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**FIELD MANUAL**

**TREATMENT OF  
BIOLOGICAL WARFARE  
AGENT CASUALTIES**

**HEADQUARTERS, DEPARTMENTS OF THE ARMY, THE NAVY, AND  
THE AIR FORCE, AND COMMANDANT, MARINE CORPS**

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**17 July 2000**

Change 1

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DEPARTMENTS OF THE ARMY,  
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TREATMENT OF BIOLOGICAL WARFARE AGENT CASUALTIES

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TREATMENT OF BIOLOGICAL WARFARE AGENT CASUALTIES

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- When was the sample/specimen collected?
- Who has maintained custody of the sample/specimen?
- What has been done with the sample/specimen at each change of custody?

**CAUTION**

Each change of custody must be recorded with date and time of change.

*b.* The samples/specimens must be appropriately packaged, labeled, and evacuated to the designated laboratory for confirmation of a BW attack. The standard chain of custody for sample/specimen evacuation is as follows:

- Sampling unit.
- Unit S2 (Intelligence Officer [US Army]), medical operations officer, or other designated person.
- Technical escort unit or other command-designated escort personnel.
- In-theater supporting medical laboratory, if in operation.
- Continental US laboratory.

**1-12. Identification Methods for Biological Warfare Agents**

The following are identification methods for BW agents:

- Isolation of the etiologic agent by culture (possible in one to two days for some agents).
- Detection of agents by enzyme immunoassay, mass spectrometry, animal inoculation, or other methods.
- Antibody detection (specific immunoglobulin [IgM] may appear within 3 days).
- Genome detection by PCR.
- Detection of metabolic products of the infectious or toxic agent in clinical specimens.

### 1-13. Therapy

★ *a. Endemic Disease versus Biological Agent.* Specific therapies are discussed for each agent. Most of these are based on standard treatment guidelines. However, some of the prophylaxis regimens and therapies recommended in this manual vary from those found in standard references and may include off-label indications. This is because—

- A BW exposure (aerosol) may produce a disease with clinical features different from the naturally occurring disease. For example, inhalation (BW) versus cutaneous (endemic) anthrax. Cases of endemic disease due to inhalation of some of these agents are rare and clinical experience is limited. Human challenge studies can be done with only a limited number of agents for obvious ethical and safety reasons. Accordingly, some of the prophylactic and treatment regimens have been developed from in vitro studies, animal models, and limited human data.

- An adversary may develop a BW agent resistant to the standard antibiotic therapy.

*b. Endemic Disease Therapy.* For endemic and epidemic disease therapies, see FM 8-33 and the civilian textbooks listed in the references.

### 1-14. Case Reporting and Epidemiological Assessment

It is imperative that clinicians report cases of suspected BW-related illnesses to the appropriate line and medical chains of command. Prompt epidemiological investigations must begin and preventive measures implemented to control the disease or reduce the number of cases.

### ★ 1-15. Prevention

Most morbidity and mortality from BW threat agents is preventable. Immunizations, pre-exposure chemoprophylaxes, post-exposure chemoprophylaxes, and protective clothing are available to provide protection. Personnel must have all required immunizations administered prior to entering an AO where BW agent employment is a threat. All immunizations should be administered in sufficient time to provide the initial protection before troops are deployed to the AO; when administration prior to deployment is impossible, troops must receive the immunizations as soon as the mission permits in the AO. Some immunizations are used in conjunction with pre-exposure chemoprophylaxes or post-exposure chemoprophylaxes to provide protection. The supporting PHS/PVNTMED units/staffs can assist commanders in determining which specific immunizations and chemoprophylaxes are required for the AO. The corps/division/wing/equivalent service/joint task force commander will decide whether to begin, continue, or discontinue the administration of chemoprophylaxes based on the BW threat. The intelligence officer, chemical officer, and surgeon advise the commander on appropriate courses of action. For those BW agents that a specific immunization is not available, the use of protective equipment combined with chemoprophylaxes may be employed to provide protection.

*a. Active Immunization.* As of January 1999, vaccines are available for the following potential BW agent threats:

- Anthrax.
- \*Argentine hemorrhagic fever.

standard precautions as outlined in the Centers for Disease Control and Prevention (CDC) Guidelines for Isolation Precautions in Hospitals will be followed. If plague, smallpox, and viral hemorrhagic fevers (VHF) can be reasonably excluded on the basis of analysis of clinical specimens and environmental samples, patients may be evacuated using Standard Precautions and the disease-specific precautions discussed for each suspect BW agent in the following chapters.

(3) Biological warfare attacks may occur with multiple agents with short and prolonged incubation times (botulinum toxin, 12 to 36 hours and smallpox, 7 to 17 days). Multiple agents can lead to the presence of coinfection-acute illness with short incubation and incubating smallpox (which may declare itself after patients have been evacuated for evaluation/treatment of the short incubating disease). Therefore, consideration should be given to quarantining patients for 17 days after AE from the BW area if plague or smallpox cannot be excluded. Reevaluate patients carefully for recurrent fever or other changes in clinical status. If clinical or laboratory findings suggest prodromal or syndromic smallpox, plague, or VHFs, institute appropriate isolation until the diagnosis is clarified. Specific control measures must be applied as presented for the following diseases/BW agent casualties:

(a) *Plague*. Plague is an internationally quarantinable disease (IQD). Do not evacuate across international borders unless authorized by the theater surgeon. Evacuate in cohorts of plague patients only on dedicated AE aircraft; treat in theater. Pneumonic plague is highly transmissible person-to-person. Droplet precautions are added to standard precautions for patients with pneumonic plague until sputum cultures are negative.

(b) *Smallpox*. Currently eradicated and no longer listed as IQD. Immediately notify the line and medical chain of command upon diagnosis. Do not evacuate across international borders unless authorized by the theater surgeon. Evacuate in cohorts of smallpox patients only on dedicated AE aircraft; treat in theater. Smallpox is transmissible person-to-person. Strict quarantine is required. Standard, contact, and airborne isolation precautions are to be observed. All contacts should be vaccinated and quarantined/grouped together for at least 17 days following the most recent exposure.

(c) *Viral hemorrhagic fevers*. The World Health Organization (WHO) does not require quarantine for hemorrhagic fevers, with the exception of yellow fever. However, due to international concerns, do not evacuate hemorrhagic fever patients across international borders unless authorized by the theater surgeon. Evacuate in cohorts of hemorrhagic fever patients only on dedicated AE aircraft. Medical evacuation may result in increased morbidity and mortality for patients with hemorrhagic fever; treatment at a local facility is preferred. Person-to-person transmission is possible for the duration of illness. If necessary, patients may be evacuated using standard, contact, plus respiratory droplet isolation precautions.

(d) *Infectious disease of unknown etiology*. Evaluate patient evacuation risk based on the patients' signs/symptoms complex and theater threat list. Assume infection with the agent requiring the most stringent infection control procedures (based on the possible threats in the theater and the clinical picture). Ensure that appropriate patient care is performed while providing the crew and aircraft with the highest level of protection.

(e) *Summary*. In summary, many BW agent casualties may be safely evacuated using basic infection control guidelines. Plague, smallpox, and the hemorrhagic fevers pose significant challenges.

These patient movements will require approval of the destination country, over-flight privileges, and approval of any country where the aircraft will land for servicing or where patients will remain overnight. Countries from which approval is sought are bound by Article 37 of the *Geneva Conventions for the Amelioration of the Condition of the Wounded and Sick in Armed Forces in the Field of 12 August 1949* to ensure humanitarian treatment to wounded and sick. That should include approval under most circumstances of transit of those injured by exposure to biological agents. Additionally, some countries, notably Germany, have already developed procedures for expedited approval of transit of dangerous/hazardous goods in their air space. That information is contained in the DOD Foreign Clearance Guide. Coordination between the theater or USTRANSCOM commander/surgeon and the Department of State is required for such movements.

### **1-22. Aeromedical Isolation Team**

The USAMRIID maintains an aeromedical isolation team (AIT). The AIT is a rapid response team with worldwide airlift capability. The AIT is designed to safely evacuate and manage patients with potentially lethal communicable diseases under high-level containment. Indications for deployment include cases of a highly contagious, lethal, or unidentified disease, including cases from a suspect BW attack. Diagnosis and medical care will be provided at USAMRIID. The AIT can only transport a limited number of patients. The AIT **CANNOT** provide for mass casualty evacuation. Such evacuation can enhance early identification of a BW agent; thus, enabling early development of treatment recommendations for medical providers in the TO. The AIT also offers a portable containment laboratory, limited environmental decontamination, and specialized consultative expertise.

### **★ 1-23. Investigational New Drugs and Off-Label Indications**

*a.* On 30 September 1999, the President of the United States issued Executive Order (EO) 13139, Improving Health Protection of Military Personnel Participating in Particular Military Operations, which outlines the conditions under which investigational new drugs (IND) and off-label pharmaceuticals could be administered to US service members. This publication discusses numerous pharmaceutical products, some of which are IND. In certain other cases, licensed pharmaceuticals are discussed for use in a manner or for a condition other than that for which they are licensed (Example: An off-label indication).

*b.* Executive Order 13139 does not intend to alter the traditional physician-patient relationship or individual physician prescribing practices. Health care providers remain free to exercise clinical judgment and prescribe licensed pharmaceutical products as they deem appropriate for the optimal care of their patients. This policy does, however, potentially influence recommendations that might be made by US government agencies and that might be applied to large numbers of service members outside of the individual physician-patient relationship. Key summary points from EO 13139 include:

- The EO describes the Secretary of Defense responsibilities regarding the use of IND products or off-label use of products as antidotes to chemical, biological, or radiological weapons.

- The EO stipulates that the US Government will administer only FDA-approved products for their labeled uses. (However, off-label indications and IND usage rules may apply as discussed below and in other areas of this publication.)



- The EO details IND product use parameters and controls.
- The EO requires individual service member informed consent before IND administration.

However, only the President may waive this informed consent requirement upon request of the Secretary of Defense if—

- Service member informed consent is not feasible.
- Informed consent is contrary to the best interest of the service member.
- Obtaining informed consent is not in the best interest of national security.

## CHAPTER 2

# BACTERIAL AGENTS

## Section I. INTRODUCTION

### 2-1. General

Bacterial organisms comprise the greatest number of pathogens in the list of potential BW agents. They include the etiologic agents of anthrax, brucellosis, cholera, glanders, melioidosis, plague, Q fever, and tularemia. Of these, anthrax is the most likely BW threat that troops will encounter in an AO. See Appendix B for guidance on medical management of BW agent casualties.

## Section II. ANTHRAX

### 2-2. General

*a. Etiologic Agent.* The spores of *Bacillus anthracis*, an encapsulated gram-positive bacillus. Sporulation occurs under adverse environmental conditions and when vegetative bacteria are exposed to air; the spores are extremely hardy and can survive extremes of temperature, dryness, and flooding. When conditions improve, the spores germinate to produce vegetative bacteria.

*b. Reservoir.* The soil, with worldwide distribution.

*c. Transmission.* The stage in the bacterial life cycle, which poses a health hazard, is the spore. Grazing animals contract spores from the vegetation. Humans contract spores via contact with infected animals, their hides, wool, or other products; from ingesting contaminated meat; or from inhaling spores during the processing of wool for textiles. Biting flies in sub-Saharan Africa may also transmit anthrax to humans. Humans usually do not contract anthrax directly from the soil, unless they work with fertilizers (bonemeal) prepared from infected animals. Also, humans can contract spores from inhalation of aerosolized spores released during a BW attack.

*d. Endemic Disease.* Endemic infectious disease is contracted by inhalation, cutaneous exposure, oropharyngeal exposure, and ingestion.

(1) Cutaneous anthrax accounts for more than 90 percent of all anthrax cases worldwide. Disease results when *Bacillus anthracis* spores are introduced into the skin via inoculation of small cuts/abrasions or inapparent skin lesions. It may possibly be introduced by biting flies. Cutaneous anthrax features a painless necrotic ulcer with a black eschar and local edema. The case fatality rate for untreated cutaneous anthrax is up to 20 percent, but with early, effective therapy is reduced to less than 5 percent.

(2) Oropharyngeal and GI diseases occur following the ingestion of anthrax spores, usually from consuming meat from infected animals. The clinical features of oropharyngeal and GI anthrax are discussed below in paragraph 2-6.

(3) Inhalation anthrax occurs when individuals working with animal hides, wool, or bonemeal inhale the spores. Also, inhalation anthrax may occur from inhalation of aerosolized spores released during a BW attack. The clinical features of inhalation anthrax are discussed below in paragraph 2-6.

### **2-3. Biological Warfare Agent Delivery**

Aerosolized spores may be delivered by missiles, bomblets, artillery fires, point release, or airborne line release. Contamination of food and water may also be used.

