BIOTERRORISM

PREPAREDNESS FOR HEALTHCARE PROFESSIONALS
BIOTERRORISM:
PREPAREDNESS FOR HEALTHCARE PROFESSIONALS

Course # 2028
Contact Hours: 5 Hours

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About the Author/Editor

Diana Harland, BS, CCRC, received her degree in Microbiology from the University of Texas at El Paso. She worked in pre-clinical research in retrovirology while in undergraduate school and again after graduation at Texas Biomedical Research Institute (formerly Southwest Foundation for Biomedical Research) in San Antonio, Texas. While at SWFBR, she worked in the department of Virology and Immunology at biosafety level 3-4 (BSL-3/BSL-4). She has extensive training in NIH, OSHA, and CDC guidelines for sterility and asepsis in tissue culture and retrovirology. She holds a certificate in bioterrorism from Tulane University School of Public Health and Tropical Medicine and the University of Alabama at Birmingham School of Public Health. She is a member of the Austin Disaster Relief Network (infrastructure for the city of Austin, TX disaster response) and the Association for Clinical Research Professionals.

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Purpose and Goals

The goal of this course to raise the level of preparedness by educating the healthcare professional in the agents of bioterrorism. Unfortunately, terrorism is not limited to biological hazards; there is also great concern regarding chemical terrorism, as well as radiological, and nuclear terrorism. This course will also briefly cover chemical, radiological and nuclear terrorism so that, should a biological or other hazardous incident occur (be it naturally occurring or intentionally driven), the healthcare worker can be instrumental in knowing how to handle, report, and effectively deal with these potentially deadly agents and situations.

Instructional Objectives

Upon completion of this course, the learner will be able to:
1. Define bioterrorism and the reasons why the threat of bioterrorism is a very real possibility in today’s society.
2. List the general characteristics of biological agents that make them effective in causing terror.
3. Relate how the CDC implements the Health Alert Network in the U.S.
5. List PPE required by first responders and state the correct procedure for decontamination of victims when victims of mass casualty incidents are brought to the hospital and the substance released is an unknown substance.
6. Identify anomalies that may signal the occurrence of a bioweapon attack.
7. Outline the reasons why category “A” agents of bioterrorism are given the highest priority by the CDC.
8. Explain why B. anthracis is so highly infectious, and define the three types of anthrax, including their clinical presentation, diagnosis, and treatment.
9. Describe criteria for pre-exposure vaccine for prevention, post exposure treatment and decontamination for Anthrax.
10. Describe the variola virus and the clinical presentation of smallpox as well as vaccination against the disease.
11. Compare and contrast the symptoms and treatment of plague and tularemia.
12. Recognize the types of botulism and their causes, and explain how botulism is treated.
13. Outline the viral hemorrhagic fevers, their epidemiology, and the isolation precautions necessary for healthcare workers.
14. Recognize the symptoms associated with chemical exposure and describe the process of chemical decontamination for victims of chemical emergencies.
15. Compare chemical versus nuclear explosions.
16. Explain the most important factors in protection from radiation and fallout, recognize the best locations for sheltering in place, and describe the symptoms of acute radiation syndrome.

Introduction

There has been much public concern over the years about the threat of bioterrorism. Bioterrorism is defined as the use of a biologic agent to intentionally cause disease against civilian populations for the purpose of creating terror. A biological agent is a living organism or other infectious agent that is capable of replicating in a host victim’s body. The U.S. military currently recognizes more than 10 different countries (including Russia, Iran, Syria, Israel, and North Korea) that are suspected of having offensive biological weapons programs in place.

In past years, the United States also possessed its own stockpile of bioweapons, including anthrax, until 1972 when the Biological and Toxin Weapons Convention (BTWC) treaty was signed by President Nixon. Under this treaty, nations are prohibited from developing, producing, or retaining (stockpiling) bioweapons or the equipment or means of delivering them. Unfortunately, there is no real way to monitor compliance, and evidence of biological weapons has even been found in certain countries that have signed this treaty.

Because the threat of public harm through the use of a biological agent is a very real possibility in today’s society, all Americans, especially those involved in healthcare, must be particularly vigilant. Experts on bioterrorism and disaster preparedness now agree that there is no longer a question of “if” an incident will occur but a question of “when” the next incident will occur. Healthcare workers may be required to take on the role of first responders who see patients with unusual symptoms, or act as first responders in the case of a mass casualty incident. They will play increasingly important roles in saving lives.
History

The use of bioweapons has occurred throughout history. Prior to 500 BC, the Assyrians poisoned enemy water wells with rye ergot (a fungus that infects rye and other grains), causing many symptoms of illness including hallucinations, psychosis, and mania in those who drank the water. In 1346, the Tartars captured corpses of persons who had died of plague over the city walls of Caffa (the city of Feodosiya in the present day Ukraine), contributing to the Black Death that took the lives of millions in Europe and killed an estimated 30 to 60 percent of the population. The first use of bioweapons in America came during the French and Indian War when Lord Jeffrey Amherst gave blankets infected with smallpox to the Indian allies of the French, causing deadly smallpox epidemics in the native population. More recently in 2001, anthrax was sent in envelopes through the mail to two U.S. Senators and to several different news media, infecting 22 people and killing five others.

Biological Agents and Terror

General Characteristics

The use of biological agents is especially good at causing terror in a population primarily because they are invisible to the human eye. These agents are also generally odorless, tasteless, and undetectable without the means of laboratory aids. They can be spread through air, food sources, water, surfaces, fomites (inanimate objects such as pens, toys, or doorknobs that are contaminated with an infectious organism and can serve in their transmission), or direct contact with an infected individual. It may take days for an infected individual to show symptoms of disease. Some agents, such as the bacteria responsible for anthrax or the bacteria responsible for botulism poisoning, can exist in a dormant endospore form that is resistant to heat, cold, radiation, drying, and even disinfectants for many years before causing infection. Furthermore, bioweapons are easier to obtain and to use than nuclear weapons. All these characteristics cause a great fear of the unknown, leaving the public feeling that they are vulnerable and out of control. Public panic is further fueled by misinformation, rumors, and the belief that resources are limited and available to only a select few of the population.

The U.S. Terrorism Advisory System

In January 2011, the United States Department of Homeland Security (DHS) announced a new terrorism advisory scale called the National Terrorism Advisory System (NTAS). Under this new system, the public is to be alerted with whatever information Homeland Security is able to give so that the public can protect itself at the individual, family, and community levels. Alerts are to be issued under the categories of either elevated (credible terrorist threat against the United States) or imminent (credible, specific, and impending threat against the United States). Information on threat assessment and steps to take in response to threats are to be given through the use of news media and social media networks. A sunset provision is also included, which means individual threat alerts will be issued for a specific time period and then will expire unless the threat evolves or new information becomes available.

The Health Alert Network

The Health Alert Network (HAN), sponsored by the Centers for Disease Control (CDC), is a program that provides vital health information and the infrastructure to support the dissemination of that information at state and local levels and beyond. Currently, all 50 states, 8 territories, the District of Columbia, and several large city and county health departments are all connected to the HAN. According to the CDC, a vast majority of state-based HAN programs have over 90% of their population covered under the umbrella of HAN.

The HAN also ensures that each community has:

• rapid and timely access to emergent health information
• a group of highly trained professional personnel
• evidence-based practices and procedures for effective public health preparedness, response, and service on a 24/7 basis

The HAN Messaging System directly and indirectly transmits various types of messages via email or RSS feed to over one million recipients. Messages are categorized based on level of importance as follows:

1. Health Alerts: Highest level of importance that warrants immediate attention.
2. Health Advisories: Important information for a specific incident or situation that may not require immediate action.
3. Health Updates: Information regarding an incident or situation that is unlikely to require immediate action.
4. Info Service Messages: General information that is not necessarily considered to be of an emergent nature.

Healthcare professionals can be added to the HAN by using the link http://www.bt.cdc.gov/HAN/updates.asp available at the CDC website and following the directions to enter a recipient’s email address, information preferences, state, and zip code.

The Biowatch Program

The Biowatch program began after the U.S. anthrax attacks in 2001. It consists of a system of filters placed within existing Environmental Protection Agency (EPA) filters that monitor air quality. These filters, located in major metropolitan cities, can detect pathogens released into the air and thus provide warning of a potential bioterrorism event. Analysis of filter contents is done at state and local levels and is coordinated by the CDC. More information is available at the DHS website at www.dhs.gov.

The Strategic National Stockpile

Figure 1: Unmarked truck with supplies from the SNS. Photo taken from the CDC.
The Strategic National Stockpile (SNS) is managed by both the Department of Health and Human Services (HHS) and the Department of Homeland Security (DHS). In the event of an emergency, the U.S. holds a reserve supply of vaccines, antibiotics, chemical antidotes, life support medications, and medical/surgical supplies that are warehoused in armed, guarded, unmarked, and classified geographic locations throughout the country. Should a bioweapon attack occur, needed supplies can be deployed wherever necessary. In the early hours of an event, Push Packages consisting of pharmaceuticals, medical supplies, and antidotes can be delivered where necessary within 12 hours of federal request (see Figure 1). If more pharmaceuticals or supplies are needed, Vendor Managed Inventory (VMI) is structured to have additional supplies arrive within 24-36 hours. All supplies from the SNS are free to those populations in need.

