RESPONDING TO POTENTIAL BIOTERRORISM AGENTS-

A primer for US Coast Guard ashore and afloat units

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INTRODUCTION

Bioterrorism is as much a threat in the marine environment, as it is on land. Thus, it is important for persons afloat to be familiar with potential threats, and especially critical for those responsible for health care underway to have an understanding of the medical aspects of bioterrorism.

Medical defense against and treatment for biological terrorism is an unfamiliar area to most providers of health care during peacetime. However, effective medical counter-measures are available against many of the bacteria, viruses, and toxins that might be used as biological weapons against people.

Biological weapons are classified as either incapacitating or lethal. These biological agents are delivered as an aerosol to be inhaled, in contaminated food or water to be ingested, or by direct contact to the skin or eyes. There are thousands of biological agents that could theoretically be utilized in bioterrorism warfare. Though for an agent to be effectively utilized it must be:

1) easily produced in large quantities;
2) sufficiently potent as a weapon;
3) effectively delivered to target populations without losing potency.

The global biological terrorism threat is serious, and the potential for devastating casualties is high for certain biological agents. However, with appropriate use of medical countermeasures either already developed or under development, the illness and death can be greatly reduced.

The goal of this section is to serve as a reference and to help the reader develop an understanding of the biological threats and the medical supplies useful in defending against these threats.

DISTINGUISHING BETWEEN NATURAL AND INTENTIONAL DISEASE OUTBREAKS

The potential mechanisms of release of a biologic agent are many. Contaminated food or water sources are certainly a possibility. As much as possible, food and water should be obtained from reputable and secure sources. Biologic agent exposure could come in the form of an aerial release from an aircraft, from an exploded munition or from an aerosolizing device. Crewmembers should be wary of suspicious persons in or around the ship and of suspicious packages, parcels, etc. However, in spite of precautions taken, it is likely that the initial exposure to the biological agent will be undetected.

Therefore, a covert biological agent attack may first be apparent if many patients become sick with similar symptoms due to the released disease agent. However, many

diseases caused by weaponized biological agents present with nonspecific clinical features that could seem like other, more common diseases. Table 1 identifies things that may suggest there has been a biologic attack. While a helpful guide, these features can also be present in a naturally occurring disease outbreak. Conversely, a bioterrorist attack may have none of these features.

Table 1. Features that may be Present with a Biologic Warfare or Terrorist Attack

- The presence of an unexpected or unusual disease
- The presence of a large epidemic with a similar disease or syndrome
- More severe disease than is usually expected for a specific biologic agent or failure to respond to standard therapy
- Unusual routes of exposure for a biologic agent, such as the inhalational route for diseases that normally occur through other exposures
- A disease that is unusual for a given geographic area or transmission season
- Disease normally transmitted by a vector that is not present in the local area
- Multiple simultaneous or serial epidemics of different diseases in the same population
- A single case of disease by an uncommon agent (smallpox, some viral hemorrhagic fevers)
- A disease that is unusual for an age group
- Unusual strains or variants of organisms
- Higher attack rates in those exposed in certain areas, such as inside a building if released indoors, or lower rates in those inside a sealed building if released outside
- Disease outbreaks of the same illness occurring in noncontiguous areas
- A disease outbreak with an impact on animals as well as humans
- Intelligence of a potential attack, claims by a terrorist or aggressor of a release, and/or discovery of munitions or tampering

I. Maintain an index of suspicion. The shipboard health-care provider must always suspect that a disease may be due to biological weapons. An early suspicion is needed for a rapid diagnosis that is essential for the early treatment needed to save the patient's life.

II. Protect Thyself. Before you approach a potential biological casualty, you must first take steps to protect yourself - using physical, chemical, and/or immunologic tools. Physical protection is often a protective mask such as a HEPA-filter or simple surgical mask. These provide adequate protection against most biological (although not against chemical) threats. Chemical protection includes the pre- and/or post-exposure administration of antibiotics. Immunological protection involves vaccines, which are generally not available for most bio-terrorism diseases.

III. Assess the Patient. First use the "ABC's" – airway, breathing and circulation. The initial "ABC's" assessment begins before decontamination and should be brief. A patient history may include questions about illnesses in other personnel, the presence of unusual food and water sources, vector exposure, immunization history,

travel history, occupational duties, and personal protection status. Physical exam should focus on the pulmonary (lung) and neuromuscular (nerve and muscle) systems, as well as any unusual dermatologic (skin) and vascular (blood vessel/heart) findings

IV. Decontaminate as Appropriate. The incubation period of biological agents makes it unlikely that victims of a bio-terrorism attack will present for medical care until days after an attack, when the need for decontamination is past. If decontamination is needed, simple soap and water bathing will usually suffice. Certainly, standard decontamination solutions (such as hypochlorite), typically employed in cases of chemical agent contamination, would be effective against all biological agents (more information is provided in the decontamination section of this chapter). In fact, even 0.1% bleach reliably kills anthrax spores, the hardiest of biological agents. Exercise caution when using caustic substances, especially on human skin.

V. Establish a Diagnosis. Following decontamination (where warranted), the focus is making a diagnosis. Diagnostic specimens should be obtained from representative patients and these should be sent to the clinical laboratory. Nasal swabs (important for culture and PCR (a test for exposure to certain biologic agents), even if you are unsure *which* organisms to test for), blood cultures, serum, sputum cultures, blood and urine for toxin analysis, throat swabs, and environmental samples should be considered and obtained, if possible.