### **2-4. Environmental Detection**

Nuclear, biological, and chemical teams or other bioenvironmental engineering (BEE) personnel operating similar detection equipment accomplish detection. Preventive medicine/PHS/BEE personnel perform detection in water supplies. Detection in food supplies may be performed by veterinary, PVNTMED, or PHS personnel. Detection in animals may be performed by veterinary personnel.

### **2-5. Prevention**

*a. Pre-exposure Prophylaxis.* Prevention may be accomplished by immunization plus chemoprophylaxis.

(1) *Immunization.* Anthrax vaccine is given in six doses at 0, 2, and 4 weeks and 6, 12, and 18 months, with annual boosting. A minimum of three doses administered within 6 months prior to the exposure may confer protective immunity.

★ (2) *Chemoprophylaxis.* While the FDA has not approved the use of pre-exposure antibiotics, empiric evidence indicates their use may significantly reduce morbidity and mortality. Therefore, they should be considered for use on a case-by-case basis and used as indicated for post-exposure preventive measures. Such use would require application of IND protocols (see paragraph 1-23).

*b. Post-exposure Prophylaxis.* Use immunization with chemoprophylaxis to prevent the clinical manifestation of the disease.

(1) *Anthrax vaccine.* For personnel who have completed the six-dose series and are up to date on boosters, or who have received at least three initial doses within 6 months prior to exposure, no additional doses are indicated, except to complete the series as previously scheduled. For personnel who have not received any immunizations, begin series and give a minimum of three doses; complete the six-dose series, if possible. Use of anthrax vaccine post-exposure requires application of an IND protocol.

★ (2) *Chemoprophylaxis.* Chemoprophylaxis is recommended as an adjunct to immunization for post-exposure prophylaxis. All personnel exposed to aerosolized anthrax should be administered Ciprofloxacin hydrochloride tablets (500 mg) orally every 12 hours for 60 days. When Ciprofloxacin

hydrochloride tablets are not available, doxycycline hyclate tablets (100 mg) should be taken orally every 12 hours for 60 days. The duration of chemoprophylaxis administration for individuals without receipt of any vaccine should be extended until they receive at least three doses of vaccine. Chemoprophylaxis should be withdrawn under careful observation and with access to an MTF with intensive care and consultative assets. If fever develops following the withdrawal of chemoprophylaxis, empiric therapy for anthrax is indicated pending etiologic diagnosis.

## **2-6. Biological Warfare Clinical Presentation**

*a. Incubation Period.* The incubation for anthrax is hours to 7 days. Most cases present within 48 hours post-exposure.

*b. Signs and Symptoms.*

(1) *Inhalation anthrax.* Inhalation anthrax will begin with nonspecific symptoms of fever, malaise, and fatigue. A nonproductive cough and vague chest discomfort may be present. These initial symptoms may be followed by a short period of symptomatic improvement, hours to 3 days in duration. This will be followed by an acute phase, including the abrupt onset of severe respiratory distress with dyspnea, stridor, diaphoresis, and cyanosis. Bacteremia and toxemia, septic shock, metastatic infection (meningitis in approximately 50 percent of the cases), and death usually occurs within 24 to 36 hours from the onset of the acute phase.

(2) *Oropharyngeal or gastrointestinal anthrax.* Oropharyngeal or GI anthrax can occur following ingestion of food contaminated with anthrax spores.

(a) Oropharyngeal anthrax will present with initial symptoms of fever, sore throat, and difficulty swallowing. The disease may progress to an acute phase with symptoms including a necrotic ulcer or eschar involving the hard palate, tonsils, or posterior oropharyngeal wall, edema of cervical tissues (possibly resulting in upper airway obstruction), and cervical lymphadenopathy. Most acute cases progress to septic shock and death.

(b) Gastrointestinal anthrax begins with vague initial symptoms featuring fever, anorexia, nausea, and vomiting. Abdominal pain, bloody vomiting, bloody diarrhea, and possibly massive abdominal swelling (ascites) may follow these symptoms. Also, septic shock and death may follow these symptoms.

## **2-7. Diagnosis**

During the incubation period, nasal swabs and specimens of respiratory secretions sent for PCR are the most important diagnostic specimens. During the early disease, blood and respiratory secretions may be sent for rapid identification by genetic typing (PCR). A rapid diagnostic test is available that detects toxin antigens in the blood during the acute phase. Chest x-ray may be normal or show hilar adenopathy early in the illness and may show a widened mediastinum and pleural effusions during the acute phase.

## **2-8. Treatment**

*a. Triage Categories.* Patients presenting with initial signs of inhalation anthrax should be placed in the Immediate category, as early aggressive treatment is lifesaving. Depending on the numbers of cases and available resources, patients presenting in the acute phase of inhalation anthrax should be placed in the Immediate or Expectant categories.

### *b. Medical Management.*

(1) Supportive care includes maintaining the airway, providing resuscitative fluids, and providing vasopressors as indicated for shock.

(2) Specific therapy includes the administration of ciprofloxacin (400 mg intravenous [IV] every 12 hours) or doxycycline (200 mg IV loading dose, followed by 100 mg IV every 12 hours). Specific therapy may also include administration of penicillin (4 million units IV) every 4 hours, if isolate is sensitive to penicillin.

(3) A tracheostomy is indicated for upper airway obstruction due to oropharyngeal anthrax. Surgical debridement of cutaneous lesions is contraindicated. Surgical drainage of the mediastinum for inhalation anthrax is not recommended.

*c. Prognosis.* The number of cases of inhalation anthrax occurring during the antibiotic era is too small to establish case fatality rates and efficacy of treatment. Almost all inhalation anthrax cases in which treatment was begun after onset of significantly severe symptoms have been fatal, regardless of treatment. Despite medical therapy, most patients with inhalation anthrax die within 24 hours of the onset of the acute phase of the illness. However, in nonhuman primate trials, animals have responded to aggressive therapy. The prognosis for oropharyngeal and GI anthrax is poor, with case fatality rates 50 to 100 percent, even with aggressive therapy.

## **2-9. Control of Patients, Contacts, and Treatment Areas**

- Report all cases to line and medical chains of command.
- Employ Standard Precautions for handling, treating, and moving all active cases.
- Use sporicidal agents, such as disinfectant strength iodophors, in MTFs for general area disinfection. Antiseptic strength iodophors are not sporicidal. Hypochlorite solutions may be attenuated by organic matter, but will provide a disinfectant capability when used in a 5-percent solution. The hypochlorite solution should be replaced frequently. Autoclaving, steam sterilizing, or burning is required for complete eradication of spores.

## **2-10. Medical Evacuation**

Patients with anthrax may be evacuated with other categories of patients. Anthrax is not transmissible person to person. Standard Precautions should be observed during evacuation.

(5) The addition of streptomycin is indicated if presentation (acute pneumonia) and sputum studies suggests plague.

*c. Prognosis.* The extent of infection will vary with inoculum, individual's underlying state of health, availability of protective mask or other respiratory protective devices, and other factors. Late activation or recrudescence can result years or decades later.

### **2-36. Control of Patients, Contacts, and Treatment Areas**

Apply Standard Precautions in management of patients and contacts. Glanders, melioidosis, and smallpox may present with diffuse pustular rashes; strict isolation and quarantine would be indicated until smallpox can be excluded. Contact precautions are indicated while caring for patients with skin involvement. Glanders, melioidosis, and smallpox may present as acute pulmonary disease with purulent sputum. Respiratory isolation pending exclusion of plague is prudent if sputum studies disclose gram-negative bacilli with bipolar "safety pin" appearance when using Wright's or methylene blue stains.

### **2-37. Medical Evacuation**

Patients may be evacuated using Standard Precautions following the exclusion of plague.

## **Section VI. PLAGUE**

### **2-38. General**

*a. Etiologic Agent.* *Yersinia pestis* (*Y. pestis*) is a gram-negative bacillus of the family *Enterobacteriaceae*.

*b. Reservoir.* The primary reservoir is rodents. Domestic cats and wild carnivores can also transmit plague to humans.

*c. Transmission.* In endemic or epidemic plague, the disease is transmitted via infected fleas from rodent to human, dog or cat to human, or person to person. Respiratory droplet transmission can occur person to person or cat to person. Respiratory transmission is enhanced in humid climates. Plague may also be transmitted via cat bites or scratches.

*d. Endemic Disease.*

(1) Bubonic plague features the acute onset of fever and prostration in association with acute, painful lymphadenitis in the lymph node group draining the site of the fleabite. A skin lesion at the portal of entry (site of fleabite) is seen in less than 25 percent of cases; clinically apparent lymphangitis does not occur. The disease progresses with bacteremia, resulting in metastatic infection, septic shock, and

thrombosis of small arteries, resulting in digital gangrene. Pneumonia due to hematogenous metastasis occurs in approximately 25 percent of cases. The case fatality rate for untreated bubonic plague is approximately 60 percent, but is less than 5 percent with prompt, effective therapy.

(2) Primary pneumonic plague occurs after inhalation of organisms, which may occur via aerosol transmission from a person or animal with secondary or primary pneumonic plague.

(3) Septicemic plague may evolve from any form of plague. It features the acute onset of bacteremia, septic shock, and thrombosis with or without antecedent lymphadenitis. Prognosis for pneumonic and septicemic pneumonic plague is poor; the fatality rate is 100 percent for untreated cases.

### **2-39. Biological Warfare Agent Delivery**

The primary threat is by aerosol release or by contamination of food and water.

### **2-40. Environmental Detection**

The NBC reconnaissance teams may collect the agent from an aerosol cloud. Preventive medicine/PHS/BEE personnel may collect suspect soil or water samples. Veterinary/PVNTMED/PHS personnel may collect samples from suspect contaminated food. A plague BW attack may result in simultaneous onset of disease in humans, rodent reservoirs, and possibly domestic and wild animals not usually associated with plague.

### **2-41. Prevention**

*a. Repellents.* Use of insect repellents, approved for human use, will provide a level of protection from bites by infected fleas.

*b. Immunization.* The currently available inactivated whole cell vaccine is not recommended for protection from the BW agent; it does not protect laboratory animals from aerosolized plague. However, the vaccine is effective in preventing bubonic plague among troops deployed in endemic/epidemic areas (see endemic disease, above).

★ *c. Pre-exposure Prophylaxis.* While the FDA has not approved the use of pre-exposure antibiotics, empiric evidence indicates their use may significantly reduce morbidity and mortality. Therefore, they should be considered for use on a case-by-case basis and used as indicated for post-exposure preventive measures. Such use would require application of IND protocols (see paragraph 1-23).

*d. Post-exposure Prophylaxis.* Administer doxycycline 100 mg orally every 12 hours for one week or ciprofloxacin 500 mg orally every 12 hours for one week.

### **2-42. Biological Warfare Clinical Presentation**

*a. Incubation.* 2 to 10 days.

*d. Endemic Disease.*

(1) Clinical syndromes vary with portal of entry, inoculum, strain virulence, and the host's underlying state of health. Infection may be subclinical or fulminant. With the exception of typhoidal tularemia, the clinical syndromes are characterized by the combination of focal processes featuring ulceration at the portal of entry, and regional adenopathy involving the node groups draining the portal of entry. Following aerosol exposure, an undifferentiated febrile illness (typhoidal tularemia) or an acute pneumonia featuring fever, coughing, substernal chest tightness, and pleuritic chest pain may present. Usually, coughing is nonproductive; hemoptysis is rare. Physical findings may vary. Examination may be normal, or disclose rales, friction rubs, or findings consistent with consolidation or effusions.

(2) Pharyngeal tularemia presents as an acute pharyngitis following ingestion of contaminated food or water. The chief complaint is a severe sore throat. Physical findings include fever, exudative pharyngitis and/or tonsillitis, and possibly pharyngeal ulcers. Also, findings may include a pharyngeal membrane similar to that seen in diphtheria. Regional adenopathy may present in cervical, preauricular, and retropharyngeal node groups with occasional abscess formation.

(3) Oculoglandular disease presents following inoculation of the conjunctivae via aerosol, splashes, or direct contact (contaminated fingers). This disease presents as an acute conjunctivitis and may feature small conjunctival ulcers or papules. Complications may include corneal ulceration and dacryocystitis, but visual loss is rare. Regional adenopathy is a conspicuous feature of this illness, with preauricular or preauricular adenopathy. Severe cases of adenopathy may mimic parotiditis. Differential diagnosis should include other causes of Parinaud oculoglandular syndrome, including adenovirus infection, cat scratch disease, syphilis, herpetic infection, and pyogenic bacterial infection.

**2-58. Biological Warfare Agent Delivery**

The primary threat is by aerosol release, or by contamination of food or water supplies.