The Ideal Bioweapon

As a rule, bioweapons are unreliable, and when used they carry a high level of uncertainty as to the outcome of a battle. There is also high collateral damage associated with their use. To be an ideal bioweapon, the agent of choice would need to be both highly infective and highly virulent, with no available vaccine. An ideal bioagent would also have to be 5µ or smaller in size so that inhalation of the agent would cause it to go into the lung alveoli. Once there, it could be quickly ingested by phagocytosis of alveolar macrophages, making it difficult for the body to eliminate it. Agents that have a particle size of 20µ or more are taken up by mucous flow and transported to the digestive tract where elimination by the body is much easier.

Methods of Delivery for Bioweapons

The goal or challenge of bioweapon delivery is to deliver the agent in a swift manner and with the greatest strategic effect. Bioweapons can be delivered through aerosolization, through animals, through food and water contamination, through the postal system (as in the 2001 anthrax spores mailed through the U.S. postal system), and through person to person contact. The most favored of these methods is aerosolization.

### Table 1: Minimum Personal Protective Equipment Required for Hospital-based First Receivers of Victims from Mass Casualty Incidents Involving the Release of Unknown Hazardous Substances

<table>
<thead>
<tr>
<th>ZONE</th>
<th>MINIMUM PPE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hospital Decontamination Zone</strong></td>
<td>1. Powered air-purifying respirator (PAPR) that provides a protection factor of 1,000. The respirator must be NIOSH-approved.</td>
</tr>
<tr>
<td></td>
<td>2. Combination 99.97% high-efficiency particulate air (HEPA)/organic vapor/acid gas respirator cartridges (also NIOSH-approved).</td>
</tr>
<tr>
<td></td>
<td>3. Double layer protective gloves.</td>
</tr>
<tr>
<td></td>
<td>4. Chemical resistant suit.</td>
</tr>
<tr>
<td></td>
<td>5. Head covering and eye/face protection (if not part of the respirator).</td>
</tr>
<tr>
<td></td>
<td>7. Suit openings sealed with tape.</td>
</tr>
<tr>
<td><strong>Hospital Post-decontamination Zone</strong></td>
<td>1. Normal work clothes and PPE, as necessary, for infection control purposes (e.g., gloves, gown, and appropriate respirator).</td>
</tr>
</tbody>
</table>

Source: OSHA Best Practices for Hospital-based First Receivers of Victims from Mass Casualty Incidents Involving the Release of Hazardous Substances

Personal Protective Equipment and Decontamination

Each healthcare facility should have in place a Hazard Vulnerability Analysis (HVA) [required by the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) for accreditation of healthcare facilities], and an Emergency Management Plan (EMP). These must both be conducted/developed and updated within the last year and tailored to each individual facility. Because healthcare facilities may have limited information on an agent that has been released, these facilities must conduct research on hazard assessments for the basis of proper Personal Protective Equipment (PPE) selection. PPE selection must be for a wide range of substances since no material will protect against all possible hazards.

Table 1 shows the minimum PPE recommended by OSHA for first receivers when the area covered is not the release site of the agent, the hazardous substance is unknown, and other eligibility conditions have been met (for conditions see the OSHA website at http://www.osha.gov/dts/osta/bestpractices/html/hospital_firstreceivers.html#3). Hospitals
must use National Institute of Occupational Safety and Health (a division of the CDC) NIOSH-approved CBRN (chemical, biological, radiological, and nuclear) respirators when the HVA reveals a potential weapon of mass destruction threat. No healthcare worker should wear or use specialized PPE or respiratory protective equipment without proper training and fit testing.

The Occupational Safety and Health Administration (OSHA) has identified healthcare workers at a hospital or healthcare facility who receive victims contaminated during a mass casualty incident for treatment as first receivers. This distinguishes them from first responders that include firefighters, law enforcement, and emergency medical personnel. OSHA has published best practice guidelines that help healthcare facilities select the minimum PPE that OSHA anticipates generally will be needed to protect first receivers faced with a wide range of unknown hazards. The guidelines cover protection for first receivers during overt releases of biological agents, as well as releases of chemicals and radiological particles that may produce victims who may need decontamination prior to administration of medical care. The guidelines are intended for mass casualty incidents as they affect first receivers at hospitals, but concepts can also apply to mobile casualty care facilities and temporary shelters should a catastrophic incident occur that involves thousands of victims. Assumptions are made by OSHA that the hospital or healthcare facility is not the primary incident site and that exposure comes from victims, their clothing, and their personal belongings, rather than the location where the hazardous substance was released.

One of the most important factors in consideration of PPE for the healthcare worker is to limit the amount of toxic agent to which he/she is exposed. When victims have been exposed to a hazardous substance, OSHA recommends the first step in the decontamination process to be removal of the victim’s clothing by cutting it away with blunt-nose shears to avoid any further unnecessary exposure to the victim or the worker. Clothing removal is estimated to remove 75-90% of the contaminant on the victim. Contaminated clothing and possessions should then be placed in an approved hazardous waste container that is isolated outdoors. The second step is showering of the victim with tepid water and a liquid soap that has good surfactant properties but is not harsh on skin (good examples are hand or dishwashing soaps such as Joy, Dawn, Ivory, and various shampooes) for a minimum of 5 minutes under running water. Scrubbing should proceed downward from head to toes to remove the contaminant from the hair and skin. This step is also promoted by the U.S. Army for removal of biological agents as well as chemical agents and radiological particles. Lastly, to further minimize exposure, first responders should remove all PPE (see Table 2) and shower themselves. PPE and showers also be decontaminated.

Table 2 shows the recommended procedure for removing PPE and decontamination as outlined by the U.S. Department of Health and Human Services Agency for Toxic Substances and Disease Registry (ASTDR).


### Biosafety Levels

The CDC and the National Institute of Health (NIH) have specified certain biocontainment or lab biosafety levels (levels of precaution that prevent workers from infection) necessary to identify and research various pathogenic agents. A summary of the biosafety levels BSL-1 through BSL-4 is shown in Table 3.
Recognizing a Bioweapon Attack

With the exception of smallpox, all of the potential category A agents (see the section entitled Category “A” Agents of Bioterrorism) are originally diseases of animals. Should a bioweapon attack occur, it is very likely that animal populations will become ill either before illness is seen in humans or simultaneously as humans become ill. A bioweapon attack may have unusual circumstances or characteristics that are not normally seen with a particular disease. Because of potentially long incubation periods, persons who become ill may not seek care for days or weeks. Healthcare workers may be one of the first groups to observe such anomalies and should be aware of anything unusual. **Table 4** lists anomalies that may signal the occurrence of a bioweapon attack.

Reporting Suspected Cases or Exposure to a Bioterrorist Agent

Each facility should have in place procedures for reporting of any suspected or confirmed cases or any exposure of patients or staff to a bioterrorist agent. Immediate notification to local and state public health agencies is required. A list

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**Table 3: Summary of Recommended Biosafety Levels for Infectious Agents**

<table>
<thead>
<tr>
<th>BSL</th>
<th>Agents</th>
<th>Practices</th>
<th>Primary Barriers and Safety Equipment</th>
<th>Facilities (Secondary Barriers)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Not known to consistently cause diseases in healthy adults</td>
<td>Standard microbiological practices</td>
<td>No primary barriers required</td>
<td>Laboratory bench and sink required</td>
</tr>
<tr>
<td></td>
<td>Agents associated with human disease</td>
<td>BSL-1 practice plus:</td>
<td>PPE, laboratory coats and gloves; eye, face protection, as needed</td>
<td>BSL-1 plus:</td>
</tr>
<tr>
<td></td>
<td>Routes of transmission include parenteral injury, ingestion, mucous membrane exposure</td>
<td>Limited access, biohazard warning signs, “Sharps” precautions</td>
<td>Primary barriers: BSCs or other physical containment devices used for all manipulations of agents that cause splashes or aerosols of infectious materials</td>
<td>Autoclave available</td>
</tr>
<tr>
<td>2</td>
<td>Indigenous or exotic agents that may cause serious or potentially lethal disease through the inhalation route of exposure</td>
<td>BSL-2 practice plus: Controlled access, Decontamination of all waste, Decontamination of laboratory clothing before laundering</td>
<td>Primary barriers: PPE: Protective laboratory clothing, gloves, face, eye and respiratory protection, as needed</td>
<td>BSL-2 plus: Physical separation from access corridors, Self-closing, double-door access, Exhausted air not recirculated</td>
</tr>
<tr>
<td></td>
<td>Dangerous/exotic agents which post high individual risk of aerosol-transmitted laboratory infections that are frequently fatal, for which there are no vaccines or treatments</td>
<td>BSL-3 practice plus: Clothing change before entering, Shower on exit, All material decontaminated on exit from facility</td>
<td>BSL-3 plus: All procedures conducted in Class III BSCs or Class I or II BSCs in combination with full-body, air-supplied, positive pressure suit</td>
<td></td>
</tr>
</tbody>
</table>