Without laboratory confirmation, a diagnosis must be made on clinical grounds. Chemical and biological terrorism diseases can be generally divided into those that present "immediately" with little or no incubation period (principally the chemical agents) and those with a longer incubation period (principally the biological agents). Moreover, bio-terrorism diseases are likely to present as one of a limited number of clinical syndromes. Plague, tularemia, and Staphylococcal Enterotoxin B (SEB) disease all may present as pneumonia. Botulism and Venezuelan Equine Encephalitis (VEE) may present with peripheral and central neuromuscular findings, respectively. Table 2 provides additional information.

VI. Render Prompt Treatment. Treatment is usually most effective during the incubation period, before the patient is sick. Treatment of the suspected diagnosis, even if not "proven" by the laboratory, is often indicated. Table 3 lists diseases requiring prompt therapy. Persons with respiratory disease, such as patients with undifferentiated febrile illnesses who might have early anthrax, plague, or tularemia, may also be treated immediately. Doxycycline (an antibiotic), for example, is effective against most strains of *B. anthracis* (anthrax), *Y. pestis* (plague), and *F. tularensis* (tularemia) as well as against *C. burnetii* (Q fever) and the *Brucellae* (brucellosis). The antibiotics ciprofloxacin and other tetracyclines and fluoroquinolones might also be considered. Beginning such therapy just "buys time" for a definitive diagnosis, it is not a substitute for a precise diagnosis.

RESPIRATORY	
Rapid-Onset	**Delayed-Onset**
• **Nerve Agents** • **Cyanide** • **Mustard** • **Lewisite** • **Phosgene** • **SEB Inhalation (biologic)**	• **Inhalational Anthrax** • **Pneumonic Plague** • **Pneumonic Tularemia** • **Q Fever** • **SEB Inhalation** • **Ricin Inhalation** • **Mustard (chemical)** • **Lewisite (chemical)** • **Phosgene (chemical)**
NEUROLOGICAL	
Rapid-Onset	**Delayed-Onset**
• **Nerve Agents** • **Cyanide**	• **Botulism-peripheral symptoms** • **VEE-CNS symptoms**

Table 2. Diagnostic Matrix: Chemical & Biological Casualties.

VII. Practice Good Infection Control. Standard precautions provide adequate protection against most infectious diseases, including potential bio-terrorist agents. Anthrax, tularemia, brucellosis, glanders, Q-Fever, VEE, and the toxin-mediated diseases are not generally contagious (transmitted person to person), and victims can be safely managed using standard precautions. Under certain circumstances, however, one of three forms of transmission-based precautions would be warranted. Smallpox victims should, wherever possible, be managed using airborne precautions. Pneumonic Plague warrants the use of droplet precautions, and certain Viral Hemorrhagic Fevers (VHFs) require contact precautions. (see section on "Patient Isolation Precautions")

RESPIRATORY	
Rapid-Onset	**Delayed-Onset**
• **Cyanide**	• **Inhalational Anthrax** • **Pneumonic Plague** • **Pneumonic Tularemia**
NEUROLOGICAL	
Rapid-Onset	**Delayed-Onset**
• **Nerve Agents**	• **Botulism**

Table 3. Chemical & Bio-Terrorism Diseases Potentially Requiring Prompt Empiric Therapy.

VIII. Alert the Proper Authorities. The ship's captain should immediately be immediately notified of any suspected bioterrorist-related illnesses. In addition, the port authorities, law enforcement and public health officials at the next port of entry must be notified.

BACTERIAL AGENTS

Bacteria generally cause disease in human beings and animals by invading host tissues or by producing toxins (poisons). Many disease-causing bacteria utilize both mechanisms. Bacterial diseases usually respond antibiotic therapy. Under special circumstances some types of bacteria can transform into spores. The spore of the bacterial cell is more resistant to cold, heat, drying, chemicals and radiation than the bacterium itself. Spores are a dormant form of the bacterium and, like the seeds of plants; they can germinate (grow) when conditions are favorable.

ANTHRAX

Historical Use: In World War I, a German operative attempted to use anthrax laced sugar lumps to contaminate Norwegian horses and reindeer being used as draft animals. In World War II, the British conducted experiments using contaminated cattle food. In 1979, near a Russian biological facility, 77 persons became ill with anthrax and 66 died due to an accidental release. Iraq reportedly completed research with anthrax during the Gulf War. In 1995 the Japanese cult group, Aum Shrinryko, unsuccessfully attempted to use anthrax as a weapon.

Potential Threat: The primary means is to disperse the anthrax spores in a form that allows them to be aerosolized and inhaled into the body.

Signs and Symptoms: Incubation period is generally 1-6 days, although longer periods have been noted. Fever, malaise, fatigue, cough and mild chest discomfort progresses to severe respiratory distress with shortness of breath, sweating, stridor, bluish-tinged skin, and shock. Death typically occurs within 24-36 hours after onset of severe symptoms.

Diagnosis: Physical findings are non-specific. A widened mediastinum may be seen on Chest X-ray (CXR) in later stages of illness. The organism is detectable by Gram stain of the blood and by blood culture late in the course of illness.

Mortality: Untreated, the inhalational form of anthrax is almost always fatal. In the recent cases it was shown that with treatment approximately 60% of the patients survived.

Treatment: Although effectiveness may be limited after symptoms are present, high dose (often intravenous) antibiotic treatment with ciprofloxacin, doxycycline or penicillin should be undertaken. Supportive therapy may be necessary.

