of disease, and the rapid identification of the causative agents will greatly increase the ability to plan an appropriate medical and public health response. Good epidemiological information will also allow the appropriate follow-up of those potentially exposed, as well as help determine public information guidelines and responses to the media [32].

The general steps for epidemiological assessment of any disease can be applied to a biological warfare or terrorist attack. First, public health authorities and healthcare personnel should formulate a case definition to determine the number of actual cases (verify the epidemic) and, from that, the approximate attack rate. The potential exists for hysteria to be confused with actual disease; therefore, objective criteria should be used to document the number of people affected. Once a case definition has been determined, description of the epidemic can be completed with respect to the timing, place, and characteristics of those who are ill. The investigation must be done expeditiously, but even rudimentary information can be of assistance in determining the source and potential consequences of an outbreak [32].

The disease pattern that develops is an important factor in differentiating between a natural epidemic and a terrorist or warfare attack. In most naturally occurring epidemics, there is a gradual rise in disease incidence as individuals are progressively exposed to an increasing number of patients, vectors, or fomites that spread the pathogen. In contrast, those exposed to a biological warfare attack would all come in contact with the agent at approximately the same time. Even taking into account varying incubation periods based on exposure dose and physiological differences, a compressed epidemic curve, with a peak in a matter of days or even hours, would occur [32].

PROTOCOLS: INTERIM RECOMMENDED NOTIFICATION PROCEDURE FOR LOCAL AND STATE PUBLIC HEALTH DEPARTMENT LEADERS IN THE EVENT OF A BIOTERRORIST INCIDENT



Source: [36] *Figure 2*

Other possible clues to a biological warfare or terrorist attack include the following [1; 32]:

- High disease rates among exposed individuals
- A naturally vector-borne disease occurring in an area that lacks the appropriate vectors for normal transmission
- More than one epidemic occurring at the same time
- Suspicious activity or discovery of a potential delivery system, such as a spray device
- Higher morbidity and mortality than normally expected for a disease
- A rapidly increasing disease incidence (hours or days) in a normally healthy population
- An epidemic curve rising and falling in a short period of time
- Unusual increase in people with fever or respiratory symptoms seeking treatment
- An endemic disease emerging quickly at an unusual time or geographic location
- Lower attack rates among people who had been indoors compared to those outdoors
- Clusters of patients arriving from a single locale
- Large numbers of rapidly fatal cases
- Any patient presenting with an uncommon disease, such as pneumonic anthrax, tularemia, or plague

Due to the rapid progression to illness and potential for dissemination of the agents, diagnostic laboratory confirmation may take too long. A response may be based on the recognition of high-risk syndromes that should alert healthcare practitioners to the possibility of a bioterrorism-related outbreak [32]. If an attack with biological agents is suspected, the proper authorities, whether military or civilian, should be notified immediately. Emergency response authorities should contact the CDC Emergency Preparedness and Response Branch at 770-488-7100 [36]. All others who suspect an emergency should call 911 ***(Figure 2)***.

APIC BIOTERRORISM READINESS PLAN

The Association for Professionals in Infection Control and Epidemiology (APIC) has prepared a review of some of the factors involved in managing a bioterror attack. A brief summary of their suggestions follow.

POSTEXPOSURE PROPHYLAXIS

Up-to-date prophylaxis recommendations should be obtained in consultation with local and state health departments and the CDC. Facilities should ensure that policies are in place to identify and manage healthcare workers exposed to infectious patients [1].

More specific recommendations, a reference list, a directory of FBI field offices, and a directory of State and Territorial Public Health Directors are included in the APIC Bioterrorism Readiness Plan, which can be found on the APIC website (http://www.apic.org) [1].