**Table 4: Anomalies That May Signal the Occurrence of a Bioweapon Attack**

1. Dead animals, especially if there are multiple animal species involved.
2. A disease with no natural vector present, for example, plague in the absence of rats or fleas.
3. Unusual illnesses in certain populations or certain age groups.
4. Groups of people with the same disease in geographical areas that are not adjacent or near to each other.
5. Groups of people who were indoors and are ill or show higher morbidity than those people who were outdoors, indicating an indoor attack. Conversely, groups of people who were outdoors who are ill or show higher morbidity than those people who were indoors, indicating an outdoor attack.
6. A disease that occurs in an unusual geographic area.
7. A large number of persons with the same disease.
8. A disease in a population at an unusual time of the year, for example, flu in the summer months.
9. A disease with a shorter incubation than is normally expected, indicating that persons have been exposed to higher amounts of an agent than in a natural occurrence.
10. A disease that is not normally antibiotic resistant and now shows antibiotic resistance.
11. A disease that shows failure to respond to usual therapy.
12. A disease caused by an unusual or different strain of an organism than what is normally seen.
13. A disease caused by an unknown organism.
14. A disease that has been transmitted in an unusual way, especially if the transmission route involves food or water.
15. A disease that is common but now shows a higher morbidity than usual or mortality where it is not expected.
17. A single case of an uncommon disease such as smallpox or inhalational anthrax.
18. Any unexplained diseases or deaths.

Table taken from U.S. Department of Health and Human Services, CDC and NIH Biosafety in Microbiological and Biomedical Laboratories 5th ed.
of state health departments can be found through the CDC website at http://www.cdc.gov/mmwr/international/relres.html. The CDC Division of Bioterrorism Preparedness and Response can be reached at 404-639-0385. The CDC also maintains a 24/7 Emergency Operations Center, telephone number 770-488-7100, for healthcare professionals and government officials (local, state, and federal agencies) to assist with questions on emergency patient care. It is not for the general public, who are instead advised to call 911 in the event of an emergency.

Classification of Agents of Bioterrorism

Category “A” Agents of Bioterrorism

There are literally thousands of microbes that could potentially be used in an attack of bioterrorism. Of particular concern, as established by the CDC, are the agents classified as Category “A” agents of bioterrorism. These microbes are given the highest priority because:
1. They are easily transmitted from person to person or are easily dispersed.
2. They result in high morbidity and high mortality rates.
3. They have the potential to cause widespread panic and social disruption of the public.
4. They require special preparedness to deal with should an outbreak occur.

Category A agents of bioterrorism include:
1. Bacillus anthracis—Anthrax
2. Variola major, Variola minor—Smallpox
3. Yersinia pestis—Plague
4. Francisella tularensis—Tularemia
5. Clostridium botulinum—Boothenism
6. The Viral Hemorrhagic Fevers
   a. Filoviruses—Ebola hemorrhagic fever; Marburg fever
   b. Arenaviruses—Lassa fever; Argentine hemorrhagic fever; Bolivian hemorrhagic fever; Venezuelan hemorrhagic fever; Brazilian hemorrhagic fever, etc.

Because the CDC considers these microbes to be of the highest priority, this course will focus on the Category “A” agents, with particular attention to anthrax and smallpox.

Category “B” Agents of Bioterrorism

Agents with a categorization of second highest priority are classified as Category “B” agents of bioterrorism. These agents are moderately easy to disperse, their infection results in a moderate degree of morbidity with low mortality, and their outbreak will cause the CDC to enhance its diagnostic capacity and disease surveillance. These agents include:
1. Brucellosis spp.—Brucellosis
2. Clostridium perfringens—Epsilon toxin
3. Salmonella spp.; Escherichia coli; Shigella spp.—Foodborne illness safety threats
4. Burkholderia mallei—Glanders
5. Burkholderia pseudomallei—Meliodosis
6. Chlamydia psittaci—Psittacosis
7. Coxiella burnetti—Q fever
8. Ricinus communis—Ricin toxin
9. Staphylococcal enterotoxin B—produces a multi-symptom disease resembling sepsis (e.g., Toxic shock syndrome)
10. Rickettsia prowazekii—Typhus fever
11. Alphaviruses—Viral encephalitis
12. Vibrio cholera; Cryptosporidium parvum—Waterborne illness safety threats

Category “C” Agents of Bioterrorism

The third highest priority agents are classified as Category “C” agents of bioterrorism. These microbes have the potential to be engineered for large scale use because they are readily available and can be easily produced and disseminated. An attack with agents from this category would produce high morbidity and mortality. Agents include emerging microbes such as Nipah virus and Hantavirus.

The Category “A” Agents

Anthrax

Etiology

Anthrax is a zoonotic disease primarily found in cattle, sheep, horses, and goats. The name anthrax means “coal” in Greek and was named for the coal black-colored lesions that are classic of the cutaneous form of the disease. Anthrax is caused by the bacterium Bacillus anthracis, a Gram-positive, non-motile, spore-forming rod that is typically seen in boxcar formation. Anthrax is a toxin-mediated disease, meaning it is the toxin produced by the bacteria, not the bacteria itself, that causes injury. B. anthracis produces a capsule that prevents leukocytes from being able to phagocytize or lyse it, and it also produces three proteins known as protective antigen (PA), lethal factor (LF), and edema factor (EF). Alone, the three proteins are not toxic, but in combination in the body they are responsible for massive bleeding, edema, tissue destruction, and ultimate death of the infected person. All these characteristics together explain why these bacteria can produce such a rapid, severe, and potentially fatal disease and why body defenses are unable to overcome them.

Epidemiology

Anthrax is spread by spores; it is not known to be spread by human-to-human contact. Humans can contract anthrax through the handling of products from infected animals (such as wool and hides) when spores invade the skin via scratches and wounds. Anthrax can also be contracted through the consumption of the insufficiently cooked meat of an infected animal, through direct inhalation of the spores, and through the bites of flies. The endospores of B. anthracis can live in the soil for decades and still return to their vegetative (active and therefore infectious) state. For humans, the greatest risk for contracting anthrax is through aerosolization of spores.

There are 20,000 to 100,000 cases of anthrax worldwide per year, occurring primarily in the developing countries. Anthrax is rare in the U.S. because very few animals are infected due to routine
inspection of animals and slaughterhouses.

Clinical Presentation, Diagnosis, and Treatment

A. Cutaneous Anthrax

This form of infection accounts for 95% of cases. Itching of the affected area occurs a few hours after initial inoculation. A painless hemorrhagic papule then develops after 1-12 days (average of 7 days), followed by an ulcer. As the ulcer dries, a black scar or eschar forms, and this will fall off in 1-2 weeks and heal with possible scarring (see Figures 2-4).

Diagnosis is made in part based on the presence of a painless ulcer. Spider bites can be differentiated because these lesions are typically painful. Gram stains and bacterial cultures of the lesion may be obtained. A blood culture should be collected in all patients.

Treatment of bioterrorism-related cutaneous anthrax consists of a 60 day course of first-line therapy oral antibiotics ciprofloxacin or doxycycline. It is important that lesions be kept clean and covered and that all contaminated dressings are properly handled and disposed. Isolation precautions are standard with added contact precautions if wound drainage is excessive. If there are signs of systemic involvement, extensive edema, or if lesions are present on the head or neck, treatment is intravenous therapy with a multidrug regimen that includes ciprofloxacin, followed by oral therapy. Naturally acquired cutaneous anthrax can be treated with oral ciprofloxacin or doxycycline for 7-10 days in uncomplicated cases. There is less than 1% mortality in treated cases.

B. Gastrointestinal Anthrax

This form of anthrax is rare, accounting for less than 1% of all anthrax cases, and results from consumption of the meat of infected animals. Infection may involve the intestines (intestinal anthrax) or the mouth or throat (oropharyngeal anthrax). The incubation period is 1 to 6 days.

Symptoms of intestinal anthrax begin with nausea, vomiting, abdominal pain, and fever. As time progresses, there is an increase of watery diarrhea, then massive amounts of bloody diarrhea, and extreme exhaustion. Edema is present in the lower trunk. This type of anthrax is very difficult to diagnose. Cases can still be treated at the point of bloody diarrhea if the treatment is extremely aggressive. Without treatment, there is cyanosis and death. The mortality rate is 20-60%.