Prophylaxis: Oral ciprofloxacin or doxycycline for known or imminent exposure. An FDA-licensed vaccine is only available for military personnel at the present time.

Isolation and Decontamination: Standard precautions for healthcare workers. This disease is not transmissible person-to-person. Environmental decontamination can be accomplished with a 0.5% hypochlorite solution.

BRUCELLOSIS

Historical Use: In the 1940's the Japanese cultured brucella for use in Manchuria. It was the first biological weapon to be weaponized at the U.S. Pine Bluff arsenal in 1954. This stockpile was destroyed in 1969.

Potential Threat: Brucella is primarily delivered in an aerosol form.

Signs and Symptoms: Illness, when present, typically presents with fever, headache, muscle pain, joint pain, back pain, sweats, chills, and generalized malaise. Other manifestations include depression, mental status changes, and vertebral osteomyelitis. Fatalities are uncommon.

Diagnosis: Diagnosis requires a high index of suspicion, since many infections present as non-specific febrile illnesses or are asymptomatic.

Mortality: Brucellosis is rarely fatal (<2%), but can persist for months.

Treatment: Antibiotic therapy with doxycycline and rifampin or doxycycline in combination with other medications (such as an aminoglycoside) for six weeks is usually sufficient in most cases.

Prophylaxis: There is no human vaccine available against brucellosis. Antibiotic prophylaxis should be considered for high-risk exposure to a confirmed biological terrorism exposure.

Isolation and Decontamination: Standard precautions are appropriate for providers of healthcare. Person-to-person transmission has been reported via tissue transplantation and sexual contact. Environmental decontamination can be accomplished with a 0.5% hypochlorite solution.

DIARRHEAL DISEASES

Historical Use: In 1984 the Rajneesh cult used *Salmonella* to contaminate salad bars in Oregon. This was an attempt to alter the results of a local election. Over 700 persons became ill. In another case a disgruntled worker used *Shigella* in the U.S. She contaminated pastries and then served them to coworkers. There has not been reported use of *E. Coli* by a bioterrorist.

Potential Threat: Bacteria would be used to contaminate food supplies.

Signs and Symptoms: The three organisms cause diarrhea, nausea, and abdominal pain. *Shigella* and *E.Coli* are more likely to cause bloody diarrhea along with the nausea and

abdominal pain. *Salmonella* usually occurs 12 to 36 hours after ingesting contaminated food or water. *Shigella* usually occurs 1 to 3 days later. *E. Coli* (also known as hemorrhagic colitis) usually occurs after 2 to 8 days.

Diagnosis: Definitive diagnosis requires culture obtained from the feces or by rectal swab.

Mortality: A low fatality rate would be anticipated. They would be used by terrorists more interested in creating large numbers of ill persons as opposed to fatalities.

Treatment: Diarrheal diseases caused by bacteria are potentially treatable with antibiotics. However, antibiotic treatment can actually make things worse (e.g. in *E. Coli* disease it may increase the risk of renal failure). The most important thing is to replace lost fluids.

Prophylaxis: There is no vaccine available against diarrheal diseases caused by these bacteria.

Isolation and Decontamination: It can be spread from person to person by contact with contaminated fecal material (e.g. diapers). The most important prevention strategy is hand-washing. Quarantine is not necessary for these diseases.

GLANDERS AND MELIOIDOSIS

Historical Use: During the U. S. Civil War glanders occurred naturally, especially in areas of stabled horses. In WWII it caused problems for the military on the German Eastern Front. The glanders organism was weaponized by the Soviets during the Cold War.

Potential Threat: The bacterial agents that cause glanders and meliodosis can be delivered as an aerosol or by direct contact with infected material.

Signs and Symptoms: Incubation period ranges from 10-14 days after inhalation. Onset of symptoms may be abrupt or gradual. Inhalational exposure produces fever (common in excess of 102 F.), shaking chills, sweats, muscle pain, headache, chest pain with respirations, enlarged cervical lymph nodes, enlarged liver and/or spleen, and generalized papular/pustular eruptions. Acute pulmonary disease can progress and result in bacteria in the blood and acute blood poisoning. Both diseases are almost always fatal without treatment.

Diagnosis: CXR may show seed-like lesions, small multiple lung abscesses, or infiltrates involving upper lungs, with solidification and cavitation.

Mortality: Untreated, the fatality rate is up to 95%.

Treatment: Therapy will vary with the type and severity of the clinical presentation but may include sulfonamides, tetracyclines and chloramphenicol. Patients with localized disease may be managed with oral antibiotics for a duration of 60-150 days. More severe illness may require intravenous therapy and more prolonged treatment.

Prophylaxis: Currently, no pre-exposure or post-exposure prophylaxis is available.

Isolation and Decontamination: Standard Precautions for healthcare workers. Person-to-person airborne transmission is unlikely, although secondary cases may occur through improper handling of infected secretions. Contact precautions are indicated while caring for patients with skin involvement. Environmental decontamination using a 0.5% hypochlorite solution is effective.

PLAGUE

Historical Use: It was recorded as a disease in 541 A.D. In the 1300's Tartar forces catapulted bodies of plague victims into the besieged Genoese city of Kaffa. In WWII the Japanese dropped infected fleas in parts of Manchuria. During the Vietnam conflict there were a few cases in US troops due to bites from the Oriental Rat Flea.

Potential Threat: It would primarily be delivered as an aerosol.