**2-59. Environmental Detection**

The NBC reconnaissance teams collect aerosol samples for supporting laboratory analysis and confirmation. Medical personnel collect medical specimens for supporting laboratory analysis and confirmation. Veterinary/PVNTMED/PHS personnel collect suspect contaminated food samples for supporting laboratory analysis and confirmation. Preventive medicine/PHS/BEE personnel collect suspect contaminated water samples for supporting laboratory analysis and confirmation.

**2-60. Prevention**

*a. Miscellaneous.* The military protective mask provides protection of the respiratory tract from exposure to aerosol organisms. All food must be thoroughly heated before consumption to kill any organisms. Water must be thoroughly disinfected before consumption.



*b. Pre-exposure Prophylaxis.*

- A live attenuated vaccine is available as an IND. It is given by scarification. The vaccine has been shown to be safe and effective in preventing laboratory-acquired tularemia and experimental infection in volunteers.

★

- The use of ciprofloxacin or doxycycline as a pre-exposure chemoprophylaxis may confer protection against tularemia, based on *in vitro* susceptibilities. See paragraph 1-23 for off-label indications and IND requirements.

*c. Post-exposure Prophylaxis.* Post-exposure prophylaxis following a BW attack include—

- Administer doxycycline 100 mg orally every 12 hours for 2 weeks; or tetracycline 500 mg orally every 6 hours for 2 weeks; or ciprofloxacin 500 mg orally every 12 hours for 2 weeks.

- Chemoprophylaxis is not recommended following potential natural exposures (tick bite, rabbit or other animal exposures).

**2-61. Biological Warfare Clinical Presentation**

*a. Incubation.* 1 to 21 days (usually 3 to 5 days).

*b. Signs and Symptoms.* The BW agent presentations of tularemia will be the pneumonic and typhoidal forms as discussed in paragraph 2-57 above. Oculoglandular disease could possibly occur following inoculation of the conjunctivae.

**2-62. Diagnosis**

*a.* Serologic testing is the preferred procedure for laboratory confirmation. Confirmation of diagnosis requires a four-fold increase in titer; serologies may need to be repeated at 7 to 10 day intervals. Agglutination tests and ELISA are also available. A gram stain of expectorated sputum is usually unrewarding; generally, the organism is not visualized on stains of clinical specimens. Cultures are not advised for diagnostic purposes. The organism does not grow on standard bacteriologic growth media. *F. tularensis* can be cultured on special supportive media containing cystine or another sulfhydryl source. However, cultures of the organism pose a significant occupational hazard to laboratory personnel. When cultures for *F. tularensis* are submitted, laboratory personnel must be alerted, as these cultures must be processed at Biosafety Level 3. Blood specimens may be submitted for mouse/egg inoculation.

*b.* Radiographic findings are nonspecific and may include subsegmental or lobar infiltrates, apical or miliary infiltrates, cavitation, pleural effusions, and hilar adenopathy.

**2-63. Treatment**

*a. Triage Categories.* Triage categories will vary according to the severity of the illness, available resources, and personnel. Patients presenting during the early stages of tularemia pneumonia are

**EMT** emergency medical treatment

★ **EO** Executive Order

*F. Francisella*

**F** Fahrenheit

**FDA** Food and Drug Administration

**FM** field manual

**GI** gastrointestinal

**gm** gram(s)

**GU** genitourinary

**HEPA** high efficiency particulate air

**HFRS** hemorrhagic fever with renal syndrome

**HIV** human immunodeficiency virus

**HSS** health service support

**IATA** International Air Transportation Association

**IgG** immunoglobulin class G

**IgM** immunoglobulin class M

**IM** intramuscular(ly)

**IND** investigational new drug

**IQD** internationally quarantinable disease

**IV** intravenous

**JBPDS** Joint Biological Point Detection System

**JPO-BIO** Joint Program Office for Biological Defense

**JSLIST** Joint service lightweight integrated suit technology

**kg** kilogram(s)

**km** kilometer(s)

**LRBDS** Long-Range Biological Standoff Detection System

**MCRP** Marine Corps Reference Publication

**MES** medical equipment sets

**mg** milligram(s)

**ml** milliliter(s)

**MOPP** mission-oriented protective posture

**MRI** magnetic resonance imaging

**MTF** medical treatment facility

**NATO** North Atlantic Treaty Organization

**NAVMED P** US Navy Medical Publication

**NBC** nuclear, biological, and chemical

**PCR** polymerase chain reaction

**PHS** public health service

**PPW** patient protective wrap

**PSP** paralytic shellfish poisoning

**PVNTMED** preventive medicine

**Q fever** Query fever

**QSTAG** Quadripartite Standardization Agreement

**RDIC** resuscitation device, individual chemical

**RNA** ribonucleic acid

**S.** *Staphylococcus*

**S2** Intelligence Officer (US Army)

**epizootic** A disease that is only present in an animal population for limited periods, but has a high morbidity rate.

**etiologic** Cause of the disease/illness.

**inoculum** The amount of microorganisms introduced into a host.

★ **off-label indication** The use of licensed medications for purposes that are not approved by the FDA. Off-label usage is common practice in general medical care.

**passive immunization** The administration of pre-formed antibodies to confer immunity to a specific pathogen or toxin.

**sample** Material collected from a source other than an animal or man for laboratory analysis (such as water sample or soil sample).

**specimen** Material collected from a man or animal for laboratory analysis (such as tissue or blood specimen).

**Standard Precautions** Handwashing after patient contact. Using gloves when touching blood, body fluids, secretions, excretions, and contaminated items. Using mask, eye protection, and gown during procedures likely to generate splashes or sprays of blood, body fluids, secretions, or excretions. Handling contaminated patient-care equipment and linens in a manner that prevents the transfer of microorganisms to people or equipment. Practicing care when handling sharps and using a mouthpiece or other ventilation device as an alternative to mouth-to-mouth resuscitation, when practical. Placing the patient in a private room if they contaminate the environment, when feasible.

**toxin agents** Poisonous by-products of living organisms used to cause disease, illness or death in susceptible individuals.

**viral agents** A group of viruses that have been selected as BW agents because of their ability to produce disease, illness, and death in susceptible individuals.

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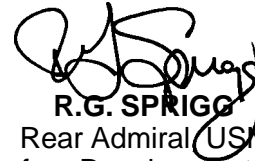


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## TREATMENT OF BIOLOGICAL WARFARE AGENT CASUALTIES

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## PREFACE

### Purpose

This publication serves as a guide and a reference for trained members of the Armed Forces Medical Services and other medically qualified personnel on the recognition and treatment of biological warfare

(BW) agent casualties. Information contained in this publication may also be relevant for the diagnosis and treatment of patients with naturally acquired diseases or illnesses due to pathogens with BW potential.

## Scope

- a.* This publication—
- (1) Classifies and describes potential BW agents.
  - (2) Provides procedures for collecting, handling and labeling, shipping, and identifying potential BW agents.
  - (3) Describes procedures for medical diagnosing, treating, and management of BW casualties.
  - (4) Describes medical management and treatment in BW operations.
- b.* The material in this publication is applicable to both the conventional battlefield and the integrated environment of the battlefield. (For the purpose of this publication, the “integrated environment” is intended to mean warfare and/or contingency operations where nuclear, biological, and chemical [NBC] weapons/agents are being employed or have a high probability of being employed in addition to conventional weapons.)
- c.* The treatment modalities contained in this manual differ from standard textbooks in that they apply to BW agent exposures. The method of exposure for most BW agents is by inhalation; whereas, the endemic disease exposure (if applicable) is by other means. Some are by ingestion, some by arthropod bites, and others by dermal contact with the agent. This does not preclude service members becoming BW casualties by these means.
- d.* The use of the term “level of care” in this publication is synonymous with “echelon of care” and “role of care.” The term “echelon of care” is the old North Atlantic Treaty Organization (NATO) term. The term “role of care” is the new NATO and American, British, Canadian, and Australian (ABCA) term.

## Standardization Agreements

This manual is in consonance with the following NATO Standardization Agreements (STANAGs) and ABCA Quadripartite Standardization Agreements (QSTAGs):

TITLE	NATO STANAG	QSTAG
Warning Signs for the Marking of Contaminated or Dangerous Land Areas, Complete Equipments Supplied and Stores	2002	
Reporting Nuclear Detonations, Biological and Chemical Attacks, and Predicting and Warning of Associated Hazards and Hazard Areas	2103	187
First Aid and Hygiene Training in NBC Operations	2358	

### **User Comments**

Users of this publication are encouraged to submit recommendations to improve the publication. Comments should be keyed to the page, paragraph, and line(s) of the text where the change is recommended. The proponent for this publication is the United States (US) Army Medical Department Center and School (AMEDDC&S). Comments should be forwarded to: **Commander, AMEDDC&S, ATTN: MCCS-FCD, 1400 East Grayson Street, Fort Sam Houston, Texas 78234-6175.**

### **Gender Statement**

Unless this publication states otherwise, masculine nouns and pronouns do not refer exclusively to men.

### **Use of Trade Names/Trademarks**

Use of trade names/trademarks in this publication is for illustrative purposes only. Their use does not constitute endorsement by the Department of Defense (DOD).

### **References**

References listed should be consulted for details beyond the scope of this publication.

## CHAPTER 1

# INTRODUCTION

### 1-1. The Threat of Biological Warfare Agents Against United States Forces and Civilian Populations

*a.* Biological warfare is the intentional use of viruses, bacteria, other microorganisms, or toxins derived from living organisms to cause death or disease in humans, animals, or plants.

*b.* In 1943, the US began research in and experimentation with several human and plant pathogens for use as BW weapons. In 1969, the US adopted a policy to cease offensive BW research and never again to produce, stockpile, weaponize, or use biological agents. By 1970 all offensive BW research was terminated. The US biological arsenal was destroyed by the end of 1972. In addition, the US is a party of the 1972 Biological Weapons Convention (BWC), which prohibits offensive BW agent research, stockpiling, weaponization, and use. However, several foreign governments and terrorist organizations have continued to develop offensive BW programs. The US conducts research to develop vaccines, chemoprophylaxes, diagnostic tests, and therapies to minimize the potential impact of a BW attack.

*c.* Biological warfare has interested several foreign governments and terrorist organizations for a number of reasons—

- Biological warfare agents are relatively easy to obtain. Naturally occurring viruses and bacteria which cause disease are obtainable from soil, water, animal reservoirs, clinical specimens, and clinical and research laboratories. Also, the development of recombinant genetic engineering has introduced the potential to genetically modify viruses and bacteria to enhance their ability to cause disease. Such modifications may include antibiotic resistance, enhanced invasiveness or toxin production, or enhanced ability to evade host immune defenses.

- Biological warfare agents are relatively easy and inexpensive to produce. The technology used to produce antibiotics, vaccines, and other industrial and food products can easily be converted to BW agent production. Such technology is readily available and is commonly used by industry; therefore, production of BW agents may be easily concealed.

### 1-2. Modes of Delivery

*a.* Biological warfare agents are unconventional weapons and can be delivered by unconventional means. Conventional explosive munitions are inefficient delivery systems for BW; the heat generated by the explosion will inactivate most of the BW agent. In addition, an explosion will generate a wide range of particle sizes with only a fraction of the weaponized BW agent being aerosolized in particles of a size suitable for deposition in the lower respiratory tract. The efficiency of explosive munitions delivering a viable BW agent is in the range of 1 to 2 percent.

*b.* Biological warfare agents are most effectively delivered as an aerosol. Aerosolized particles 1 to 5 microns ( $\mu$ ) in diameter are most efficiently delivered to their target (the air sacs of the lung). Larger particles either settle onto environmental surfaces, or are deposited in the upper respiratory tract and eliminated by mucociliary clearance. Due to the aerodynamics of particle flow through the respiratory tract, most particles smaller than 1  $\mu$  in diameter are exhaled and result in inefficient delivery to the lung.

*c.* Aerosol generators capable of generating particles of optimal size are easily constructed by adapting available agricultural and industrial sprayers. Aerosols may be delivered via point source (stationary release point, bomblets, or other devices equipped with sprayers) or from a line source (such as a moving vehicle or cruise missile releasing agent).

*d.* Biological warfare agents may be used to contaminate food or water systems/supplies. Heat destroys most pathogens and toxins; thus, to be effective most agents would have to be used on food that will be served raw or added after the food is prepared and presented for serving. Dilution can reduce the concentration of pathogens and toxins below an effective level. Standard water purification methods (chlorination and filtration) inactivate most pathogens and toxins. Therefore, a successful BW attack on a water system would have to occur after treatment.

*e.* Biological warfare agents have been delivered by covert injection.