Symptoms of oropharyngeal anthrax include extreme throat pain, enlarged cervical lymph nodes, and difficulty swallowing. Ulcers may be seen in the throat or mouth. An airway must be placed in the patient at the point where there is difficulty in swallowing because, as the infection progresses, there is great edema of the neck and submandibular areas.

Treatment of GI anthrax is not well documented but should consist of an aggressive intravenous multi-drug antibiotic therapy with ciprofloxacin as the primary antibiotic, and one to two additional antimicrobials followed by at least 60 days of oral therapy. Isolation precautions are standard.

C. Inhalation Anthrax

Inhalation anthrax has two phases. Phase one begins with a flu-like upper respiratory illness. Symptoms include mild fever, fatigue, a non-productive cough, and malaise. Substantial chest discomfort and shortness of breath (dyspnea) may be present. After a few days, there is slight improvement. Phase two progresses rapidly and results in death within 24 hours. Symptoms include nausea, vomiting, severe respiratory distress, cyanosis, edema of the chest and neck, and cardiovascular collapse. The lungs and alveoli are destroyed. Death results from suffocation and effects of the toxin.

Diagnosis at the onset of disease is difficult because of its non-specific flu-like presentation. A thorough patient history is essential to determine if exposure to spores may have occurred. A key symptom of phase one is dyspnea (shortness of breath), which is present in only 6% of influenza cases. Inhalation anthrax from the 2001 U.S. postal cases showed an 81% incidence of dyspnea. Substantial chest discomfort is also more common in inhalation anthrax than in cases of influenza. The classic chest radiograph will show mediastinal widening that is due to hemorrhage and massive edema. This results from the exotoxin released by increasing concentrations of anthrac bacilli in the regional lymph nodes that drain pulmonary alveoli. This is an important indication of inhalation anthrax. If a CT scan is done, it will show hemorrhagic mediastinitis (inflammation of the tissues of the mediastinum), and this is diagnostic of inhalation anthrax. A blood culture should always be taken because B. anthracis is present in blood cultures even in the early stage of the disease.

Treatment of inhalation anthrax is also an intravenous multidrug therapy with ciprofloxacin (recommended over doxycycline) as the primary antibiotic, and one to two additional antimicrobials with good CNS penetration, followed by at least 60 days of oral therapy. Isolation precautions are standard. Without treatment, mortality is nearly 100%, and with treatment mortality is 75%.

D. Complications of Anthrax Infection

Septicemic anthrax is due to invasion of the anthrax bacilli into the bloodstream and may be secondary to infection of any of the above types of anthrax but more frequently follows inhalation or gastrointestinal anthrax. Untreated cases of cutaneous anthrax will progress to septicemic anthrax in 1 in 5 or 20% of cases. Symptoms include edema of the head and neck that interferes with breathing, swallowing,
and vision. Infection is spread along lymphatic channels. The treatment for septicemic anthrax is a very aggressive course of intravenous antibiotic therapy with a multidrug regimen that includes ciprofloxacin (unless contraindicated), followed by oral therapy.

Anthrax meningitis may also result from any form of anthrax as bacilli spread to the central nervous system. CNS tissues become hemorrhagic and filled with edema. Symptoms include fever, deteriorating mental function, and seizures. Death can result in as few as 2-4 days. Mortality is about 100%.

E. Important Notes about Anthrax Medications

Originally, penicillin was considered to be a first-line antibiotic for treatment of anthrax. After the 2001 postal anthrax attacks, however, this has changed. Naturally occurring isolates of B. anthracis have been shown to produce the class of enzymes known as beta-lactamases that inactivate penicillins, cephalosporins, and similar antimicrobial drugs. Isolates of B. anthracis have also been shown to contain the presence of cephaparinase and penicillinase. Therefore, especially in the case of bioterrorism, penicillin alone is not recommended because of the potential for genetically altered B. anthracis. The CDC recommends ciprofloxacin and doxycycline as first line antibiotics, with preference for ciprofloxacin in any severe cases. In cases of meningitis or CNS involvement, doxycycline should not be used because it has poor penetration of the CNS. Consultation with infectious disease specialists at the CDC is highly recommended for treatment of any cases involving anthrax.

F. Pre-exposure Prophylaxis

An FDA-licensed anthrax vaccine, Anthrax Vaccine Adsorbed (AVA), is available in the U.S. for pre-exposure human use in individuals between 18 and 65 years of age and is known by the trade name BioThrax. It is not licensed for postexposure use. The U.S. Department of Defense recommends all military personnel be vaccinated against anthrax. The Advisory Committee for Immunization Practices (ACIP), a panel of experts selected by the Secretary of the HHS to provide advice to the CDC, also recommends the vaccine for anyone in the workplace who has contact with imported animal hides, furs, wool, bone meal, bristles, and animal hair (especially goat hair), as well as all persons who engage in diagnostic or investigational activities involving anthrax spores. Pregnant women should not be vaccinated because effects on the fetus are not known. The vaccine course consists of two intramuscular injections, given at 0 and 4 weeks, then three additional injections given at 6, 12, and 18 months. To maintain immunity, annual booster injections are also needed.

Currently, the U.S. holds a reserve of BioThrax vaccine in the Strategic National Stockpile. There are no commercially available doses of anthrax vaccine; all anthrax vaccine is owned and managed by the US Department of Defense. The shelf life for BioThrax is three years.

At the present time, no antibiotics are approved for pre-exposure prophylaxis to anthrax spores.

Antitoxin known as Anthrax Immune Globin (AIG), made from plasma that is taken from individuals who were previously immunized with anthrax vaccine, is available in the SNS. It can be used in addition to antibiotic therapy to treat persons showing anthrax symptoms. A monoclonal antibody called Raxibacumab (under the trade name ABthrax) that targets anthrax toxin at the point when antibiotics may no longer be effective is also available in the SNS. It is reported to improve survival rates by 64% in animal studies.

G. Postexposure Prophylaxis

For postexposure prophylaxis (PEP) of potential inhalational exposure, the CDC recommends decontamination if necessary, followed by vaccination (although the vaccine is not licensed for PEP) and antibiotic treatment. Vaccination, which in cases of bioterrorism would be available under an Investigational New Drug (IND) protocol, consists of three doses of BioThrax given at week 0, week 2, and week 4. In asymptomatic individuals, a 60 day course of ciprofloxacin with doxycycline (or other tetracycline) or penicillin is recommended. The 60 days of therapy has been considered critical and should never be reduced because of the potential spore formation of B. anthracis. Anthrax is known to recur up to 57 days after initial infection in similar studies.

Research by the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) and the National Institute of Allergy and Infectious Diseases (NIAID) has shown that when anthrax vaccine is administered with a short-term 14 day combination of antibiotics beginning one to two hours postexposure, non-human primates were completely protected from inhalation anthrax. More information can be found at http://www.pnas.org/content/103/20/7813.full. Regardless of the course duration of antibiotics, immediate prophylaxis of cases of potential exposure will be of utmost importance.

H. Decontamination of Anthrax

Handwashing with soap and water, followed by showering with soap and water, is the recommended method for decontamination of any persons who have come into contact with sources of potential B. anthracis spores. The use of bleach has not shown any advantages over soap and water. Sources of spores such as clothing, shoes, and so on, should be identified. Clothing or other potentially contaminated materials should be triple bagged in plastic bags before transportation, then incinerated or autoclaved.

The CDC recommends a 1:10 bleach solution (one part household bleach containing 5.25% sodium hypochlorite to nine parts water) as an effective sporidical solution to decontaminate any work surfaces, or surfaces confirmed to have contamination. Other approved sporidical agents may also be used. Non-sterilizable equipment should be routinely cleaned with a sporidical agent. Items that can be autoclaved should first be soaked in a sporidical solution, then autoclaved.

If there is an accidental contamination from fresh clinical samples, the area should be flooded with sporidical solution, soaked for at least 5 minutes, and then cleaned. Areas involved in accidental contamination of samples with large concentrations of spores, such as lab specimens (e.g., blood cultures or culture plates), areas with accidents that involve organic matter, or areas with contamination where there is a temperature, lower than room temperature should be gently covered to avoid aerosolization. A sporidical solution should then be liberally applied to the area and left to soak for
1 hour before cleaning. Soiled cleaning materials should be autoclaved. All cultures, infected material, or suspect material should be incinerated or autoclaved. It should be noted that boiling at 100°C does NOT kill endospores; they are known to survive for hours at boiling temperatures.

1. Reporting of Anthrax Cases

Public health and law enforcement officials should be notified immediately if a case of anthrax is diagnosed or suspected. It is essential that any lab that will be handling specimens suspected of containing anthrax be notified because clinical specimens must be handled at biosafety level 2 (BSL-2) or at biosafety level 3 (BSL-3) if higher concentrations are handled or if screening involves environmental samples (especially powders) from anthrax contaminated locations. It is also important to alert the diagnostic lab so that the suspect agent can be properly identified because Bacillus is generally considered to be a contaminant and is normally not tested.