Signs and Symptoms: Pneumonic plague begins after an incubation period of 1-6 days, with high fever, chills, headache, malaise, followed by cough (often with blood), progressing rapidly to shortness of breath, stridor, bluish-tinged skin, and death. Gastrointestinal symptoms are often present. Death results from respiratory failure, circulatory collapse, and a bleeding abnormality. Bubonic plague, featuring high fever, malaise, and painful lymph nodes (buboes) may progress spontaneously to the septicemic form (septic shock, thrombosis, DIC) or to the pneumonic (lung) form.

Diagnosis: Suspect plague if large numbers of previously healthy individuals develop severe pneumonia, especially if coughing of blood is present. Definitive diagnosis requires culture of the organism.

Mortality: Untreated bubonic plague has a 50-60% fatality rate. Pneumonic plague is usually fatal if not treated in the first 18 hours.

Treatment: Early administration of antibiotics is critical, as pneumonic plague is invariably fatal if antibiotic therapy is delayed more than 1 day after the onset of symptoms. Choose one of the following: streptomycin, gentamicin, ciprofloxacin, or doxycycline for 10-14 days. Chloramphenicol is the drug of choice for plague meningitis.

Prophylaxis: For asymptomatic persons exposed to a plague aerosol or to a patient with suspected pneumonic plague, give doxycycline 100 mg orally twice daily for seven days or the duration of risk of exposure plus one week. Alternative antibiotics include ciprofloxacin, tetracycline, or chloramphenicol. No vaccine is currently available for

plague prophylaxis. The previously available licensed, killed vaccine was effective against bubonic plague, but not against aerosol exposure.

Isolation and Decontamination: Use Standard Precautions for bubonic plague, and Respiratory Droplet Precautions for suspected pneumonic plague. *Y. pestis* can survive in the environment for varying periods, but is susceptible to heat, disinfectants, and exposure to sunlight. Soap and water is effective if decontamination is needed. Take measures to prevent local disease cycles if vectors (fleas) and reservoirs (rodents) are present.

Q FEVER

Historical Use: In World Wars I and II, troops became infected after sleeping in straw or hay contaminated by animals. In the 1950's volunteers at Camp Detrick (later changed to Fort Detrick) were exposed to Q fever by aerosol and monitored for disease progression.

Potential Threat: The bacteria causing Q fever would primarily be delivered as an aerosol.

Signs and Symptoms: Fever, cough, and chest pain with respirations may occur as early as ten days after exposure. Patients are not generally critically ill, and the illness lasts from 2 days to 2 weeks.

Diagnosis: Q fever is not a clinically distinct illness and may resemble a viral illness or other types of atypical pneumonia. The diagnosis is confirmed by a blood test.

Mortality: Mortality is less then 2%, even if untreated. Death usually is due to endocarditis (heart inflammation).

Treatment: Q fever is generally a self-limited illness even without treatment, but tetracycline or doxycycline should be given orally for 5 to 7 days to prevent complications of the disease. Q fever endocarditis (rare) is much more difficult to treat.

Prophylaxis: Antibiotic prophylaxis begun too early during the incubation period may delay but not prevent the onset of symptoms. Therefore, tetracycline or doxycycline should be started 8-12 days post exposure and continued for 5 days. This regimen has been shown to prevent clinical disease.

Isolation and Decontamination: Standard Precautions are recommended for healthcare workers. Person-to-person transmission is rare. Patients exposed to Q fever by aerosol do not present a risk for secondary contamination or re-aerosolization of the organism. Decontamination is accomplished with soap and water or a 0.5% chlorine solution on personnel.

TULAREMIA

Historical Use: Tularemia (also known as rabbit fever) was first identified as a human acquired disease in Tulare County, California. It was weaponized by the United States in the 1950's and 1960's during the U.S. Offensive Biological Warfare Program. The Soviet Union also was thought to have weaponized it.

Potential Threat: Tularemia could potentially be stabilized in either a wet, frozen, or dried form and delivered as an aerosol.

Signs and Symptoms: Ulceroglandular tularemia presents with a local ulcer and regionally enlarged lymph nodes, fever, chills, headache and malaise. Typhoidal tularemia presents with fever, headache, malaise, substernal discomfort, prostration, weight loss and a non-productive cough.

Diagnosis: Clinical diagnosis. Physical findings are usually non-specific. Chest x-ray may reveal a pneumonic (lung) process, enlarged mediastinal lymph nodes or pleural effusion (fluid in the lung spaces). Routine culture is possible but difficult. The diagnosis can be established retrospectively by a blood test.

Mortality: Without treatment, tularemia has up to a 35% fatality rate. With treatment there is approximately a 2% fatality rate.

Treatment: Administration of antibiotics (streptomycin or gentamicin) with early treatment is very effective.

Prophylaxis: A two-week course of tetracycline is effective as prophylaxis when given after exposure.

Isolation and Decontamination: Standard Precautions for healthcare workers. Organisms are relatively easy to render harmless by mild heat (55° C for 10 minutes) and standard disinfectants.

VIRAL AGENTS

Viruses are the simplest microorganisms and consist of a nucleocapsid protein coat containing genetic material, either RNA or DNA. Antibiotics do not have an effect on viruses. This chapter covers three types of viruses that could potentially be employed as bio-terrorism agents: smallpox, alphaviruses (e.g., VEE), and viral hemorrhagic fever (VHF) viruses.