### **1-3. Employment of Biological Warfare Agents**

*a.* Nuclear, biological, and chemical weapons/agents, and radiological dispersal devices are classified as weapons of mass destruction (WMD). Aerosols of BW agents may deliver incapacitating or lethal inocula over large geographic areas and produce mass casualties. The epidemic produced by the BW agent can quickly overwhelm the supporting military health service support (HSS) system or public health capabilities; thus reducing the ability of emergency response teams and emergency medical providers to respond. Limited medical resources (such as intensive care units) can quickly become overloaded with special medications being quickly exhausted early in a BW incident.

*b.* The BW agents may be plant pathogens used to destroy crops, devastate the food chain, and cause famine. Livestock and other animals of economic importance may be targeted. Contamination of water systems/supplies and the food chain with potential human pathogens is another mode of delivery to a targeted population.

*c.* The threatened use of BW agents can result in fear and panic in a population (whether under attack or being threatened to gain political advantage in political activities). The potential psychological impact of BW agents adds to an adversary's strategic threat.

*d.* Most BW agents are probably poor tactical weapons on a modern battlefield. Given that most BW agents have incubation times of several days to weeks duration, the outcome of a rapidly developing battle will be determined before the effects of a BW attack are realized. However, rapid-acting toxins (such as saxitoxin) may have tactical utility. Potential targets for delayed-onset BW agents may include areas with relatively fixed positions (logistics support facilities, aerial ports of debarkation, and seaports of debarkation).

*e.* Biological warfare agents are adaptable for terrorist operations. A BW agent with its delivery system can be easily concealed and transported. Given the difficulties in identifying a BW agent attack and the incubation periods for most BW agents, the perpetrators can escape before the BW release is apparent. The employment of BW agents is not limited to war; the potential for BW agent use exists and

can occur at anytime, anyplace, and by anyone with an intent to cause injury, disturbance, or create political discord. The employment of BW agents during political events (especially during multinational events) is a major threat.

#### 1-4. Classification of Biological Warfare Agents

Biological warfare agents may be classified according to—

- Their effects.
    - Lethal agents produce death in all or most victims.
    - Incapacitating agents produce severe disease, but not death. The potential adverse effects of an incapacitating agent on a military unit's ability to perform its mission equals or surpasses those of a lethal agent; casualties are unable to perform their mission and place high demands on available HSS assets.
  - Their taxonomy. However, such a classification system is probably of limited value in a battlefield situation.
  - Their mode of delivery (aerosol, food- or waterborne, vectorborne, or injection.)
  - The clinical syndrome they produce (such as pneumonia agents and systemic disease agents).
- However, this classification system is of questionable value since many BW agents are delivered via aerosol, resulting in both pneumonic and systemic disease. The clinical syndromes of many BW agents are similar during the early stages of disease development; classic disease-specific syndromes may not present until later in the clinical course.

#### 1-5. Portals of Entry

*a.* Biological warfare agents enter the body via the “portals of entry” of naturally occurring infectious diseases. These include the respiratory tract following inhalation of an aerosolized BW agent; the exposed mucosal surfaces (the moist surfaces of the nose, mouth, and eyes); the digestive tract following ingestion of contaminated food or water; or the inadvertent swallowing of an agent delivered as an aerosol. Intact skin provides an effective barrier against most BW agents, except mycotoxins. However, traumatic wounds, superficial abrasions, and cuts can provide portals of entry. The protective barrier of the skin can also be bypassed by injection (a technique which has been used in covert assassination).

*b.* In most instances, the disease produced by a BW attack mimics the naturally occurring infectious disease caused by the same pathogen. The delivery of a toxin to a portal of entry different from the natural portal of entry can result in a different clinical presentation. For example, staphylococcal enterotoxin B when ingested in food causes acute gastrointestinal (GI) illness; however, when delivered via aerosol to the respiratory tract, it produces respiratory disease.

## 1-6. Environmental Detection

*a.* Adequate and accurate intelligence is required in order to develop effective defenses against BW. Following the release of a BW agent aerosol, detection of the aerosol prior to its arrival over the target will enable commanders to instruct personnel to take defensive protection measures.

*b.* Aerosols of BW agents or contamination of food or water supplies are not detectable by human senses. Systems for the rapid detection and presumptive identification of several BW agent aerosols are fairly new and to date have limited fielding. Several point and standoff detection devices are planned, under development, or are being field-tested.

(1) Biological Integrated Detection System (BIDS) is a multi-component system that provides monitoring, sampling, detection, and presumptive identification. The BIDS is vehicle-based and must be located in the BW aerosol cloud to detect the agent. These technologies use components that automatically count and size particles, determine if the particles are living organisms, classify some basic cell characteristics, and use antigen-antibody analysis for presumptive identification. Improvements to this system are ongoing to increase BW agent detection and identification through the pre-planned product improvement program. See Field Manual (FM) 3-101-4 for detailed information.

(2) A Short-Range Biological Standoff Detection System (SRBSDS) is in development. This unit will employ ultraviolet and laser-induced fluorescence to detect aerosol clouds of possible BW origin at distances up to 5 kilometers (km).

(3) A Long-Range Biological Standoff Detection System (LRBSDS) employs a laser system mounted in a helicopter to scan a designated area of interest and find large, man-made aerosols suspected of containing BW agents. It enhances situational awareness and allows for early force protection. These systems are available for fixed site application or for transport platforms including fixed wing aircraft. These units will be used to provide early warning, enhance decontamination efforts, and cue other detection efforts. See FM 3-101-6 for additional information on the technical aspects of environmental detection.

(4) The Portal Shield System is the name of an Airbase/Port Biological Detection Advanced Concept Technology Demonstration (ACTD) in process, under the direction of the Joint Program Office for Biological Defense (JPO-BIO). When fully operational, it will consist of a network of biological and chemical point detectors, linked to a computer/communications control system. The biological agent detectors collect suspect aerosolized BW agents and test for their presence using an immunoassay system.

(5) The Joint Biological Point Detection System (JBPDS), currently under development, is an automatic air sampling device which will provide visual and audible alarms in the presence of BW agents.

(6) Soil contaminated with BW agent aerosols released via a line source would not leave hazardous environmental residue (one possible exception is anthrax spores which may persist and pose a health hazard near the dissemination line). Point source munitions leave an obvious signature that may alert troops to a BW attack and will leave environmental residues of a BW agent near the point of release. Environmental samples obtained near the point of release should be submitted for BW agent identification.



(7) Water reservoirs and other large water supplies are difficult to contaminate due to the effect of dilution on the concentration of toxins or microorganisms. In addition, standard water treatment methods of filtration and chlorination inactivate most viruses, bacteria, and toxins. However, several pathogens and toxins can survive standard water treatment; an example is *Cryptosporidium parvum*. Water could be used as a vehicle for biological attack if water was contaminated near the end-user.

(8) Food may be used as a vehicle for a biological attack by poisoning food supplies with pathogens or toxins. This method of attack is significant in a civilian terrorist context. Implicated food samples may be submitted for cultures and antigen (toxin) assays.

## 1-7. Diagnosis

Given that most BW agents have incubation periods, a BW attack may not be apparent until days or even weeks after the attack has occurred. Therefore, the first indication that a BW attack has occurred may be large numbers of patients simultaneously presenting with a similar disease. Such an event could be confused with a naturally occurring epidemic. Early identification of a BW attack may be further confounded by difficulties in early clinical diagnosis. Many BW-related diseases can result in vague, nonspecific symptoms during the early stages of illness and will be difficult to differentiate from numerous naturally occurring diseases. Classic, fully differentiated syndromes may not be apparent until late in the clinical course. Other potential confounding factors include lack of clinical experience with potential BW agents, and possible difference in clinical presentations from a naturally acquired disease versus an aerosolized agent. Ongoing disease surveillance and analysis of endemic and epidemic disease trends is critical in the event of covert use of biological agents. Early recognition of the first few cases of disease will enable commanders and medical personnel to implement BW defensive measures. Disease surveillance and analysis must include all military units in the area of operations (AO) to differentiate naturally occurring diseases from intentionally induced disease. The first military members who become ill serve as sentinels for all other military units. An epidemiologic investigation of any disease outbreak is key to the prompt start of countermeasures. Clinical detection should be accomplished by monitoring daily disease and nonbattle injury (DNBI) statistics. Health care providers should log all diagnoses. Preventive medicine (PVNTMED) or public health service (PHS) personnel should review these logs daily in order to identify trends that could indicate BW agent use. See Appendix A for further guidance on recognizing a BW agent casualty.

### NOTE

Rapid diagnostic tests may be available far forward to assist clinicians in early diagnosis of BW casualties. Laboratory confirmation of suspected BW employment is done at designated in-theater laboratories. The Level V (continental United States [CONUS]-based) medical laboratory provides the National Command Authorities the final confirmation and identification of BW agents encountered based on the commander's request. A documented chain of custody must be maintained on all suspect specimens from time of collection until delivered to the CONUS laboratory (see below).

**1-8. Specimen Collection**

a. A blood culture with routine media will readily detect bacterial agents, although specialized media may be required for some. Both aerobic and anaerobic cultures should be obtained. Cultures and impression smears should be taken from involved lymph nodes, sputum, pleural fluid, cerebrospinal fluid (CSF), tissues, or body fluids as clinically indicated.

b. Acute serum (at least 3 milliliters [ml] for suspected infectious agents and at least 20-ml serum for suspected intoxications) should be collected as early as possible after onset of symptoms. Blood samples also should be obtained from exposed persons who are not yet symptomatic. Convalescent sera from survivors and asymptomatic unit members should be obtained 3 to 4 weeks later.

c. Tissue samples obtained at autopsy should be collected in multiple aliquots; minimally, one (25-50 grams [gm]) to freeze for microbiology or toxicology testing and one in formalin for histopathology testing should be obtained. Where possible, additional specimens for other procedures, such as immunofluorescence or polymerase chain reaction (PCR) studies, should be obtained. Organs sampled should include lung, mediastinal lymph nodes, spleen, liver, and other tissues as clinically indicated. Gross lesions and adjacent normal tissue should be taken from affected areas in any organ. Postmortem blood (up to 20 ml) should be obtained and submitted as serum and clot or cells.

d. Table 1-1 provides information on the types and amounts of specimens to collect from personnel exposed to aerosolized BW agents. Proper collection of specimens is dependent on the time frame following exposure. Specimen collection is described for “early post-exposure, clinical, and convalescent/terminal/postmortem” time frames. These time frames are not rigid and will vary according to the concentration of the agent used, the agent strain, and predisposing health factors of the patient.

**NOTE**

*Blood specimens:* Several choices are offered based on availability of the blood collection tubes. Do not send blood in all the tubes listed, but merely choose one. Tiger-top tubes that have been centrifuged are preferred over red-top clot tubes with serum removed from the clot, but the latter will suffice. Blood culture bottles are also preferred over citrated blood for bacterial cultures. See FM 8-10-7 for additional information on specimen collection procedures.