Smallpox

Etiology

Smallpox is caused by either of the double stranded DNA, brick-shaped viruses Variola major or Variola minor, members of the orthopoxvirus family. Variola major causes a more severe form of the disease with a more severe rash, higher fever, and up to 30% mortality. V. major accounts for four types of infection:

1. Ordinary: most frequent; accounts for 90% of cases
2. Modified: mildest and occurring in previously vaccinated persons
3. Flat: lesions do not project above the skin surface; rare, severe, and usually fatal
4. Hemorrhagic: hemorrhages occur in the skin and mucous membranes; rare, severe, and usually fatal

Variola minor causes a less severe form of the disease with less than 1% mortality. Smallpox virus infects only humans and has no animal reservoir.

Epidemiology

Cases of smallpox have been documented throughout history, and this disease is one of the most devastating diseases known to mankind. It is believed that the mummiﬁed remains of Ramses V of Egypt (reigned from 1149-1145 BC) show that he died of smallpox infection, making this pharaoh the oldest known victim with actual visible signs of the pox pustules. Smallpox has shown great morbidity and mortality throughout the ages and has even destroyed entire civilizations including the Incas, the Aztecs, and many Native American tribes. In survivors, blindness, osteomyelitis, arthritis, and disﬁguring scars were common. Because there is no treatment for smallpox, vaccination is the only way to prevent the disease. After great efforts through vaccination programs, the World Health Organization (WHO) declared smallpox to be eradicated in 1979. There is now no variola virus in the world except for the virus stored in laboratory stockpiles. The only two WHO authorized reference sites are the CDC in Atlanta, GA, and the VECTOR institute in Koltsovo, Russia.

Smallpox is spread through ﬂuids and scabs from the pustules characteristic of the disease (see Figure 5), and requires prolonged face-to-face contact. Since pustules ﬁrst form in the mouth, saliva that is spread through coughing, sneezing, speaking, or breathing can transmit the virus to others. Although indirect contact is less efﬁcient for the virus to spread, fomites may also spread the virus. It is uncertain if genetically engineered smallpox virus would be spread in the same manner as the naturally occurring virus. The incubation period is 7 to 17 days, with an average of 12 to 14 days postexposure for symptoms to begin. During this incubation, people are not contagious. The greatest problem faced by epidemiologists, however, is the fact that identiﬁcation of the index case (the ﬁrst person found to have the disease leading to the diagnosis of others with the same disease in a population) occurs weeks postexposure, and by the time a diagnosis is made, there may have been many persons exposed. It is most likely that variola would be released by airborne dispersion if used as a bioweapon.

Clinical Presentation, Diagnosis, and Treatment

Smallpox begins with an acute ful-like prodrome phase which can last up to 4 days. Symptoms can include high fever (101-104°F), chills, back pain, body aches, headache, vomiting, abdominal pain, malaise, and rigors. Patients are possibly contagious. The next phase is early rash when small red spots appear on the mouth and tongue. Persons are highly contagious at this time. As mouth sores break down, rash appears on the skin and can spread to all body parts in 24 hours. Fever may fall and the patient feels better. It should be noted here that patients are contagious in all phases involving rash. After the 3rd day, the rash becomes raised pustules. On the 4th day, the bumps become filled with thick, opaque ﬂuid and have a characteristic depression in the center (like a “belly button”) that is diagnostic of smallpox. Fever will usually rise again and remain until scabs form. A pustular rash phase, lasting about 5 days, follows as bumps become sharply raised pustules that are round and ﬁrm. The lesions are in the deep layers of skin and feel hard as if an object is embedded there. Next is the pustules and scabs phase, lasting
another 5 days, when pustules form a crust and then a scab. Most pustules will have scabs by the end of the second week of rash. A Resolving Scabs phase follows, lasting about 6 days. As scabs fall off, the area on the skin will eventually become a pitted scar. The person is considered no longer contagious when the last scab is gone. The total disease duration is about 4 weeks.

Smallpox can be differentiated from chicken pox by the pattern of rash on the body (see Figure 6). Smallpox is distributed in centrifugal fashion, with lesions appearing on the periphery of the body. The rash is common on the palms and soles. Chickenpox rash is distributed in centripetal fashion, with more rash appearing on the trunk, and few or no lesions on the palms and soles. Chickenpox can also be distinguished from smallpox because the fever begins at the same time as the rash (as opposed to smallpox with a 2-4 day fever Prodromal stage and no lesions), and the lesions will be in different stages (as opposed to smallpox with lesions all in the same stage). Diagnosis is made by patient history of a prodromal stage prior to rash, with fever greater than 102°F, and at least one symptom including headache, backache, vomiting, chills, or abdominal pain. Observation of the lesions characteristic of smallpox with lesions all in the same stage of development are also diagnostic. Any samples sent for laboratory identification must be collected by a previously vaccinated individual and examined only at a designated biosafety level 4 (BSL-4) laboratory. Any cases of suspected smallpox must be immediately reported to public health officials. Infectious disease specialists at the CDC should be consulted.

There is no treatment for smallpox. Patients can be managed with supportive care and should be isolated until all scabs have separated. It is debatable whether vaccinia immunoglobulin (VIG) is helpful in severe cases.

Vaccination

Routine vaccination of Americans was ended in 1972. At present, there is uncertainty as to whether or not there is any residual immunity in persons vaccinated prior to 1972; therefore, the CDC considers these persons to be susceptible. In the event of an attack of bioterrorism using smallpox, vaccination of any persons exposed to the virus is highly recommended. The CDC has stated that vaccination within 3 days of exposure will prevent or significantly lessen the severity of smallpox symptoms in the vast majority of people, and vaccination 4-7 days postexposure likely offers some protection from the disease or may modify the severity of disease. An outbreak of smallpox can be halted by vaccinating a “ring” of people around each case and their contacts. Mass vaccination of the public is only a last resort.

The available vaccine (either ACAM2000 or Dryvax) is made with live attenuated (decreased pathogenicity) vaccinia virus, not variola virus. Vaccination is done on the deltoid (recommended by the CDC) with a bifurcated needle. A vaccination is considered successful if there is a “take” or sufficient reaction induced. The take consists of papule and vesicle formation, followed by a well-formed pustule, then a scab, and finally scab detachment and a resulting scar. In addition to the localized reaction and scar formation, headache, and body aches, the vaccine has other important potential side effects:

1. **Inadvertent inoculation.** The vaccination site must be kept well covered to prevent inadvertent inoculation (transfer) to other sites on the body. This is the most common adverse reaction. Rate = 529 per million persons vaccinated.

2. **Generalized vaccinia.** Occurs when the virus spreads throughout the body via the bloodstream. Rate = 250 per million persons vaccinated.

3. **Erythema multiforme.** A rash characterized by symmetric red patchy areas. Rate = 165 per million persons vaccinated.

4. **Postvaccinal encephalitis.** A life-threatening, demyelinating acute inflammation of the brain. Rate = 12.3 per million vaccinated.

5. **Eczema vaccinatum.** A life-threatening reaction that occurs in persons with eczema or atopic dermatitis when the vaccinia virus spreads to these areas. This can also occur if the eczema or dermatitis is inactive at the time of vaccination, or if a person has even only once had eczema or other skin conditions. Rate = 38.5 per million vaccinated.

6. **Progressive vaccinia.** A life-threatening reaction that occurs when lesions go through muscle down to the bone. Rate = 1.5 per million persons vaccinated.

7. **Mortality rate.** The mortality rate from vaccination is 1 to 2 per million persons vaccinated, equal to the mortality rate resulting from flu vaccination.

The vaccine is contraindicated in various persons, including children under 12 months, pregnant or breastfeeding mothers, persons with heart conditions, immunodeficient individuals, persons undergoing immunosuppressive therapy, persons with active eye disease, and those who are severely ill. A complete list of contraindications and more information on the vaccine can be found at http://www.bt.cdc.gov/agent/smallpox/.

**PPE, Infection Control, and Decontamination**

Isolation precautions are combined standard, contact, and airborne until all scabs have separated. The CDC recommends that fit-tested N95 masks be used by anyone caring for smallpox patients in a controlled healthcare setting. After confirmation of vaccine take, healthcare workers are no longer required to wear N95 masks. For contaminated patient areas, PPE must include disposable gowns and gloves that are disposed of prior to leaving those areas. Laundry and linens must be bagged and laundered on the premises by only vaccinated workers, or first autoclaved if laundered by non-vaccinated persons. Laundry should be washed in hottest water and hot air dried. Disposable items should be used whenever possible. Food should be prepared on the premises or brought in using disposable serving ware. More information is available on the CDC website at http://emergency.cdc.gov/agent/smallpox/response-plan/files/guide-c-part-1.pdf.