DISASTER PLANS

Every medical facility should have a plan in place to delineate how to deliver care in the event of a large-scale bioterrorist event. This disaster plan should be created with input from the infection control committee, administration, emergency department, laboratory directors, and nursing directors [1]. Processes for triage, safe housing, and care for potentially large numbers of affected individuals should be included in the bioterrorism plan. The needs of the facility will vary based on the size of the regional population served. Triage and management planning for large-scale events may include the following [1]:

- Establishing communication networks and lines of authority required to coordinate on-site care
- Planning for cancellation of nonemergency services and procedures
- Identifying sources able to supply vaccines, immune globulin, antibiotics, and antitoxins

- Planning for efficient evaluation and discharge of patients
- Developing discharge instructions for noninfectious patients
- Identifying sources for additional medical equipment and supplies
- Planning for the allocation or re-allocation of scarce equipment
- Determining the ability to handle a sudden increase in the number of cadavers on site

PSYCHOLOGICAL ASPECTS OF BIOTERRORISM

Fear and panic can be expected from patients and healthcare providers following a bioterrorism-related event [1]. Public mental health crises may be an issue, and horror, anger, unrealistic concerns about infection, and fear of contagion will have to be handled. Collaboration with emergency response agencies will be essential as will be working relationships with mental health support personnel [1].

Clearly explaining risks, offering careful, rapid medical evaluation, and avoiding unnecessary isolation for quarantine can minimize panic [1]. Anxiety can be treated with reassurance or anxiolytics [1]. Providing bioterrorism readiness education and inviting active, voluntary involvement in the planning process and in drills may alleviate staff fears [1].

PUBLIC INFORMATION

In the event of bioterrorism, clear, consistent information should be provided in fact sheets to patients, visitors, and the general public [1]. Visitors may be strictly limited, and the reasoning behind this should be explained. Facilities should plan in advance the methods of communication to inform the public. Failure to provide a public forum for information exchange has the danger of increasing anxiety and misunderstanding and increasing fear [1].

CONSIDERATIONS FOR NON-ENGLISH PROFICIENT PATIENTS

Obtaining a detailed patient history is a vital aspect of diagnosing many bioterrorism-related conditions, particularly those that are rare or that display similar signs and symptoms to other conditions. Furthermore, communication with patients regarding diagnostic procedures and treatment regimens depends on clear communication between the patient and clinician. When there is an obvious disconnect in the communication process between the practitioner and patient due to the patient's lack of proficiency in the English language, an interpreter is required. The interpreter should be considered an active agent in the diagnosis and/or treatment processes, negotiating between two cultures and assisting in promoting culturally competent communication and practice [38].

In the increasingly multicultural landscape of the United States, interpreters are a valuable resource to help bridge the communication and cultural gap between patients or caregivers and practitioners. Interpreters are more than passive agents who translate and transmit information from party to party. When they are enlisted and treated as part of the interdisciplinary clinical team, they serve as cultural brokers, who ultimately enhance the clinical encounter. When interacting with patients for whom English is a second language, the consideration of the use of an interpreter and/or patient education materials in their native language may improve understanding and outcomes.

RESOURCES

Association for Professionals in Infection Control and Epidemiology
http://www.apic.org

Centers for Disease Control and Prevention Emergency Preparedness and Response Branch
http://www.bt.cdc.gov

World Health Organization
http://www.who.int/topics/bioterrorism/en

Department of Homeland Security
http://www.dhs.gov

U.S. Federal Emergency Management Agency (FEMA)
http://www.fema.gov
1-800-621-3362

U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID)
http://www.usamriid.army.mil

U.S. Public Health Service Commissioned Corps
http://www.usphs.gov
1-877-463-6327

Institute for Biosecurity
http://bioterrorism.slu.edu

American Dental Association
http://www.ada.org/prof/resources/topics/bioterrorism.asp

American Red Cross
http://www.redcross.org
1-800-733-2767

Salvation Army
http://www.salvationarmyusa.org

CONCLUSION

Weapons of bioterror have been used since ancient times. As scientific knowledge has progressed, so has the sophistication of weaponry utilizing biological or radiological agents. As discussed, bacterial, viral, fungal, chemical, nuclear, and other biologically harmful materials have been devised for use as weapons of terror. They can be delivered by many means to both combatants and innocent civilians. Bombs, aerosols, and direct application of toxic materials are only some of the methods that have been used to cause injury. The ease with which these many harmful agents can be obtained, produced, and delivered is alarming. Conversely, the knowledge that they have been used so rarely in our history could be evidence that our fear of these weapons may actually be greater than the reality of their danger.

Fortunately, there has also been a considerable amount of research into the ways in which these weapons can be neutralized. In addition, antidotes, vaccines, and other means have been discovered to help protect the public or treat those who become victims of an attack. All medical personnel must be prepared with the knowledge and ability to perform their role as front-line respondents in the event that biological or radiological weapons are used.

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