*Table 1-1. Specimen Collection for Suspect Biological Warfare Agents*

EARLY POST-EXPOSURE	CLINICAL	CONVALESCENT/TERMINAL/ POSTMORTEM
<p><b>ANTHRAX</b> 0 TO 24 HOURS. NASAL AND THROAT SWABS, AND INDUCED RESPIRATORY SECRETIONS FOR CULTURE, FA, AND PCR.</p>	<p>24 TO 72 HOURS. SERUM (TT OR RT) FOR TOXIN ASSAYS. BLOOD (E,C,H) FOR PCR. BLOOD (BC OR C) FOR CULTURES.</p>	<p>3 TO 10 DAYS. SERUM (TT OR RT) FOR TOXIN ASSAYS. BLOOD (BC OR C) FOR CULTURE. PATHOLOGY SPECIMENS.</p>

Table 1-1. Specimen Collection for Suspect Biological Warfare Agents (Continued)

EARLY POST-EXPOSURE	CLINICAL	CONVALESCENT/TERMINAL/ POSTMORTEM
<p><b>PLAGUE</b> 0 TO 24 HOURS. NASAL SWABS, SPUTUM, AND INDUCED RESPIRATORY SECRETIONS FOR CULTURE, FA, AND PCR.</p>	<p>24 TO 72 HOURS. BLOOD (BC AND C) FOR CULTURE AND BLOODY SPUTUM (C) FOR FA. SERUM (TT OR RT) FOR F-1 ANTIGEN ASSAYS. BLOOD (E, C, OR H) FOR PCR.</p>	<p>&gt;6 DAYS. SERUM (TT OR RT) FOR IgM, LATER FOR IgG. PATHOLOGY SPECIMENS.</p>
<p><b>TULAREMIA</b> 0 TO 24 HOURS. NASAL SWABS, SPUTUM, AND INDUCED RESPIRATORY SECRETIONS FOR CULTURE, FA, AND PCR.</p>	<p>24 TO 72 HOURS. BLOOD (BC OR C) FOR CULTURE. BLOOD (E, C, OR H) FOR PCR. SPUTUM FOR FA AND PCR.</p>	<p>&gt;6 DAYS. SERUM (TT OR RT) FOR IgM AND LATER IgG, AGGLUTINATION TITERS. PATHOLOGY SPECIMENS.</p>
<p><b>MELIOIDOSIS/GLANDERS</b> 0 TO 24 HOURS. NASAL SWABS, SPUTUM, AND INDUCED RESPIRATORY SECRETIONS FOR CULTURE AND PCR.</p>	<p>24 TO 72 HOURS. BLOOD (BC OR C) FOR CULTURE. BLOOD (E, C, OR H) FOR PCR. SPUTUM AND DRAINAGE FROM SKIN LESIONS FOR PCR AND CULTURE.</p>	<p>&gt;6 DAYS. BLOOD (BC OR C) AND TISSUE FOR CULTURE. SERUM (TT OR RT) FOR IMMUNOASSAYS. PATHOLOGY SPECIMENS.</p>
<p><b>BRUCELLOSIS</b> 0 TO 24 HOURS. NASAL SWABS, SPUTUM, AND INDUCED RESPIRATORY SECRETIONS FOR CULTURE AND PCR.</p>	<p>24 TO 72 HOURS. BLOOD (BC OR C) FOR CULTURE. BLOOD (E, C, AND H) FOR PCR.</p>	<p>&gt;6 DAYS. BLOOD (BC OR C) AND TISSUE FOR CULTURE. SERUM (TT OR RT) FOR IMMUNOASSAYS. PATHOLOGY SPECIMENS.</p>
<p><b>Q FEVER</b> 0 TO 24 HOURS. NASAL SWABS, SPUTUM, AND INDUCED RESPIRATORY SECRETIONS FOR CULTURE AND PCR.</p>	<p>2 TO 5 DAYS. BLOOD (BC OR C) FOR CULTURE IN EGGS OR MOUSE INOCULATION. BLOOD (E, C, AND H) FOR PCR.</p>	<p>&gt;6 DAYS. BLOOD (BC OR C) FOR CULTURE IN EGGS OR MOUSE INOCULATION. PATHOLOGY SPECIMENS.</p>
<p><b>BOTULISM</b> 0 TO 24 HOURS. NASAL SWABS AND INDUCED RESPIRATORY SECRETIONS FOR PCR (CONTAMINATING BACTERIAL DNA) AND TOXIN ASSAYS. SERUM (TT OR RT) FOR TOXIN ASSAYS.</p>	<p>24 TO 72 HOURS. NASAL SWABS AND RESPIRATORY SECRETIONS FOR PCR (CONTAMINATING BACTERIAL DNA) AND TOXIN ASSAYS.</p>	<p>&gt;6 DAYS. USUALLY NO IgM OR IgG. PATHOLOGY SPECIMENS (LIVER AND SPLEEN FOR TOXIN DETECTION).</p>

Table 1-1. Specimen Collection for Suspect Biological Warfare Agents (Continued)

EARLY POST-EXPOSURE	CLINICAL	CONVALESCENT/TERMINAL/ POSTMORTEM
<p><b>RICIN INTOXICATION</b>  <i>0 TO 24 HOURS.</i>                      NASAL SWABS AND INDUCED RESPIRATORY SECRETIONS FOR PCR (CONTAMINATING CASTOR BEAN DNA) AND TOXIN ASSAYS. SERUM (TT OR RT) FOR TOXIN ASSAYS.</p>	<p><i>36 TO 48 HOURS.</i>                      SERUM (TT OR RT) FOR TOXIN ASSAY. TISSUE FOR IMMUNOHISTOLOGICAL STAINING. PATHOLOGY SPECIMENS.</p>	<p><i>&gt;6 DAYS.</i>                      SERUM (TT OR RT) FOR IgM AND IgG IN SURVIVORS.</p>
<p><b>STAPH ENTEROTOXICOSIS</b>  <i>0 TO 3 HOURS.</i>                      NASAL SWABS AND INDUCED RESPIRATORY SECRETIONS FOR PCR (CONTAMINATING BACTERIAL DNA) AND TOXIN ASSAYS. SERUM (TT OR RT) FOR TOXIN ASSAYS.</p>	<p><i>2 TO 6 HOURS.</i>                      URINE FOR IMMUNOASSAYS. NASAL SWABS AND INDUCED RESPIRATORY SECRETIONS FOR PCR (CONTAMINATING BACTERIAL DNA) AND TOXIN ASSAYS. SERUM (TT OR RT) FOR TOXIN ASSAYS.</p>	<p><i>&gt;6 DAYS.</i>                      SERUM FOR IgM AND IgG.</p>
<p><b>T-2 TOXICOSIS</b>  <i>0 TO 24 HOURS POST EXPOSURE.</i>                      NASAL AND THROAT SWABS AND INDUCED RESPIRATORY SECRETIONS FOR IMMUNOASSAYS, HPLC/MASS SPECTROMETRY</p>	<p><i>1 TO 5 DAYS.</i>                      SERUM (TT OR RT) AND TISSUE FOR TOXIN DETECTION.</p>	<p><i>&gt;6 DAYS POST EXPOSURE.</i>                      URINE FOR DETECTION OF TOXIN METABOLITES.</p>
<p><b>EQUINE ENCEPHALOMYELITIS</b>                      (VEE, EEE, AND WEE VIRUSES)  <i>0 TO 24 HOURS.</i>                      NASAL SWABS AND INDUCED RESPIRATORY SECRETIONS FOR RT-PCR AND VIRAL CULTURE.</p>	<p><i>24 TO 72 HOURS.</i>                      SERUM (TT OR RT) AND THROAT FOR CULTURE. SERUM (E, C, H, TT, OR RT) FOR RT-PCR. THROAT SWABS UP TO 5 DAYS FOR CULTURE THEN CSF SERUM (TT OR RT) FOR ANTIGEN ELISA.</p>	<p><i>&gt;6 DAYS.</i>                      SERUM (TT OR RT) FOR IgM. PATHOLOGY SPECIMENS PLUS BRAIN.</p>
<p><b>POX</b>                      (SMALL POX AND MONKEYPOX)  <i>0 TO 24 HOURS.</i>                      NASAL SWABS AND INDUCED RESPIRATORY SECRETIONS FOR PCR AND VIRAL CULTURE.</p>	<p><i>2 TO 5 DAYS.</i>                      SERUM (TT OR RT) FOR VIRAL CULTURE.</p>	<p><i>&gt;6 DAYS.</i>                      SERUM (TT OR RT) FOR VIRAL CULTURE. DRAINAGE FROM SKIN LESIONS/ SCRAPINGS FOR MICROSCOPY, EM, VIRAL CULTURE, AND PCR. PATHOLOGY SPECIMENS.</p>

Table 1-1. Specimen Collection for Suspect Biological Warfare Agents (Continued)

EARLY POST-EXPOSURE	CLINICAL	CONVALESCENT/TERMINAL/ POSTMORTEM	
<b>EBOLA</b>			
0 TO 24 HOURS. NASAL SWABS AND INDUCED RESPIRATORY SECRETIONS FOR RT-PCR AND VIRAL CULTURE.	2 TO 5 DAYS. SERUM (TT OR RT) FOR VIRAL CULTURE.	>6 DAYS. SERUM (TT OR RT) FOR VIRAL CULTURE. PATHOLOGY SPECIMENS PLUS ADRENAL GLAND.	
<b>LEGEND:</b>			
BC	Blood culture	H	Heparin
C	Citrated blood	HPLC	high-pressure liquid chromatography
CSF	cerebrospinal fluid	IgG	immunoglobulin class G
DNA	deoxyribonucleic acid	IgM	immunoglobulin class M
E	EDTA	PCR	polymerase chain reaction
EEE	eastern equine encephalitis	RT	Red Top, if TT is not available
ELISA	enzyme-linked immunosorbent assay	RT-PCR	reverse transcriptase/polymerase chain reaction
EM	electron microscopy	TT	Tiger top
F-1	fraction-1	VEE	Venezuelan equine encephalitis
FA	fluorescent antibody	WEE	western equine encephalitis

## 1-9. Specimen Labeling

a. Each container should be labeled with name, numerical identities, type of specimen, and date of collection. Included should be—

- A brief description of the illness and gross autopsy findings.
- Place, date, and time of death.
- Place, date, and time of collection.
- Pathologist or individual trained in forensics.
- The individual's unit.

b. All serum samples should be completely labeled with patient's name, numerical identifier, unit, date, originating medical facility, and medical treatment facility (MTF) to receive results (if different from submitting facility). Routine laboratory slips should be included with each sample. Data on laboratory slips should include the number of days since the onset of symptoms and the reason that samples were obtained.

c. Clinical and operational data should be included for all samples, together with a form to establish chain of custody. This requirement must be strongly and clearly delineated since evidence may well be politically or militarily sensitive.

#### **1-10. Specimen Handling and Shipment**

a. All specimens from suspected BW casualties should be submitted through the designated laboratory chain for processing. Specimens must be clearly marked for special testing and the chain of custody procedures maintained. Each sample/specimen will be placed in a watertight receptacle made of glass, plastic, or metal with a screw cap closure, the screw cap will be reinforced with adhesive tape. Serum specimens will be placed individually in a second plastic vial or zip-top bag to prevent leakage. Absorbent material (such as vermiculite) sufficient to absorb the entire content of the primary receptacle is placed between the primary and secondary packaging; for serum specimens placed in a plastic vial, the absorbent material will be placed between the plastic vial and another secondary packaging material. The secondary packaging should be of a material that prevents leakage. The entire contents should be placed in an insulated shipping container with cold packs or dry ice. When ice is used, the outer package must be leak proof. When dry ice is used, the outer container must permit release of carbon dioxide gas. For transportation out of theater, the samples/specimens must be packaged in an International Air Transportation Association (IATA) or Department of Transportation 49, Code of Federal Regulation 173 approved container.

b. It is the responsibility of the physician at forward MTFs or the laboratory officer, in concert with a physician at a hospital, to ensure that suspect specimens are submitted correctly and expeditiously to an appropriate diagnostic laboratory.

c. Specimens sent rapidly (less than 24 hours) to analytical laboratories require only wet ice or refrigeration at 2° to 8° Celsius (C). However, if the time span increases beyond 24 hours, contact the US Army Medical Research Institute for Infectious Disease (USAMRIID); telephone hot-line (1-888-USA-RIID) for other shipping requirements such as shipment on dry ice or in liquid nitrogen. *Blood specimens:* Several choices are offered based on availability of the blood collection tubes. Do not send blood in all the tubes listed, but merely choose one. Tiger-top tubes that have been centrifuged are preferred over red-top clot tubes with serum removed from the clot, but the latter will suffice. Blood culture bottles are also preferred over citrated blood for bacterial cultures.

#### **1-11. Chain of Custody Responsibilities**

a. A strict chain of custody must be maintained for every sample/specimen collected. Use Department of the Army (DA) Form 4137 (Evidence/Property Custody Document) or Department of Defense (DD) Form 1911 (Materiel Courier Receipt) for each sample/specimen collected. The DA Form 4137 or DD Form 1911 must accompany the sample/specimen during transport from the point of collection to the final receiving laboratory. Each time the sample/specimen is transferred to another individual, the receiving person must sign the document to show that they received the sample/specimen. When a DA Form 4137 or DD Form 1911 is not available, the information must be recorded in such a manner that a clear chain of custody can be verified. Regardless of whether the DA Form 4137, the DD Form 1911, or another record document is used, the document will provide the answer to the following questions:

- When was the sample/specimen collected?
- Who has maintained custody of the sample/specimen?
- What has been done with the sample/specimen at each change of custody?

**CAUTION**

Each change of custody must be recorded with date and time of change.

*b.* The samples/specimens must be appropriately packaged, labeled, and evacuated to the designated laboratory for confirmation of a BW attack. The standard chain of custody for sample/specimen evacuation is as follows:

- Sampling unit.
- Unit S2 (Intelligence Officer [US Army]), medical operations officer, or other designated person.
- Technical escort unit or other command-designated escort personnel.
- In-theater supporting medical laboratory, if in operation.
- Continental US laboratory.

**1-12. Identification Methods for Biological Warfare Agents**

The following are identification methods for BW agents:

- Isolation of the etiologic agent by culture (possible in one to two days for some agents).
- Detection of agents by enzyme immunoassay, mass spectrometry, animal inoculation, or other methods.
- Antibody detection (specific immunoglobulin [IgM] may appear within 3 days).
- Genome detection by PCR.
- Detection of metabolic products of the infectious or toxic agent in clinical specimens.