No products are registered by the Environmental Protection Agency (EPA) as specific for variola virus inactivation on surfaces. Since variola is physically and biochemically similar to Vaccinia, which is inactivated by low or intermediate level disinfecting products, it is presumed that these products would be effective against Variola as well. Most healthcare facilities use higher level disinfectants than those which inactivate
Plague

Etiology

Plague is caused by the bacterium *Yersinia pestis*, a member of the *Enterobacteriaceae* family. *Y. pestis* is a gram-negative coccobacillus that shows a characteristic “safety pin” appearance with staining. These bacteria are easily destroyed by sunlight and drying but may survive up to 1 hour when released into the air. *Y. pestis* causes three main types of plague in humans: bubonic, septicemic, and pneumonic. Pharyngeal plague, meningeal plague, and ocular plague are less common forms.

Epidemiology

Plague has long been recorded in history. The pandemic Plague of Justinian (541-542 AD), was due to bubonic plague likely originating in China. It was spread through the importing of enormous amounts of grain from Egypt to Constantinople as rats and fleas on grain ships infested the grain. The Black Death pandemic (1347-1351) that occurred in China, Asia, Europe, and Africa followed later, killing an estimated 75-100 million people. The “black death” referred to the characteristic black color due to cyanosis and gangrene of the fingers and toes as the disease progressed. A third pandemic that began in China in 1855 killed more than 12 million in China and India alone and involved both bubonic and pneumonic forms. Remnants of this pandemic are the likely source for the *Y. pestis* currently present in the U.S.

Plague is transmitted to humans by fleas that have bitten an infected animal and then bite a human. Plague can also be transmitted by handling an infected animal or by close person-to-person contact in cases of pneumonic plague. The WHO reports 1,000 to 3,000 cases of worldwide plague each year. Plague naturally occurs in animals throughout the Western United States. According to the CDC, human cases in the U.S. occur in two main regions: 1) northern New Mexico, northern Arizona, and southern Colorado, primarily from rock squirrels and their fleas, and 2) California, southern Oregon, and far western Nevada, primarily from ground squirrels and their fleas. Domestic cats are also easily infected and can bring infected fleas or rodents into the home. Dogs are sometimes infected. There are 10-20 cases of plague in the U.S. each year, primarily in rural areas.

It is most likely that *Y. pestis* would be aerosolized in an attack of bioterrorism, causing the contagious pneumonic form of plague.

Clinical Presentation, Diagnosis, and Treatment

Bubonic plague has an incubation period of 2 to 6 days. Initial symptoms include fever, headache, exhaustion, and general malaise, followed by painful swollen lymph nodes. The diagnostic sign of plague is the presence of very large, swollen, painful, and hot lymph nodes (especially in the groin area) called buboes (see Figure 7). The disease progresses rapidly and can lead to septicemic plague as bacteria invade the bloodstream. If antibiotic therapy is not started, pneumonic plague may follow. Primary pneumonic plague has an incubation period of 1 to 3 days. Patients present with high fever, chills, cough, and bloody sputum. Diagnosis of plague is made by patient history, symptoms, and blood and lymph node specimen cultures. Lab identification must be handled at a minimum of biosafety level 2 (BSL-2) or at biosafety level 3 (BSL-3) if cultures have potential for antibiotic resistance or there is aerosol production.

Patients suspected of having plague should be isolated and promptly treated with streptomycin or gentamicin as preferred antibiotics. Doxycycline is also effective as an alternative drug. Tetracycline is usually substituted for streptomycin to minimize toxicity after several days of therapy. Treatment may also include incision and drainage of buboes. Without antibiotic treatment, bubonic plague has a 13.5% mortality rate, septicemic plague has a near 100% mortality rate, and pneumonic plague has a 57% mortality rate.

Prophylactic antibiotic treatment with ciprofloxacin or doxycycline for 10 days is recommended for any contacts of persons or pets with confirmed or suspected pneumonic plague. Prophylactic treatment is not necessary for contacts of bubonic or septicemic plague. Antibiotic therapy is also recommended for any persons exposed to flea bites of wild rodents or tissues and fluids of an infected animal during an outbreak of plague.

In 1999, plague vaccine production was stopped because it was unlikely to protect from primary pneumonic plague. There is now no commercially available vaccine in the U.S., but new vaccines being developed against primary pneumonic plague are in clinical trials. It is the law that all cases of suspected plague be immediately reported to local and state public health departments and that a diagnosis is confirmed by the CDC. The CDC must then report all plague be immediately reported to local and state public health departments and that a diagnosis is confirmed by the CDC. The CDC must then report all

PPE, Infection Control, and Decontamination

Isolation precautions are standard for persons with bubonic plague, with droplet precautions added for anyone with pneumonic plague until 48 hours of antibiotic therapy have elapsed. Droplet precautions are also recommended for all patients until pneumonia has been ruled out and treatment has begun. Any laboratory spills should be covered in absorbent material and flooded with a 1:10 bleach solution that is left on for 30 minutes and then cleaned. Exposed skin should be cleaned with a nonabrasive soap and water. Any contaminated material should be disposed of in biohazard waste bags and autoclaved. Workers exposed in the field must wear protective clothing, gloves, boots, and positive
pressure HEPA filtered respirators. PPE must be decontaminated or disposed of as biohazardous waste.

**Tularemia**

**Etiology**

Tularemia, also known as rabbit fever or deer fly fever, is a highly infectious zoonotic disease that is endemic in many parts of the world and in North America. It is caused by the gram-negative, nonmotile coccobacillus Francisella tularensis. *F. tularensis* is an intracellular bacterium that lives and multiplies within the host’s macrophage cells.

**Epidemiology**

Tularemia is spread by the bite of ticks, deer flies, or other arthropods; contact with an infected animal (most commonly rabbits) ingestion of undercooked meat of infected animals; ingestion of contaminated water; or inhalation of contaminated dusts or aerosols. There are about 150 cases of naturally occurring tularemia per year in the U.S., and it has been reported in every state except Hawaii. Domestic cats are very susceptible and can transmit the disease to humans. *F. tularensis* in natural conditions can survive extended periods in cold, moist environments.

It is most likely that *F. tularensis* would be aerosolized in an attack of bioterrorism, causing primarily the pneumonic form of the disease.

**Clinical Presentation, Diagnosis, and Treatment**

Patients with tularemia present with different symptoms depending on how the bacteria enters the body. Onset may be abrupt, with fever, chills, headache, body aches, and sore throat. Nausea, vomiting, and diarrhea may also be present. Up to 20% of patients may show a blotchy rash that may become pustular. Other symptoms may vary by site of bacterial entry:

1. **Ulceroglandular:** Most common form, from either the bite of a tick or deerfly or from handling an infected animal. A skin ulcer forms at the site, and swelling of lymph glands in the armpit or groin is common.
2. **Glandular:** Likely occurs when bacteria enter through an unseen abrasion; similar to ulceroglandular but without an ulcer.
3. **Oculoglandular:** Occurs when a person touches the eye and transfers the bacteria there. Symptoms include purulent conjunctivitis of the eye, periorbital edema, and swelling of lymph glands in front of the ear.
4. **Oropharyngeal:** Occurs from consuming contaminated meat (usually rabbit) or water. Symptoms include sore throat, exudative tonsillitis, mouth ulcers, and swollen lymph glands in the neck.
5. **Pneumonic:** Most serious form, contracted after breathing dust or aerosols containing the bacteria or when other forms of tularemia are left untreated and disease progresses to the lungs via the bloodstream. Symptoms include dry cough, subternal chest pain, and difficulty breathing.
6. **Typhoidal (septicemic):** Symptoms include fever, chills, weight loss, and malaise, and possibly pneumonia. Difficult to diagnose because there is usually an absence of ulcers and lymphadenopathy.

Diagnosis of tularemia is difficult because the disease is rare and symptoms resemble those of other illnesses. Routine lab work is not diagnostic. A thorough patient history showing exposure to animals or insect bites is important. Diagnosis is generally made with serological testing. Blood and tissue cultures showing growth of *F. tularensis* are also diagnostic. Labs should be alerted if *tularemia* is suspected because special culture media is required for bacterial propagation. Additionally, lab identification must be handled at biosafety level 2 (BSL-2) or at biosafety level 3 (BSL-3) if procedures are more complicated or might produce aerosols.

The CDC recommends intravenous antibiotic treatment with streptomycin as the drug of choice and gentamycin as an acceptable alternative. A 10-day course is recommended. Tetracyclines and chloramphenicol (used for a minimum of 14 days) should be used with caution due to relapses and primary treatment failure. Although ciprofloxacin and fluoroquinolones are not approved for treatment, there has been good efficacy in both animals and humans. *F. tularensis* is resistant to penicillins and first generation cephalosporins. Patients should respond quickly with correct antibiotic treatment, and dramatic changes should be observed within 24-48 hours.