SMALLPOX

Historical Use: When the Spanish invaded the Americas, it is estimated over 3.5 million Aztec Indians died in 2 years from the disease. The British during the French and Indian War (1754-67) gave smallpox-contaminated bedding to local Indian leaders. The Japanese used in experimentally on POW's during WWII.

Potential Threat: Smallpox can effectively be delivered as an aerosol.

Signs and Symptoms: Clinical manifestations begin acutely with malaise, fever, shaking chills, vomiting, headache, and backache. 2-3 days later lesions appear which quickly progress from macules to papules, and eventually to pustular vesicles. They are more abundant on the extremities and face, and develop synchronously.

Diagnosis: Clinical suspicion is based on the presentation of the above symptoms.

Mortality: The fatality rate has varied from 20 to 95% in unvaccinated persons, but is generally considered to be about 30%.

Treatment: At present there is no effective medication therapy, and treatment of a clinical case remains supportive.

Prophylaxis: Immediate vaccination or revaccination should be undertaken for all personnel exposed.

Isolation and Decontamination: Droplet and Airborne Precautions for a minimum of 17 days following exposure for all contacts. Patients should be considered infectious until all scabs separate and quarantined during this period. Strict quarantine of asymptomatic contacts should be done. If quarantine is not possible, require contacts to check their temperatures daily. Any fever above 38° C (101° F) during the 17-day period following exposure to a confirmed case would suggest the development of smallpox. The contact should then be isolated immediately until smallpox is either confirmed or ruled out and remain in isolation until all scabs separate.

VENEZUELAN EQUINE ENCEPHALITIS (VEE)

Historical Use: It was weaponized by the United States in the 1950's and 1960's before the U. S. Offensive Biowarfare Program was terminated. It was considered for use as a "humane" weapon against the Viet Cong during the early Vietnam War. However it was not utilized. It was discussed as a preinvasion agent to lessen resistance in Cuba in the early 60's. It was not used. There are no reported cases of VEE as a bioweapon.

Potential Threat: The primary means of dispersal is in aerosol form. This virus can theoretically be produced either wet or dry. A biowarfare attack could also occur by infecting Equidae, an appropriate mosquito vector, and initiating an epidemic.

Signs and Symptoms: Incubation period 1-6 days. Acute systemic febrile illness with encephalitis develops in a small percentage (4% children; < 1% adults). Generalized malaise, spiking fevers, shaking chills, severe headache, pain in the eyes with exposure to light, and muscle pain for 24-72 hours may be seen. Nausea, vomiting, cough, sore throat, and diarrhea may follow. Full recovery from malaise and fatigue takes 1-2 weeks. The incidence of CNS disease and associated morbidity and mortality would be much higher after a bio-terrorism attack.

Diagnosis: Clinical diagnosis. Physical findings are non-specific.

Mortality: Adults with VEE have a fatality rate of less than 1%. In children with severe encephalitis the fatality rate is 20%. Full recovery takes 1 to 2 weeks.

Therapy: Treatment is supportive only. Treat uncomplicated VEE infections with analgesics to relieve headache and myalgia. Patients who develop encephalitis may require anticonvulsants and intensive supportive care to maintain fluid and electrolyte balance, ensure adequate ventilation, and avoid complicating secondary bacterial infections.

Prophylaxis: There is no post-exposure prophylaxis.

Isolation and Decontamination: Patient isolation and quarantine is not required. Standard Precautions augmented with vector control while the patient is febrile. There is no evidence of direct human-to-human or horse-to-human transmission. The virus can be destroyed by heat (80^{o}C for 30 min) and standard disinfectants.

VIRAL HEMORRHAGIC FEVERS (VHF)

Historical Use: There is no good evidence of previous use as a warfare agent.

Potential Threat: VHF diseases can potentially be delivered as an aerosol.

Signs and Symptoms: VHFs are febrile illnesses that can feature flushing of the face and chest, petechiae, bleeding, edema, abnormally low blood pressure, and shock. Malaise, muscle pain, headache, vomiting, and diarrhea may occur in any of the hemorrhagic fevers.

Diagnosis: Definitive diagnosis rests on specific viral lab tests. Significant numbers of personnel with a hemorrhagic fever syndrome should suggest the diagnosis of a viral hemorrhagic fever.

Mortality: The fatality rate varies from disease to disease. It can be as low as 5% and as high as 88%, such as in Ebola.

Treatment: Intensive supportive care may be required. Antiviral therapy with ribavirin may be useful in several of these infections (Available only as Investigational New Drug under protocol).

Prophylaxis: The only licensed VHF vaccine is yellow fever vaccine. Prophylactic ribavirin may be effective for Lassa fever, Rift Valley fever, and Crimean-Congo Hemorrhagic Fever (CCHF) (Available only as IND under protocol).

Isolation and Decontamination: Contact isolation, with the addition of a surgical mask and eye protection for those coming within three feet of the patient, is indicated for

suspected or proven Lassa fever, CCHF, or filovirus (Ebola, Marburg) infections. Respiratory protection should be upgraded to airborne isolation, including the use of a fit-tested HEPA-filtered respirator, a battery powered air-purifying respirator, or a positive pressure supplied air respirator, if patients with the above conditions have prominent cough, vomiting, diarrhea, or hemorrhage. Decontamination is accomplished with hypochlorite or phenolic disinfectants.