### 1-13. Therapy

*a. Endemic Disease versus Biological Agent.* Specific therapies are discussed for each agent. Most of these are based on standard treatment guidelines. However, some of the post-exposure prophylaxis regimens and therapies recommended in this manual vary from those found in standard references. This is because—

- A BW exposure (aerosol) may produce a disease with clinical features different from the naturally occurring disease. For example, inhalation (BW) versus cutaneous (endemic) anthrax. Cases of endemic disease due to inhalation of some of these agents are rare and clinical experience is limited. Human challenge studies can be done with only a limited number of agents for obvious ethical and safety reasons. Accordingly, some of the prophylactic and treatment regimens have been developed from in vitro studies, animal models, and limited human data.

- An adversary may develop a BW agent resistant to the standard antibiotic therapy.

*b. Endemic Disease Therapy.* For endemic and epidemic disease therapies, see FM 8-33 and the civilian textbooks listed in the references.

### 1-14. Case Reporting and Epidemiological Assessment

It is imperative that clinicians report cases of suspected BW-related illnesses to the appropriate line and medical chains of command. Prompt epidemiological investigations must begin and preventive measures implemented to control the disease or reduce the number of cases.

### 1-15. Prevention

The effects of most BW threat agents are preventable. Immunizations, pre-exposure chemoprophylaxes, post-exposure chemoprophylaxes, and protective clothing are available to provide protection. Personnel must have all required immunizations administered prior to entering an AO where BW agent employment is a threat. All immunizations should be administered in sufficient time to provide the initial protection before troops are deployed to the AO; when administration prior to deployment is impossible, troops must receive the immunizations as soon as the mission permits in the AO. Some immunizations are used in conjunction with pre-exposure chemoprophylaxes or post-exposure chemoprophylaxes to provide protection. The supporting PHS/PVNTMED units/staffs can assist commanders in determining which specific immunizations and chemoprophylaxes are required for the AO. For those BW agents that a specific immunization is not available, the use of protective equipment combined with chemoprophylaxis may be employed to provide protection.

*a. Active Immunization.* As of January 1999, vaccines are available for the following potential BW agent threats:

- Anthrax.
- \*Argentine hemorrhagic fever.



- \*Botulinum toxin.
- \*\*Plague.
- \*Q fever.
- \*Rift Valley Fever.
- Smallpox.
- \*Tularemia.
- \*Venezuelan equine encephalitis (VEE).
- Yellow Fever.

\* Investigational new drug (IND) is available only under Food and Drug Administration (FDA)-approved protocol with informed consent.

\*\* Not effective for inhalation BW exposure.

*b. Chemoprophylaxes.* Chemoprophylaxes are available for anthrax, plague, Q fever, and tularemia. See the following chapters for details on vaccines and chemoprophylaxes for specific BW agents.

## 1-16. Protective Equipment

*a.* The currently fielded chemical protective equipment will provide protection against BW agents. This equipment includes the military protective mask (MCU-2A/P and M40), battle dress overgarment (BDO), Joint service lightweight integrated suit technology (JSLIST), protective gloves, and overboots. When worn alone, the protective mask will provide a high level of protection against inhalation BW agents. Maintenance of the protective mask is essential to provide maximum protection; replacement of the filter elements is of the utmost priority. The filters must be replaced when—

- The wearer has been exposed to a suspect BW agent.
- The elements are immersed in water.
- The elements are crushed, cut, or otherwise damaged.
- Excessive breathing resistance is encountered.
- Thirty days have elapsed in the combat theater of operations (TO).
- Supply bulletins indicate a lot number has expired.

- Ordered by the commander.

*b.* If a protective mask is not available, other means may provide some protection to the respiratory tract. Animal experiments have shown that a double layer of the battle dress uniform (BDU) T-shirt is an effective respiratory filter against ricin and saxitoxin and in an emergency, may be effective against other BW agents. See FM 3-4 for additional information on protective measures.

### 1-17. First Aid

For most BW agent casualties, first aid consists of basic procedures to protect against further exposure as described below. When specific first aid procedures exist for a specific BW agent, the procedures will be discussed within the text for that agent.

*a. Self-Aid.* Take pre-exposure and post-exposure chemoprophylaxes as directed by your commander/leader. Seek medical evaluation for fever and other signs of illness.

*b. Buddy Aid.* A buddy should assist any service member who develops fever and is not able to move on his own, as the mission permits. A buddy should request medical assistance in all cases.

*c. Combat Lifesaver Aid.* Individuals with swelling of the cervical (neck) tissue may benefit from an oropharyngeal airway or endotracheal intubation to prevent or treat upper airway obstruction.

#### NOTE

The combat lifesaver is a US Army nonmedical person trained in enhanced first aid procedures.

### 1-18. Protective Measures and Handling of Casualties

*a.* Depending on the AO, command guidance may dictate the assumption of mission-oriented protective posture level 1 (MOPP1). However, MOPP4 (protective mask, BDO, protective gloves, and overboots) will be assumed immediately—

- When the local alarm or command is given.
- When entering an area known to be or suspected of being contaminated with an NBC agent.
- When casualties are being received by personnel at the patient receiving/decontamination area from an area where suspect BW agents have reportedly been used.

*b.* If individuals find themselves alone without command/leadership guidance, they must mask IMMEDIATELY and assume MOPP4 when—

- Their position is under attack by artillery, mortar or rocket fire, or by aircraft bombs if NBC agents have been used in the AO, or if the threat of their use is significant.
- Their position is under attack by aircraft spray.
- Mist or smoke of an unknown source is present or approaching.
- A suspicious odor, liquid, or solid is present.
- An NBC attack is suspected.

**NOTE**

The mask should be worn until the “all clear” signal is given.

*c.* The decision to lower the level of protection is often more difficult to make than warning the force. Lowering the level of protection or removing the protective mask before the contamination is gone can prove just as fatal as no protection at all. However, staying in protective gear for long periods of time can significantly degrade operations. While most BW agents are considered nonpersistent, this can vary based on weather conditions. As a general rule after conducting a biological hazard prediction, if the trailing edge of the hazard area indicates the BW contamination has passed and there are no other indications of BW attacks (example: negative BIDS/LRBSDS results), then units may be directed to conduct unmasking procedures (see FM 3-4).

*d.* Casualties unable to continue wearing protective equipment should be held and/or transported within patient protective wraps designed to protect the patient against further chemical-biological agent exposure.

*e.* Collective protection by the use of either a hardened or unhardened shelter equipped with an air filtration unit providing positive pressure airflow can offer protection for personnel in the biologically contaminated environment. An airlock ensures that no contamination will be brought into the shelter systems. However, these shelters are costly to produce and maintain, are difficult to deploy, and may be scarce. In the absence of a dedicated structure, enhanced protection can be afforded within most buildings by sealing cracks and entry ports, and providing filtration with high efficiency particulate air (HEPA) filters within existing ventilation systems. Personnel must be decontaminated prior to entering the collective protection unit.

**1-19. Patient Decontamination**

All casualties should be decontaminated at their unit; however, some may require immediate lifesaving care or may become contaminated en route to an MTF. Potentially contaminated patients arriving at an MTF must be decontaminated before they are admitted into the clean treatment area. Medical personnel perform

triage and provide emergency medical treatment (EMT) in the patient decontamination area while supervising the decontamination personnel. See FM 8-10-7 and United States Air Force (USAF) wartime medical decontamination team (WMDT) concept of operations (CONOPS) for patient decontamination procedures.

## **1-20. Infection Control**

Infection control procedures should be reinforced for mass casualty situations with undifferentiated febrile illness following a suspected BW attack. Isolate patients and use respiratory droplet precautions, in addition to standard precautions, until plague and smallpox can be reasonably excluded. Isolation should be in designated tents or other structures. The use of surgical masks on patients is appropriate when separate tents or structures are not available. Infection control practices could then be modified after the agent is identified. Most agents require only standard precautions. Specific precautions are discussed for each agent in the following chapters.

## **1-21. Medical Evacuation**

*a.* When preparing casualties for medical evacuation, attempts should be made to identify the agent through analytical analysis of environmental samples. Also attempt to perform early diagnosis based on clinical manifestations and rapid laboratory diagnostic tests (enzyme-linked immunosorbent assays [ELISA] and PCR) to provide medical evacuation personnel additional information to protect themselves and patients from possible exposure to contagious diseases.

*b.* Potentially contaminated casualties should be decontaminated prior to evacuation; however, patients may have to be evacuated that have not been completely decontaminated. Measures must be taken to prevent contamination of ambulances and air evacuation assets when evacuating potentially contaminated casualties. Ground ambulances should be used first in a contaminated environment because they are easier to decontaminate than are air evacuation assets. This does not preclude the use of air evacuation assets in a contaminated environment. Commanders must evaluate the situation and make a determination as to which assets they will commit in the contaminated environment. Already contaminated ground and air evacuation assets should be used first. Only commit clean assets if they are required to meet the medical evacuation needs of the command.

(1) Normally, patients air evacuated by USAF aircraft must be externally decontaminated prior to loading onto the aircraft. In rare situations where decontamination is not possible due to the tactical situation, the theater and United States Transportation Command (USTRANSCOM) Commanders in Chief (CINCs) will determine whether USAF aircraft will be used for patient aeromedical evacuation (AE). The theater and USTRANSCOM CINCs must be notified of intent to use USAF aircraft for transport of BW casualties. Issues regarding the decontamination/quarantine of potentially contaminated USAF aircraft will also be determined at CINC command levels. Planners will ensure procedures are in place to assure patients, aircrew, and aircraft are appropriately protected.

(2) Once patients are externally decontaminated, further AE decisions should be based on the actual or suspected clinical diagnosis as well as the patient's condition. Since BW agent incubation times are variable, all patients should be considered potentially infectious during transport. As a minimum,

standard precautions as outlined in the Centers for Disease Control and Prevention (CDC) Guidelines for Isolation Precautions in Hospitals will be followed. If plague, smallpox, and viral hemorrhagic fevers (VHF) can be reasonably excluded on the basis of analysis of clinical specimens and environmental samples, patients may be evacuated using Standard Precautions and the disease-specific precautions discussed for each suspect BW agent in the following chapters.

(3) Biological warfare attacks may occur with multiple agents with short and prolonged incubation times (botulinum toxin, 12 to 36 hours and smallpox, 7 to 17 days). Multiple agents can lead to the presence of coinfection-acute illness with short incubation and incubating smallpox (which may declare itself after patients have been evacuated for evaluation/treatment of the short incubating disease). Therefore, consideration should be given to quarantining patients for 17 days after AE from the BW area if plague or smallpox cannot be excluded. Reevaluate patients carefully for recurrent fever or other changes in clinical status. If clinical or laboratory findings suggest prodromal or syndromic smallpox, plague, or VHFs, institute appropriate isolation until the diagnosis is clarified. Specific control measures must be applied as presented for the following diseases/BW agent casualties:

(a) *Plague*. Plague is an internationally quarantinable disease (IQD). Do not evacuate across international borders unless authorized by the theater surgeon. Evacuate in cohorts of plague patients only on dedicated AE aircraft; treat in theater. Pneumonic plague is highly transmissible person-to-person. Droplet precautions are added to standard precautions for patients with pneumonic plague until sputum cultures are negative.

(b) *Smallpox*. Currently eradicated and no longer listed as IQD. Immediately notify the line and medical chain of command upon diagnosis. Do not evacuate across international borders unless authorized by the theater surgeon. Evacuate in cohorts of smallpox patients only on dedicated AE aircraft; treat in theater. Smallpox is transmissible person-to-person. Strict quarantine is required. Standard, contact, and airborne isolation precautions are to be observed. All contacts should be vaccinated and quarantined/grouped together for at least 17 days following the most recent exposure.

(c) *Viral hemorrhagic fevers*. The World Health Organization (WHO) does not require quarantine for hemorrhagic fevers, with the exception of yellow fever. However, due to international concerns, do not evacuate hemorrhagic fever patients across international borders unless authorized by the theater surgeon. Evacuate in cohorts of hemorrhagic fever patients only on dedicated AE aircraft. Medical evacuation may result in increased morbidity and mortality for patients with hemorrhagic fever; treatment at a local facility is preferred. Person-to-person transmission is possible for the duration of illness. If necessary, patients may be evacuated using standard, contact, plus respiratory droplet isolation precautions.

(d) *Infectious disease of unknown etiology*. Evaluate patient evacuation risk based on the patients' signs/symptoms complex and theater threat list. Assume infection with the agent requiring the most stringent infection control procedures (based on the possible threats in the theater and the clinical picture). Ensure that appropriate patient care is performed while providing the crew and aircraft with the highest level of protection.