Currently, there is a live attenuated vaccine that has been used to protect lab workers that is under FDA review. There is no immune globulin available for treatment, and no antibiotics are licensed for pre-exposure prophylaxis. Postexposure prophylaxis lasting 14 days should begin within 24 hours after exposure with either doxycycline or ciprofloxacin as the drugs of choice.

**PPE, Infection Control, and Decontamination**

Isolation precautions are standard and patient isolation is not recommended for tularemia because person-to-person transmission is rare. Standard hospital decontamination procedures for surfaces and laundry are sufficient.

**Botulinum Toxin**

**Etiology**

Botulinum toxins are produced by the anaerobic gram-positive spore-forming bacillus Clostridium botulinum and two other Clostridium species. There are seven neurotoxins, known as types A through G, which are produced when the bacterial spores return to the vegetative state under anaerobic conditions. The A, B, and E types cause human disease. Types C and D cause animal disease. Botulinum toxins are the most toxic compounds per weight known to man. They can be absorbed through the respiratory tract, eyes, skin breaks, and mucous membranes. The toxins can bind to the presynaptic junction of either neuromuscular or autonomic nerve junctions. Once bound, the damage is irreversible. The toxins work to block neuromuscular transmission by preventing the release of acetylcholine across the nerve synapse. Recovery can occur only if the neuron develops a new axon, a process that may take several months. Without treatment, death occurs due to paralysis of respiratory muscles. Botulinum toxin is also used for medical purposes, including treatment of strabismus, muscle pain disorders, excessive underarm sweating, and chronic migraines. It is also used in cosmetic procedures (Botox).

**Epidemiology**

Cases of botulism have been described...
Table 5: Characteristics of Filoviruses and Arenaviruses

<table>
<thead>
<tr>
<th>Family</th>
<th>Virus &amp; mortality rate</th>
<th>Disease</th>
<th>Natural Reservoir</th>
<th>Regions Found</th>
</tr>
</thead>
<tbody>
<tr>
<td>Filoviridae</td>
<td></td>
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<tr>
<td>Marburg</td>
<td>(mortality up to 25%)</td>
<td>Marburg Fever</td>
<td>Likely to be Fruit bats</td>
<td>Marburg W. Germany, Yugoslavia, Africa</td>
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<tr>
<td>Ebola</td>
<td>(mortality as high as 90% with certain strains of Ebola)</td>
<td>Ebola HF</td>
<td></td>
<td>Tropical Regions of Africa</td>
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<td>Arenaviridae</td>
<td></td>
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<tr>
<td>Lassa</td>
<td>(&lt;10% of cases are severe but mortality can reach 25% in these)</td>
<td>Lassa Fever</td>
<td>Old world rats and mice</td>
<td>Rural W. Africa</td>
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<tr>
<td>Lujo</td>
<td></td>
<td>Unnamed HF</td>
<td></td>
<td></td>
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<tr>
<td>Junin</td>
<td>(mortality 15-30%)</td>
<td>Argentine HF</td>
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<td>Machupo</td>
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<td>Chapare</td>
<td></td>
<td>Unnamed HF</td>
<td></td>
<td>Bolivia</td>
</tr>
<tr>
<td>Whitewater Arroyo</td>
<td></td>
<td>Whitewater Arroyo HF</td>
<td></td>
<td>W. United States</td>
</tr>
</tbody>
</table>

Throughout literature, Clostridia spp. can be found throughout the world in samples taken from soil, marine sediments, household dust, and the surfaces of food.

There are Six types of botulism:

1. **Foodborne botulism** from eating foods that were improperly canned or preserved and are contaminated with preformed toxin. Occurs primarily in home- canned foods.

2. **Wound botulism** from toxin produced in an infected wound. May be found in cases secondary to surgery or trauma, in cases of sinusitis from intranasal cocaine abuse, or in cases of subcutaneous heroin injection (especially black tar heroin use in California).

3. **Infant botulism** occurs in infants under 1 year old from consumption of spores in food (honey) that germinate and colonize the intestines.

4. **Adult intestinal toxemia botulism** occurs after persons with bowel conditions that disrupt normal intestinal flora consume spore-containing food.

5. **Iatrogenic botulism** occurs from accidental overdose of pharmaceutical botulinum toxin. Cases are rare because the FDA requires doses to be below human toxicity level.

6. **Inhalational botulism** is rare and only recently seen in lab workers who accidentally inhaled toxin. There are about 145 reported cases of botulism in the U.S. per year. In a case of bioterrorism, botulinum toxin could be spread through aerosolization or through
food and water contamination.

Clinical Presentation, Diagnosis, and Treatment

Within 48 hours of exposure to the toxin, patients present with classic symptoms, including dry mouth, double vision, blurred vision, ptosis, slurred speech, dysphagia, and muscle weakness. Fever is absent, and patients are fully alert with fully intact sensation. Overall, a descending motor paralysis can be seen as respiratory muscles, arms, and legs become affected. Infants are lethargic and have a weak cry, poor muscle tone, poor feeding, and constipation.

Diagnosis is based on patient history and physical and neurologic exams and is confirmed by lab analysis. Lab identification must be handled at biosafety level 2 (BSL-2) or at biosafety level 3 (BSL-3) if procedures are more complicated or might produce aerosols. Suspected cases must be immediately reported to state health departments that will then notify the CDC.

Treatment consists of prompt dosing of antitoxin and intensive supportive therapy. If botulism is suspected, antitoxin should be given as soon as possible (prior to lab confirmation) because it can minimize subsequent nerve damage and speed recovery. It will not reverse any existing paralysis. The heptavalent botulinum antitoxin (HBAT) of equine origin is available through a CDC-sponsored FDA Investigational New Drug (IND) protocol for noninfant, naturally occurring botulism. It is now the only antitoxin available for noninfant botulism. Infant botulinum immune globin (Baby-BIG) is available from the California State Health Department. Skin testing for sensitivity to serum or antitoxin must be performed prior to administration of antitoxin. Patients placed on mechanical ventilation usually require 6 to 8 weeks of therapy but may require up to seven months. There is no current vaccine for botulism.

PPE, Infection Control, and Decontamination

Person-to-person transmission of botulism does not occur, and isolation precautions are standard. In a bioweapon situation, the primary risk of aerosolized toxin from a patient’s wound or skin is low. Anyone decontaminating a patient exposed to C. botulinum toxin should wear splash-proof and waterproof outer garments, chemical resistant gloves, eye protection, and a NIOSH approved N95 fit-tested respirator. C. botulinum is inactivated by a 1:10 dilution of household bleach with a 30 minute contact time. Botulism toxin in food is destroyed by heating food to an internal temperature of 85°C for at least 5 minutes.

The Viral Hemorrhagic Fevers

Etiology and Epidemiology

The viral hemorrhagic fevers (VHF) are a group of diseases caused by several families of viruses. These viruses damage the body’s vascular system and affect multiple organ systems. The viruses are grouped into four groups: filoviruses, arenaviruses, bunyaviruses, and flaviviruses. All are RNA viruses and they are found in areas where their natural reservoirs live; humans are not their natural reservoirs. This course will focus on the filoviruses and arenaviruses because they are in the CDC category A list. Table 5 shows characteristics of filoviruses and arenaviruses.

Filoviruses belong to the filoviridae family. The two members of this family that have been identified are Marburg virus and Ebola virus. The natural reservoir is still unknown but is suspected to be fruit bats. Transmission occurs from exposure to the natural reservoir. Once the virus is in a human, transmission is by close personal contact with an infected person, infected blood, infected body fluids, or cadavers. They are also known to spread in laboratories through small particle aerosols. Aerosol spread among humans is unclear.

Arenaviruses belong to the arenaviridae family. Members of this family are Lassa virus (Lassa fever), Junin virus (Argentine hemorrhagic fever), Machupo virus (Bolivian hemorrhagic fever), Guanarito virus (Venezuelan hemorrhagic fever), Sabia virus (Brazilian hemorrhagic fever), Whitewater Arroyo virus (white arroyo hemorrhagic fever), and most recently the Lujo virus discovered in 2009. These viruses are spread through exposure to rodents and human- to- human contact.

In a case of bioterrorism, viruses causing hemorrhagic fever could most likely be spread through aerosolization.

Clinical Presentation, Diagnosis, and Treatment

Incubation for VHFs is 3 to 21 days. Although there are differences in symptoms between the different hemorrhagic fevers, common symptoms include abrupt onset of fever, severe exhaustion, myalgia, headache, and various bleeding manifestations that range from ecchymosis to overt bleeding. Nausea, vomiting, bloody diarrhea, abdominal pain, maculopapular rash, sore throat, chest pain, and jaundice are also common symptoms. Tremor, seizures, coma, and death may follow.

Diagnosis is made by a thorough patient history and definitive lab analysis. Any suspected cases of VHF must be immediately reported to the CDC’s Viral Special Pathogens Branch. All lab work must be done at biosafety levels 3 and 4 (BSL-3 and BSL-4) due to the ability of the viruses to infect via aerosols and their ability to cause rapid onset of life-threatening disease.