BIOLOGICAL TOXINS

Toxins are harmful substances produced by living organisms (animals, plants, microbes). Features that distinguish them from chemical agents, such as VX, cyanide, or mustard, include being not man-made, non-volatile (no vapor hazard), usually not dermally (skin) active (mycotoxins are the exception), and generally much more toxic per weight than chemical agents.

This chapter will cover four toxins considered to be among the most likely to be used against U.S. military and civilian targets: botulinum toxins, ricin, staphylococcal enterotoxin B (SEB), and T-2 mycotoxins.

BOTULINUM

Historical Use: In WWII there was concern about potential delivery by the German V-1 rocket system. The British stocked up on an antidote that was not used. The Japanese cult group, Aum Shrinryko, in the 1990's did research on its use, but it was not deployed. Iraq is known to have filled over 100 munitions (bombs and missiles) with botulism toxin.

Potential Threat: Botulinum toxin could be placed in food sources or delivered as an aerosol.

Signs and Symptoms: Usually begins with cranial nerve palsies, including ptosis, blurred vision, double vision, dry mouth and throat, difficulty swallowing, and altered voice. This is followed by symmetrical descending flaccid (weak, soft) paralysis, with generalized weakness and progression to respiratory failure. Symptoms begin as early as 12-36 hours after inhalation, but may take several days after exposure to low doses of toxin.

Diagnosis: Diagnosis is primarily a clinical one. A bioterrorism attack should be suspected if multiple casualties simultaneously present with progressive descending flaccid paralysis.

Mortality: Without support for breathing, botulism has a 60% fatality rate. With prompt diagnosis and support the fatality rate is as low as 5%.

Treatment: Early administration of trivalent licensed antitoxin or heptavalent antitoxin (IND product) may prevent or decrease progression to respiratory failure and hasten recovery. Intubation and ventilatory assistance may be needed for respiratory failure. Tracheostomy may be required.

Prophylaxis: Vaccine is generally not available.

Isolation and Decontamination: Standard Precautions for healthcare workers. Toxin is not dermally (skin) active and secondary aerosols are not a hazard from patients. Decontaminate with soap and water. Botulinum toxin is inactivated by sunlight within 1-3 hours. Heat (80^{O}C for 30 min., 100^{O}C for several minutes) and chlorine also destroy the toxin.

RICIN

Historical Use: Ricin is a toxin that is obtained from castor bean plants. It was tested by the U.S. and Britain in WWII, but never used. It was used by a Bulgarian agent via a hidden needle in the end of an umbrella and fatally injected into an exiled Bulgarian.

Potential Threat: Ricin toxin can be delivered by injection, ingestion, or aerosol. It is least toxic when eaten.

Signs and Symptoms: Acute onset of fever, chest tightness, cough, shortness of breath, nausea, and joint pain occurs 4 to 8 hours after inhalational exposure. Airway necrosis and pulmonary capillary leak resulting in pulmonary edema would likely occur within 18-24 hours, followed by severe respiratory distress and death from hypoxemia (low blood oxygen) in 36-72 hours.

Diagnosis: Acute lung injury in large numbers of geographically clustered patients suggests exposure to aerosolized ricin. The rapid time course to severe symptoms and death would be unusual for infectious agents.

Mortality: The ingested mortality rate is thought to be about 2%.

Treatment: Management is supportive and should include treatment for pulmonary edema. Gastric lavage and cathartics (emetics) are indicated for ingestion, but charcoal is of little value for large molecules such as ricin.

Prophylaxis: There is currently no vaccine or prophylactic antitoxin available for human use. Use of the protective mask is currently the best protection against inhalation.

Isolation and Decontamination: Standard Precautions for healthcare workers. Ricin is non-volatile, and secondary aerosols are not expected to be a danger to health care providers. Decontaminate with soap and water. Hypochlorite solutions (0.1% sodium hypochlorite) can inactivate ricin.

STAPHYLOCOCCAL ENTEROTOXIN B (SEB)

Historical Use: SEB is a bacterial toxin that is a common cause of food poisoning. In the 1960's the U.S. studied its use as a potential agent to incapacitate large numbers of troops. Persons who became clinically ill might be incapacitated for up to 2 weeks. There were reports of Soviet use under their biological warfare program.

Potential Threat: SEB could be delivered as an aerosol or a food supply contaminate.

Signs and Symptoms: Latent period of 3-12 hours after aerosol exposure is followed by sudden onset of fever, chills, headache, muscle pain, and nonproductive cough. Some patients may develop shortness of breath and mid-chest pain. Patients tend to plateau rapidly to a fairly stable clinical state. Fever may last 2 to 5 days, and cough may persist for up to 4 weeks. Patients may also present with nausea, vomiting, and diarrhea if they swallow the toxin. Presumably, higher exposure can lead to septic shock and death.

Diagnosis: Diagnosis is clinical. Patients will present with a febrile respiratory syndrome without CXR abnormalities. Large numbers of patients presenting in a short period of time with typical symptoms and signs of SEB pulmonary exposure would suggest an intentional attack with this toxin.

Mortality: In a case of 9 laboratory workers exposed to an inhalation toxin, none died.

Treatment: Treatment is limited to supportive care. Artificial ventilation might be needed for very severe cases, and attention to fluid management is important.

Prophylaxis: Use of protective mask. There is currently no human vaccine available to prevent SEB intoxication.

Isolation and Decontamination: Standard Precautions for healthcare workers. SEB is not dermally active and secondary aerosols are not a hazard from patients. Decontaminate with soap and water. Destroy any food that may have been contaminated.