(e) *Summary*. In summary, many BW agent casualties may be safely evacuated using basic infection control guidelines. Plague, smallpox, and the hemorrhagic fevers pose significant challenges.

These patient movements will require approval of the destination country, over-flight privileges, and approval of any country where the aircraft will land for servicing or where patients will remain overnight. Countries from which approval is sought are bound by Article 37 of the *Geneva Conventions for the Amelioration of the Condition of the Wounded and Sick in Armed Forces in the Field of 12 August 1949* to ensure humanitarian treatment to wounded and sick. That should include approval under most circumstances of transit of those injured by exposure to biological agents. Additionally, some countries, notably Germany, have already developed procedures for expedited approval of transit of dangerous/hazardous goods in their air space. That information is contained in the DOD Foreign Clearance Guide. Coordination between the theater or USTRANSCOM commander/surgeon and the Department of State is required for such movements.

#### **1-22. Aeromedical Isolation Team**

The USAMRIID maintains an aeromedical isolation team (AIT). The AIT is a rapid response team with worldwide airlift capability. The AIT is designed to safely evacuate and manage patients with potentially lethal communicable diseases under high-level containment. Indications for deployment include cases of a highly contagious, lethal, or unidentified disease, including cases from a suspect BW attack. Diagnosis and medical care will be provided at USAMRIID. The AIT can only transport a limited number of patients. The AIT **CANNOT** provide for mass casualty evacuation. Such evacuation can enhance early identification of a BW agent; thus, enabling early development of treatment recommendations for medical providers in the TO. The AIT also offers a portable containment laboratory, limited environmental decontamination, and specialized consultative expertise.

CHAPTER 2

**BACTERIAL AGENTS**

**Section I. INTRODUCTION**

**2-1. General**

Bacterial organisms comprise the greatest number of pathogens in the list of potential BW agents. They include the etiologic agents of anthrax, brucellosis, cholera, glanders, melioidosis, plague, Q fever, and tularemia. Of these, anthrax is the most likely BW threat that troops will encounter in an AO. See Appendix B for guidance on medical management of BW agent casualties.

**Section II. ANTHRAX**

**2-2. General**

*a. Etiologic Agent.* The spores of *Bacillus anthracis*, an encapsulated gram-positive bacillus. Sporulation occurs under adverse environmental conditions and when vegetative bacteria are exposed to air; the spores are extremely hardy and can survive extremes of temperature, dryness, and flooding. When conditions improve, the spores germinate to produce vegetative bacteria.

*b. Reservoir.* The soil, with worldwide distribution.

*c. Transmission.* The stage in the bacterial life cycle, which poses a health hazard, is the spore. Grazing animals contract spores from the vegetation. Humans contract spores via contact with infected animals, their hides, wool, or other products; from ingesting contaminated meat; or from inhaling spores during the processing of wool for textiles. Biting flies in sub-Saharan Africa may also transmit anthrax to humans. Humans usually do not contract anthrax directly from the soil, unless they work with fertilizers (bonemeal) prepared from infected animals. Also, humans can contract spores from inhalation of aerosolized spores released during a BW attack.

*d. Endemic Disease.* Endemic infectious disease is contracted by inhalation, cutaneous exposure, oropharyngeal exposure, and ingestion.

(1) Cutaneous anthrax accounts for more than 90 percent of all anthrax cases worldwide. Disease results when *Bacillus anthracis* spores are introduced into the skin via inoculation of small cuts/abrasions or inapparent skin lesions. It may possibly be introduced by biting flies. Cutaneous anthrax features a painless necrotic ulcer with a black eschar and local edema. The case fatality rate for untreated cutaneous anthrax is up to 20 percent, but with early, effective therapy is reduced to less than 5 percent.

(2) Oropharyngeal and GI diseases occur following the ingestion of anthrax spores, usually from consuming meat from infected animals. The clinical features of oropharyngeal and GI anthrax are discussed in paragraph 2-6.

(3) Inhalation anthrax occurs when individuals working with animal hides, wool, or bonemeal inhale the spores. Also, inhalation anthrax may occur from inhalation of aerosolized spores released during a BW attack. The clinical features of inhalation anthrax are discussed in paragraph 2-6.

### 2-3. Biological Warfare Agent Delivery

Aerosolized spores may be delivered by missiles, bomblets, artillery fires, point release, or airborne line release. Contamination of food and water may also be used.

### 2-4. Environmental Detection

Nuclear, biological, and chemical teams or other bioenvironmental engineering (BEE) personnel operating similar detection equipment accomplish detection. Preventive medicine/PHS/BEE personnel perform detection in water supplies. Detection in food supplies may be performed by veterinary, PVNTMED, or PHS personnel. Detection in animals may be performed by veterinary personnel.

### 2-5. Prevention

*a. Pre-exposure Prophylaxis.* Prevention may be accomplished by immunization plus chemoprophylaxis.

(1) *Immunization.* Anthrax vaccine is given in six doses at 0, 2, and 4 weeks and 6, 12, and 18 months, with annual boosting. A minimum of three doses administered within 6 months prior to the exposure may confer protective immunity.

(2) *Chemoprophylaxis.* Ciprofloxacin hydrochloride tablets (500 milligrams [mg]) are given orally every 12 hours beginning prior to imminent anthrax attack. When Ciprofloxacin hydrochloride tablets are not available, doxycycline hyclate tablets (100 mg) are given orally every 12 hours beginning prior to imminent anthrax attack. The chemoprophylaxis should be discontinued after attack if the use of anthrax has been excluded.

*b. Post-exposure Prophylaxis.* Use immunization with chemoprophylaxis to prevent the clinical manifestation of the disease.

(1) *Anthrax vaccine.* For personnel that have completed the six-dose series and are up to date on boosters, or who have received at least three initial doses within 6 months prior to exposure, no additional doses are indicated, except to complete the series as previously scheduled. For personnel who have not received any immunizations, begin series and give a minimum of three doses; complete the six-dose series, if possible.

(2) *Chemoprophylaxis.* Chemoprophylaxis is recommended as an adjunct to immunization for post-exposure prophylaxis. Ciprofloxacin hydrochloride tablets (500 mg) should be taken orally every



12 hours for at least 4 weeks. When Ciprofloxacin hydrochloride tablets are not available, doxycycline hyclate tablets (100 mg) should be taken orally every 12 hours for at least 4 weeks. The duration of chemoprophylaxis administration for individuals without receipt of any vaccine should be extended until they receive at least three doses of vaccine. Chemoprophylaxis should be withdrawn under careful observation and with access to an MTF with intensive care and consultative assets. If fever develops following the withdrawal of chemoprophylaxis, empiric therapy for anthrax is indicated pending etiologic diagnosis.

## 2-6. Biological Warfare Clinical Presentation

*a. Incubation Period.* The incubation for anthrax is hours to 7 days. Most cases present within 48 hours post-exposure.

*b. Signs and Symptoms.*

(1) *Inhalation anthrax.* Inhalation anthrax will begin with nonspecific symptoms of fever, malaise, and fatigue. A nonproductive cough and vague chest discomfort may be present. These initial symptoms may be followed by a short period of symptomatic improvement, hours to 3 days in duration. This will be followed by an acute phase, including the abrupt onset of severe respiratory distress with dyspnea, stridor, diaphoresis, and cyanosis. Bacteremia and toxemia, septic shock, metastatic infection (meningitis in approximately 50 percent of the cases), and death usually occurs within 24 to 36 hours from the onset of the acute phase.

(2) *Oropharyngeal or gastrointestinal anthrax.* Oropharyngeal or GI anthrax can occur following ingestion of food contaminated with anthrax spores.

(a) Oropharyngeal anthrax will present with initial symptoms of fever, sore throat, and difficulty swallowing. The disease may progress to an acute phase with symptoms including a necrotic ulcer or eschar involving the hard palate, tonsils, or posterior oropharyngeal wall, edema of cervical tissues (possibly resulting in upper airway obstruction), and cervical lymphadenopathy. Most acute cases progress to septic shock and death.

(b) Gastrointestinal anthrax begins with vague initial symptoms featuring fever, anorexia, nausea, and vomiting. Abdominal pain, bloody vomiting, bloody diarrhea, and possibly massive abdominal swelling (ascites) may follow these symptoms. Also, septic shock and death may follow these symptoms.

## 2-7. Diagnosis

During the incubation period, nasal swabs and specimens of respiratory secretions sent for PCR are the most important diagnostic specimens. During the early disease, blood and respiratory secretions may be sent for rapid identification by genetic typing (PCR). A rapid diagnostic test is available that detects toxin antigens in the blood during the acute phase. Chest x-ray may be normal or show hilar adenopathy early in the illness and may show a widened mediastinum and pleural effusions during the acute phase.

## 2-8. Treatment

*a. Triage Categories.* Patients presenting with initial signs of inhalation anthrax should be placed in the Immediate category, as early aggressive treatment is lifesaving. Depending on the numbers of cases and available resources, patients presenting in the acute phase of inhalation anthrax should be placed in the Immediate or Expectant categories.

*b. Medical Management.*

(1) Supportive care includes maintaining the airway, providing resuscitative fluids, and providing vasopressors as indicated for shock.

(2) Specific therapy includes the administration of ciprofloxacin (400 mg intravenous [IV] every 12 hours) or doxycycline (200 mg IV loading dose, followed by 100 mg IV every 12 hours). Specific therapy may also include administration of penicillin (4 million units IV) every 4 hours, if isolate is sensitive to penicillin.

(3) A tracheostomy is indicated for upper airway obstruction due to oropharyngeal anthrax. Surgical debridement of cutaneous lesions is contraindicated. Surgical drainage of the mediastinum for inhalation anthrax is not recommended.

*c. Prognosis.* The number of cases of inhalation anthrax occurring during the antibiotic era is too small to establish case fatality rates and efficacy of treatment. Almost all inhalation anthrax cases in which treatment was begun after onset of significantly severe symptoms have been fatal, regardless of treatment. Despite medical therapy, most patients with inhalation anthrax die within 24 hours of the onset of the acute phase of the illness. However, in nonhuman primate trials, animals have responded to aggressive therapy. The prognosis for oropharyngeal and GI anthrax is poor, with case fatality rates 50 to 100 percent, even with aggressive therapy.

## 2-9. Control of Patients, Contacts, and Treatment Areas

- Report all cases to line and medical chains of command.
- Employ Standard Precautions for handling, treating, and moving all active cases.
- Use sporicidal agents, such as disinfectant strength iodophors, in MTFs for general area disinfection. Antiseptic strength iodophors are not sporicidal. Hypochlorite solutions may be attenuated by organic matter, but will provide a disinfectant capability when used in a 5-percent solution. The hypochlorite solution should be replaced frequently. Autoclaving, steam sterilizing, or burning is required for complete eradication of spores.

## 2-10. Medical Evacuation

Patients with anthrax may be evacuated with other categories of patients. Anthrax is not transmissible person to person. Standard Precautions should be observed during evacuation.

## Section III. BRUCELLOSIS

### 2-11. General

*a. Etiologic Agent.* The genus *Brucella* is encapsulated nonmotile bacteria consisting of short, gram-negative coccoid bacillus. There are four members of the genus *Brucella* that are human pathogens. These are *Brucella melitensis*, *Brucella abortus*, *Brucella suis*, and *Brucella canis*.

*b. Reservoir.* The following are reservoirs in nature for the disease:

- *Brucella melitensis.* Primarily sheep, goats, and camels. It may also be found in bison, elk, caribou, and some species of deer.
- *Brucella abortus.* Cattle.
- *Brucella suis.* Swine.
- *Brucella canis.* Dogs and coyotes.

The organisms may be produced in a laboratory for BW purposes, using a single cell or a small amount of the organism from a natural source.

*c. Transmission.* The disease is transmitted to humans by—

- Inhalation of aerosols or dusts that contain organisms.
- Ingestion of unpasteurized dairy products and contaminated meat.
- Inoculation of abraded skin or mucosal surfaces.

*d. Endemic Disease.*

(1) *Pathogenesis.* Following introduction into the body, *Brucella* organisms are phagocytized by polymorphonuclear or mononuclear cells and are transported to regional lymph nodes. However, *Brucella* organisms can survive intracellularly. This results in the release of bacteria from lysed cells, resulting in hematogenous metastasis to other organs, particularly organs high in reticuloendothelial content (notably the liver, spleen, bone marrow, and possibly, the lungs).

(2) *Acute disease.* Onset may be sudden or insidious (in approximately one half of all cases) with nonspecific symptoms of fever, malaise, fatigue, anorexia, weight loss, and depression. Illness persists as a systemic illness, with or without localizing signs and symptoms. Fever can be intermittent. Physical examinations may be unrevealing or may disclose fever, mild lymphadenopathy, and hepatosplenomegaly. Disease localization can occur, usually in tissues high in reticuloendothelial content.