There is no cure for the VHFs. Treatment consists primarily of supportive therapy, including maintenance of electrolytes, mechanical ventilation, and management of bleeding. Although not FDA approved, Ribavirin, available only as an IND, has been shown to be effective against arenaviruses but is not effective and not recommended for filoviruses. Ribavirin is teratogenic.

Any persons exposed to a VHF or who are contacts of a patient with a VHF should be closely monitored. Prophylactic antiviral therapy is NOT recommended. If temperature is 101°F or greater, or if other symptoms of VHF are present, and the suspected virus is not Ebola, Marburg, or a flavivirus, ribavirin should be initiated.

PPE, Infection Control, and Decontamination

Isolation precautions are strict contact precautions with airborne precautions added until a mode of transmission has been confirmed. If the disease was naturally acquired, droplet precautions can be substituted for airborne. Emphasis should be placed on sharps safety, barrier precautions, hand hygiene, and patient isolation. PPE consists of gowns, double
Chemical and Nuclear Terrorism

Although chemical and nuclear terrorism do not fall under the bioterrorism category, it is important to have a basic understanding of these other threats in situations of emergency preparedness and response.

### Chemical Terrorism

Symptoms associated with chemical exposure include chemical burns, skin blistering and redness, extreme pain, coughing, choking, dyspnea, lung and airway irritation, sore throat, tearing, conjunctival and corneal damage, blurred vision, miosis or mydriasis, nausea, vomiting, sweating, diarrhea, seizures, confusion and hallucinations.

In chemical emergencies, victims should be first assessed for an airway, adequate respiration, and a pulse. If trauma is suspected, the patient must be stabilized with a cervical collar and backboard. Because most chemical agents can penetrate clothing and are quickly absorbed through the skin, decontamination must be done as soon as possible to be most effective, preferably within 1 to 2 minutes after exposure. Contaminated clothing should be removed as quickly as possible. Any clothing that must be pulled over the head to remove should be cut off instead to prevent further exposure of eyes and mucous membranes. If possible, any exposed areas of skin should be washed with large amounts of soap and water. Eyes should be irrigated with water or saline. Contact lenses should be removed and discarded with contaminated clothing. All contaminated material and clothing should be double-bagged in plastic bags and tightly sealed. Persons who have undergone decontamination should avoid contact with others who have not been decontaminated and should avoid areas where the chemical release occurred.

Treatment for chemical exposure will vary based on the type of chemical and symptoms. Medical management guidelines for acute chemical exposure as compiled by the Agency for Toxic Substances and Disease Registry

<table>
<thead>
<tr>
<th>Chemical Explosion</th>
<th>Nuclear Explosion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amount of heat produced</td>
<td>Several thousand degrees</td>
</tr>
<tr>
<td></td>
<td>Millions of degrees where matter becomes plasma</td>
</tr>
<tr>
<td>Size of gaseous fireball</td>
<td>Several meters in diameter (1 meter = 3.28 ft)</td>
</tr>
<tr>
<td></td>
<td>1,450 ft (~442 meters) for a 10KT nuclear device</td>
</tr>
<tr>
<td></td>
<td>(442 meters) for a 10KT nuclear device</td>
</tr>
<tr>
<td>Energy Released</td>
<td>Derived from reactions between molecules</td>
</tr>
<tr>
<td></td>
<td>Derived from splitting (fission) of the ~atomic nuclei of uranium or plutonium</td>
</tr>
<tr>
<td>Amount of energy released when compared pound for pound</td>
<td>1X energy</td>
</tr>
<tr>
<td>Equivalents</td>
<td>~1000 tons of TNT</td>
</tr>
<tr>
<td></td>
<td>~10,000 tons of TNT</td>
</tr>
<tr>
<td></td>
<td>Low yield nuclear device = 1KT</td>
</tr>
<tr>
<td></td>
<td>Low yield nuclear device = 10KT*</td>
</tr>
</tbody>
</table>


‡For comparison, the blast in the Oklahoma City, OK, bombing of the Murrah Federal Building in 1995 was equivalent to 2 tons of TNT.

*Department of Homeland Security bases its planning factors on a low-yield nuclear device of 10KT (kilotons) detonated at ground level in an urban area.
Radiation emergencies could be caused by dirty bombs, nuclear blasts, attacks or problems at a nuclear facility, or accidents involving the transport of radioactive materials. Nuclear explosions are immensely more powerful than chemical explosions. Table 6 shows a comparison of chemical versus nuclear explosions. Nuclear explosions produce blast injuries, thermal injuries, and radiation injuries. The prognosis for those with both radiation and traumatic injuries is worse than the prognosis for those with radiation exposure alone.

**Radiation fallout** is the term used to describe the particles that form when vaporized dirt particles are drawn up into the mushroom cloud produced from an explosion. Radioactive materials then condense on these particles and fall back to earth. The most hazardous fallout will be visible as fine particles the size of sand. The lack of apparent fallout does not mean there is no radiation. The area of significant fallout for a 10KT (the size of blast that DHS bases its planning factors on) explosion will extend 10-20 miles from ground zero, or the initial location of the blast. Persons who take shelter within the first 60 minutes of a nuclear explosion and who shelter in place (go immediately indoors to the nearest most protective structure) will have the most effective life-saving opportunity. The most important factors in protection from radiation and fallout are:

1. **Distance.** The greater the distance between a person and radiation/fallout particles, the greater the protection. Underground rooms and basements offer greater protection than bottom floors, and middle floors in high-rise buildings offer greater protection than upper floors. Flat rooftops will collect fallout particles making upper floors a poorer choice. **Figure 8** shows the different amounts of shielding protection offered depending on the location of persons within a building. These factors apply only to fallout from a nuclear detonation and are not appropriate for reactor incidents, dirty bombs, or chemical/biological events.

2. **Shielding.** The heavier and denser the material between a person and radiation/fallout particles, the greater the protection. The more earth, rock, concrete, and so forth. between a person and fallout particles, the better.

3. **Time.** The greater the time spent in shelters away from radiation/fallout, the greater the protection. Fallout poses the greatest threat in the 2 weeks following a nuclear emergency; after 2 weeks the level of radiation is about 1% of the initial radiation level. The dose of radiation a person receives is directly proportional to the time of exposure.

**The electromagnetic pulse (EMP),** or high-density electromagnetic field that follows a nuclear weapon detonation, is similar to a lightning strike but is stronger, faster and shorter. Depending on where the detonation occurs, electronic devices connected to power sources and antennas can be damaged for many miles. This includes computers, cell

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**Figure 8: Protection/Shielding Offered by Various Locations within a Building**

*Figure used with permission: Brooke Buddemeier, Lawrence Livermore National Laboratory. Protection factors apply only to fallout from a nuclear detonation and are not appropriate for use after reactor incidents, dirty bombs, or chemical/biological events.

phones and communication systems, electrical appliances, and ignition systems of automobiles and aircraft. With a high altitude detonation, most equipment within a distance of 1,000 miles could be damaged. An EMP may also harm pacemakers and other electronic implants.

Radiation cannot be detected by the five human senses. It can only be detected by radiation monitoring equipment. Persons exposed to radiation may not realize what level or length of exposure they may have had. Symptoms of acute radiation syndrome (ARS), also known as radiation sickness or radiation poisoning, vary depending on the amount and length of radiation exposure. Prodomal symptoms include headache, fever, nausea, vomiting, and fatigue. As time progresses, symptoms include low blood cell counts, anemia, infections, neurological problems, and bleeding. Treatment is supportive therapy including antibiotics and blood products.

If a person has been exposed to radiation, clothing should be removed as soon as possible, sealed in a plastic bag, and placed as far away as feasible from humans and animals. If possible, persons should be decontaminated by showering with large amounts of soap and water, taking care not to scrub or scratch the skin. Hair should be shampooed but no conditioner used because it will bind radioactive particles to the hair. The nose should be thoroughly blown to help get rid of any radioactive particles there. Eyes and eyelids should be wiped with a clean wet cloth. Contamination that is not washed off or brushed away can cause beta burns to the skin; therefore, any action (such as brushing/dusting off as much as possible) to reduce the contamination is better than none. For more information on nuclear terrorism, see www.ready.gov or the excellent federal interagency document Planning Guidance for Response to a Nuclear Detonation available at http://www.hhs.org/hsp/documents/Planning_Guidance_for_Response_to_a_Nuclear_Detonation-2nd_Edition_FINAL.pdf.

**Conclusion**

Raising the level of preparedness among healthcare workers through education will enable them to more effectively deal with any incident they might encounter and will save countless lives. Regardless of the threat, healthcare workers can feel more confident if they have a familiarity with and knowledge of the various agents of bioterrorism, as well as a working knowledge of chemical, radiological, and nuclear threats. This preparedness will help them effectively manage an emergency situation when it arises.

**Suggested Reading and References**