T-2 MYCOTOXINS

Historical Use: Mycotoxins are compounds produced by filamentous fungi (molds). They were first reported as a potential biological weapon by the Russian military shortly after World War II though no use was reported. Mycotoxins allegedly have been used in aerosol form to produce lethal and non-lethal casualties in Laos (1975-81), Kampuchea (1979-81), and Afghanistan (1979-81). An estimated 10,000 civilians and guerilla forces were killed by "yellow rain" during this time period. Some investigators have claimed that the "yellow clouds" were, in fact, bee feces produced by swarms of migrating insects. Much controversy has centered upon the veracity of eyewitness and victim accounts, but there is evidence to make these allegations of biological warfare agent use in these areas possible. Iraq has admitted to doing basic research on mycotoxins.

Potential Threat: The primary means of dispersal is in aerosol form. The attack occurs in the form of "yellow rain" with droplets of yellow fluid contaminating clothes and the environment.

Signs and symptoms: Exposure causes skin pain, itching, redness, vesicles, necrosis and shedding of the skin. Effects on the airway include nose and throat pain, nasal discharge, itching and sneezing, cough, shortness of breath, wheezing, chest pain and bloody sputum. Toxin also produces effects after ingestion or eye contact. Severe intoxication results in prostration, weakness, ataxia, collapse, shock, and death.

Diagnosis: Should be suspected if an aerosol attack occurs in the form of "yellow rain" with droplets of variously pigmented oily fluids contaminating clothes and the environment. Confirmation requires testing of blood, tissue and environmental samples.

Mortality: In experimental animals, there was a rapid onset of shock and death within 12 to 24 hours.

Treatment: There is no specific antidote. Treatment is supportive. Soap and water washing, even 4-6 hours after exposure can significantly reduce dermal toxicity; washing within 1 hour may prevent toxicity entirely. Superactivated charcoal should be given orally if the toxin is swallowed.

Prophylaxis: The only defense is to prevent exposure by wearing a protective mask and clothing (or topical skin protectant) during an attack. No specific immunotherapy or chemotherapy is available for use in the field.

Isolation and Decontamination: Outer clothing should be removed and exposed skin decontaminated with soap and water. Eye exposure should be treated with copious saline irrigation. Secondary aerosols are not a hazard; however, contact with contaminated skin and clothing can produce secondary dermal exposures. Contact Precautions are warranted until decontamination is accomplished. Then, Standard Precautions are recommended for healthcare workers. Environmental decontamination requires the use of a hypochlorite solution under alkaline conditions such as 1% sodium hypochlorite and 0.1M NaOH with 1-hour contact time.

DETECTION

Detector systems are evolving, and represent an area of intense interest with the highest priorities within the research and development community. However, until reliable detectors are available in sufficient numbers, usually the first indicator of a biological attack in unprotected people will be those who become ill.

DECONTAMINATION

Contamination is the introduction of an infectious agent on a body surface, food or water, or other inanimate objects. Decontamination involves either disinfection or sterilization to reduce microorganisms to an acceptable level on contaminated articles,

thus rendering them suitable for use. Disinfection is the selective reduction of undesirable microbes to a level below that required for transmission. Sterilization is the killing of all organisms.

Decontamination methods have always played an important role in the control of infectious diseases. However, we are often unable to use the most efficient means of rendering microbes harmless (e.g., toxic chemical sterilization), as these methods may injure people and damage materials that are to be decontaminated. Though some sophisticated methods of decontamination may not be available underway, some fairly simple tools are available. Bio-terrorism agents can be decontaminated by mechanical, chemical and physical methods:

1) Mechanical decontamination involves measures to remove but not necessarily neutralize an agent. An example is the filtering of drinking water to remove certain water-borne biologic agents (e.g. *Dracunculus medinensis*), or in a bioterrorism context, the use of an air filter to remove aerosolized anthrax spores, or water to wash agent from the skin.

2) Chemical decontamination renders bioterrorism agents harmless by the use of disinfectants that are usually in the form of a liquid, gas or aerosol. Some disinfectants are harmful to humans, animals, the environment, and materials.

3) Physical means (heat, radiation) are other methods that can be employed for decontamination of objects.

Dermal (skin) exposure to a suspected bioterrorism aerosol should be immediately treated by soap and water decontamination. Careful washing with soap and water removes nearly all of the agent from the skin surface. Hypochlorite solution or other disinfectants are reserved for gross contamination (i.e. following the spill of solid or liquid agent from a munition directly onto the skin). In the absence of chemical or gross biological contamination, these will confer no additional benefit, may be caustic, and may predispose to colonization and resistant superinfection by reducing the normal skin flora. Grossly contaminated skin surfaces should be washed with a 0.5% sodium hypochlorite solution, if available, with a contact time of 10 to 15 minutes.

The 0.5% solution can be made by adding one 6-ounce container of calcium hypochlorite to five gallons of water. The 5% solution can be made by adding eight 6-ounce ampules of calcium hypochlorite to five gallons of water. These solutions evaporate quickly at high temperatures so if they are made in advance they should be stored in closed containers. Also the chlorine solutions should be placed in distinctly marked containers because it is very difficult to tell the difference between the 5% chlorine solution and the 0.5% solution.

To mix a 0.5% sodium hypochlorite solution, take one part Clorox and nine parts water (1:9) since standard stock Clorox is a 5.25% sodium hypochlorite solution. The solution is then applied with a cloth or swab. The solution should be made fresh daily with the pH in the alkaline range.

Chlorine solution must NOT be used in (1) open body cavity wounds, as it may lead to the formation of adhesions, or (2) brain and spinal cord injuries. However, this solution may be instilled into non-cavity wounds and then removed by suction to an appropriate disposal container. Within about 5 minutes, this contaminated solution will be neutralized and nonhazardous. Subsequent irrigation with saline or other surgical solutions should be performed. Prevent the chlorine solution from being sprayed into the eyes, as corneal opacities may result.

For decontamination of fabric clothing or equipment, a 5% hypochlorite solution should be used. For decontamination of equipment, a contact time of 30 minutes prior to normal cleaning is required. This is corrosive to most metals and injurious to most fabrics, so rinse thoroughly and oil metal surfaces after completion.

Bioterrorism agents can be rendered harmless through such physical means as heat and radiation. To render agents completely harmless, sterilize with dry heat for two hours at 160 degrees centigrade. If autoclaving with steam at 121 degrees centigrade and 1 atmosphere of overpressure (15 pounds per square inch), the time may be reduced to 20 minutes, depending on volume. Solar ultraviolet (UV) radiation has a disinfectant effect, often in combination with drying. This is effective in certain environmental conditions but hard to standardize for practical usage for decontamination purposes.

PATIENT ISOLATION PRECAUTIONS

STANDARD PRECAUTIONS

- Wash hands after patient contact.
- Wear gloves when touching blood, body fluids, secretions, excretions and contaminated items.
- Wear a mask and eye protection, or a face shield during procedures likely to generate splashes or sprays of blood, body fluids, secretions or excretions
- Handle used patient-care equipment and linen in a manner that prevents the transfer of microorganisms to people or equipment.
- Use care when handling sharps and use a mouthpiece or other ventilation device as an alternative to mouth-to-mouth resuscitation when practical.

Standard precautions are employed in the care of ALL patients

AIRBORNE PRECAUTIONS

Standard Precautions plus:

- Place the patient in a private room that has monitored negative air pressure, a minimum of six air changes/hour, and appropriate filtration of air before it is discharged from the room.
- Wear respiratory protection when entering the room.
- Limit movement and transport of the patient. Place a mask on the patient if they need to be moved.

Biothreat Diseases requiring Airborne Precautions: Smallpox.

DROPLET PRECAUTIONS

Standard Precaution plus:

- Place the patient in a private room or cohort them with someone with the same infection. If not feasible, maintain at least 3 feet between patients.
- Wear a mask when working within 3 feet of the patient.
- Limit movement and transport of the patient. Place a mask on the patient if they need to be moved.

Biothreat Diseases requiring Droplet precautions: Pneumonic Plague.

CONTACT PRECAUTIONS

Standard Precautions plus:

- Place the patient in a private room or cohort them with someone with the same infection if possible.
- Wear gloves when entering the room. Change gloves after contact with infective material.
- Wear a gown when entering the room if contact with patient is anticipated or if the patient has diarrhea, a colostomy or wound drainage not covered by a dressing.
- Limit the movement or transport of the patient from the room.
- Ensure that patient-care items, bedside equipment, and frequently touched surfaces receive daily cleaning.
- Dedicate use of non-critical patient-care equipment (such as stethoscopes) to a single patient, or group of patients with the same disease. If not feasible, adequate disinfection between patients is necessary.

Biothreat Diseases requiring Contact Precautions: Viral Hemorrhagic Fevers.

GLOSSARY OF MEDICAL TERMS

Ataxia-An inability to coordinate muscle activity during voluntary movement, so that smooth movements occur. May involve the limbs, head, or trunk.

Edema-An accumulation of an excessive amount of watery fluid in cells, tissues, or body cavities.

Endotracheal intubation-Passage of a tube through the nose or mouth into the trachea for maintenance of the airway during anesthesia or for maintenance of an imperiled airway.

HEPA-HEPA is an acronym for "high efficiency particulate arresting". These air purifiers effectively remove 99.97% of all pollen, mold spores, animal hair and dander, dust mites, bacteria, smoke particles and dust that pass though the air purifier.

Incubation period-The time period from exposure to biologic agent and the onset of symptoms.

Macula, pl. maculae-1. A small spot, different in color from the surrounding tissue. 2. A small, discolored patch or spot on the skin, neither elevated above nor depressed below the skin's surface.

Malaise-Generalized body discomfort

Mediastinum-The middle partition of the thoracic cavity, containing all the chest organs and structures except the lungs.

Necrosis-Pathologic death of one or more cells, or of a portion of tissue or organ, resulting from irreversible damage.
Osteomyelitis-Inflammation of the bone marrow and adjacent bone.
Papule-A small, circumscribed, solid elevation on the skin.
Petechia, pl. petechiae-Minute hemorrhagic (blood) spots, of pinpoint to pinhead size, in the skin, which are not blanched by pressure.
Stridor-A high-pitched, noisy respiration, like the blowing of the wind; a sign of respiratory obstruction, especially in the trachea or larynx.
Vector-The carrier, usually an animal (e.g. mosquito), that transfers the biologic agent from one host to another.

SUMMARY

Though overall the risks of a specific bioterrorist event to any specific vessel may be low, the potential danger is great enough to warrant pre-planning and preparation. For providers of medical care, the key is to suspect a bioterrorist event if a patient's illness seems strange or unusual, and then to have a plan to address the situation. This section has provided a basic introduction to this process.