(3) *Osteoarticular.* Bone and joint disease is the most common localizing complications, occurring in up to 40 percent of cases. These include bursitis, sacroiliitis, spondylitis, peripheral joint arthritis, and osteomyelitis. Vertebral osteomyelitis can result in epidural abscess resulting in spinal cord compression, and psoas abscess. In addition to developing pyogenic septic osteoarticular infection, patients may also develop reactive arthropathies. Diagnostic studies can include magnetic resonance imaging (MRI), computed tomography (CT), and technetium bone scans; plain radiographs may be insensitive early in disease.

(4) *Pulmonary infection.* Although the respiratory tract is a portal of entry for brucellosis, pulmonary disease is rare, under 15 percent. Complications may include hilar and paratracheal adenopathy, interstitial pneumonia, pulmonary nodules, pleural effusions, and empyema.

(5) *Genitourinary tract infection.* Acute orchitis or epididymo-orchitis are the most common genitourinary (GU) complications, usually in the absence of systemic symptoms or signs. Intrapartum infection is rare, but can result in abortion although there is no convincing evidence that the risk is higher than that of other bacteremic infections. Early diagnosis and therapy will prevent an adverse outcome. Chronic pyelonephritis has been reported as a rare complication.

(6) *Cardiovascular.* Endocarditis occurs in less than 2 percent of the cases, but accounts for most deaths from brucellosis. Other cardiovascular complications may include pericarditis, myocarditis, and mycotic aneurysms.

(7) *Neurologic.* Acute or chronic meningitis occurs in less than 2 percent of the cases. Depression, fatigue, and headache occurring in most cases represent nonspecific features of systemic disease.

## 2-12. Biological Warfare Agent Delivery

The primary threat is by aerosol release. A foodborne brucellosis attack is unlikely, but could be executed.

## 2-13. Environmental Detection

Currently, detection is primarily by laboratory analysis of specimens from patients presenting with the illness or by laboratory testing of foods for the organism. Veterinary/PVNTMED/ PHS/BEE personnel should collect samples from dairy products and other food items suspected of being contaminated with the organism. Field NBC reconnaissance teams may collect the agent from an aerosol cloud, but must rely on the supporting medical laboratory for identification.

## 2-14. Prevention

a. *Pre-exposure Prophylaxis.* Vaccines are not currently available for human use; attenuated vaccines for veterinary use have caused brucellosis following accidental percutaneous or mucous membrane exposures. Chemoprophylaxis has not been proven to be effective and may delay or mask the onset of the disease.

*b. Post-exposure Prophylaxis.* A 3- to 6-week course of therapy is advised following high-risk exposures to attenuated vaccines for veterinary use, which have been associated with human disease. Accordingly, a full course of therapy (see paragraph 2-17) is advised for exposed personnel following a proven brucellosis BW attack. Post-exposure chemoprophylaxis is generally not advised following possible natural exposures to endemic disease. Personnel must avoid consuming unpasteurized dairy products or uncooked foods containing the dairy products and avoid contact with suspect infected animals.

## **2-15. Biological Warfare Clinical Presentation**

- a. Incubation.* Incubation varies from 5 days to 8 weeks, usually 2 to 8 weeks.
- b. Signs and Symptoms.* See endemic disease above.

## **2-16. Diagnosis**

A definitive diagnosis is made by culturing the organism from blood, bone marrow, or other clinical specimens. The laboratory should be advised to maintain cultures for at least 4 weeks, as *Brucella* species grow slowly in vitro. The sensitivity of cultures varies with clinical specimens; 15 to 70 percent for blood, greater than 90 percent for bone marrow. Isolates may be misidentified as *Moraxella* or *Haemophilus* species in automated bacterial identification systems that lack specific profiles for *Brucella* species. Submit specimens for ELISA testing and PCR. Serologic tests are valuable for diagnosis. Most patients with brucellosis will have serum-agglutinating titers (SAT) of 1:160 or greater; lower titers must be analyzed within the patient's clinical context. The SAT will not detect antibodies to *Brucella canis*; a specific test is required. False negative tests may occur because of blocking antibodies; dilution to 1:320 or a Coomb's test is indicated for suspected cases with negative titers.

## **2-17. Treatment**

*a. Triage Categories.* Triage categories will vary with conditions and available resources. Given the subacute nature of brucellosis, most patients are candidates for the Delayed treatment category.

*b. Medical Management.*

(1) *Undifferentiated febrile illness.* Antibiotic therapy requires a combination of two medications. Administer—

- Doxycycline, 200 mg, daily for 6 weeks and rifampin, 600 mg, daily for 6 weeks or
- Doxycycline, 200 mg, daily for 6 weeks and streptomycin, 1 gm intramuscularly (IM), daily for 2 weeks.

(2) *Osteoarticular disease.* Treat as indicated in (1) above, but extend therapy to 12 weeks.

(3) *Endocarditis*. Administer antibiotic therapy as indicated in (1) above. Optimal duration of therapy is undefined; however, treatment is often continued for 6 to 9 months. Surgical heart valve replacement is usually necessary for total cure and should be strongly considered.

(4) *Central nervous system (CNS) disease*. Administer antibiotic therapy as indicated in (1) above, but extend therapy for 6 to 9 months.

(5) *Abscesses*. In addition to treatment in (1) above, drainage of abscesses should be done as surgically indicated.

*c. Prognosis*. The case fatality rate for untreated brucellosis has historically been less than 2 percent. Most fatalities in untreated cases result from endocarditis due to *Brucella melitensis*. Untreated brucellosis may result in severe morbidity for months, and occasionally years.

## 2-18. Control of Patients, Contacts, and Treatment Areas

Apply Standard Precautions for disease control. The disease is not communicable from person to person.

## 2-19. Medical Evacuation

Patients with brucellosis are evacuated with other patients. Apply Standard Precautions for disease control.

# Section IV. MELIOIDOSIS

## 2-20. General

*a. Etiologic Agent*. *Burkholderia (B.) pseudomallei* (formerly *Pseudomonas pseudomallei*), a small, gram-negative aerobic bacillus.

*b. Reservoir*. Soil and water throughout the world between 20 degrees north and south latitudes. Several animals, including sheep, goats, horses, swine, monkeys, and rodents, serve as reservoirs. However, there is no evidence that animals are important reservoirs, except that they spread the agent to new foci (soil and water).

*c. Transmission*. Inoculation of gross or inapparent skin lesions from contact with contaminated soil or water, aspiration or ingestion of contaminated water, or inhalation of contaminated dust.

*d. Endemic Disease*. Acute pulmonary disease is the most common form of the endemic disease. Acute local suppurative disease can complicate inoculation of the skin, resulting in a nodular lesion at the portal of entry, with lymphangitis and regional lymphadenopathy. Acute septicemic disease and chronic suppurative sequelae are discussed in paragraph 2-24.

## **2-21. Biological Warfare Agent Delivery**

The primary threat is aerosol release.

## **2-22. Environmental Detection**

The NBC reconnaissance team collects samples from aerosol clouds; PVNTMED/PHS/BEE personnel collect samples from soil and water sources; and veterinary/PVNTMED/PHS personnel collect samples from food supplies/sources. The supporting medical laboratory processes the samples and provides the command with initial identification of the organism.

## **2-23. Prevention**

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

## **2-24. Biological Warfare Clinical Presentation**

- a. Incubation.* 10 to 14 days following inhalation.
- b. Signs and Symptoms.*

(1) Following an aerosol attack, melioidosis will most likely present as an acute pulmonary infection. Infection can vary from a mild bronchitis to a severe necrotizing pneumonia. The illness may begin abruptly, or with a vague prodrome featuring headache, anorexia, and myalgia. Fever, often in excess of 102° Fahrenheit (F), is common. Localizing symptoms may include pleuritic or dull aching chest pain, and a cough (which may be either productive or nonproductive of purulent or bloody sputum). Physical findings may be minimal but can feature pulmonary rales. Acute pulmonary disease can progress and result in bacteremia and acute septicemic disease.

(2) The acute septicemic disease may follow a terminal course with death occurring in 7 to 10 days. Case fatality rate for acute septicemic disease exceeds 90 percent. Symptoms may include severe dyspnea, headache, pharyngitis, diarrhea, and a pustular rash. Physical findings may include high fever, tachypnea, hypotension, flushing of the skin, cyanosis, and rash (the rash may begin as a generalized papular rash that may progress to a pustular exanthem). Chest findings are variable; palpable hepatosplenomegaly may be present.

(3) Pulmonary infection can result in chronic disease, with clinical and radiographic features similar to those of tuberculosis. Chronic suppurative disease can complicate metastatic infection to other organs including the brain, myocardium, liver, bone, spleen, lymph nodes, and eyes.

## **2-25. Diagnosis**

Microscopic evaluation of exudate will feature poorly staining gram-negative bacilli; methylene blue or Wright's stain will disclose a "safety pin" bipolar appearance. Standard bacteriologic culture methods can

identify *B. pseudomallei*. Diagnosis can also be confirmed by serologic tests, with the limitations that single low titers are nondiagnostic and negative serology does not exclude the diagnosis. Given the possible presentation of an acute pneumonia and the above findings on sputum studies, the most important item in a differential diagnosis, especially in a BW context, would be plague (see paragraph 2-38). Chest x-rays may disclose infiltrates involving the upper lobes, with consolidation and cavitation. Pleural effusions and pleural-based masses are unusual radiographic findings. Leukocyte count can vary from normal to 20,000 white blood cells/cubic millimeter.

## 2-26. Treatment

*a. Triage Categories.* Triage categories will vary based upon the stage and severity of illness and available resources. Patients with signs and symptoms of acute pulmonary disease are classified as Immediate or Delayed category, depending on severity of presentation. Those presenting in septic shock are classified as Immediate or Expectant category, depending on available resources.

*b. Medical Management.* In medical management, therapy will vary with the type and severity of the clinical presentation.

(1) For localized disease, administer one of the following for a duration of 60 to 150 days:

- Amoxicillin/clavulanate, 60 mg/kilograms (kg)/day in 3 divided oral doses.
- Tetracycline, 40 mg/kg/day in 3 divided oral doses.
- Trimethoprim/sulfa (TMP, 4 mg per kg per day/sulfa, 20 mg per kg per day in divided oral doses).

(2) For localized disease with mild toxicity, administer antibiotics as follows: Combine two of the above oral regimens for a duration of 30 days, followed by monotherapy with either amoxicillin/clavulanate or TMP/sulfa for 60 to 150 days. For extrapulmonary suppurative disease, the antibiotic therapy should be administered for 6 to 12 months. Surgical drainage of abscesses is indicated.

(3) For severe and/or septicemic disease, administer antibiotics as follows: Ceftazidime, 120 mg/kg/day in three divided doses, combined with TMP/sulfa (TMP, 8 mg per kg per day/sulfa, 40 mg per kg per day in four divided doses). Initially, administer parenteral therapy for 2 weeks, followed by oral therapy for 6 months.

(4) The addition of streptomycin is indicated if presentation (acute pneumonia) and sputum studies suggests plague (see paragraph 2-38).

*c. Prognosis.* The extent of infection will vary with inoculum, individual's underlying state of health, availability of protective mask or other respiratory protective devices, and other factors. Late activation or recrudescence can result years or decades later.



## 2-27. Control of Patients, Contacts, and Treatment Areas

Apply Standard Precautions in management of patients and contacts. Melioidosis, glanders, and smallpox may present with diffuse pustular rashes; strict isolation and quarantine would be indicated until smallpox can be excluded. Contact precautions are indicated while caring for patients with skin involvement. Melioidosis, glanders, and smallpox may present as acute pulmonary disease with purulent sputum. Respiratory isolation pending exclusion of plague is prudent if sputum studies disclose gram-negative bacilli with bipolar “safety pin” when using Wright’s or methylene blue stains.

## 2-28. Medical Evacuation

Patients may be evacuated following the exclusion of smallpox and plague. Contact precautions are indicated for patients with skin involvement.

# Section V. GLANDERS

## 2-29. General

- a. *Etiologic Agent.* *B. mallei* (formerly *Pseudomonas mallei*), is a gram-negative bacillus.
- b. *Reservoir.* Horses, mules, and donkeys serve as reservoirs.
- c. *Transmission.* By the organism invading the nasal, oral, and conjunctival mucous membranes, by inhalation into the lungs, and by invading abraded or lacerated skin. Inhalation of aerosols from cultures by laboratory workers has occurred.
- d. *Endemic Disease.* The disease is not widespread. The cases have been among veterinarians, horse and donkey caretakers, abattoir workers, and laboratory personnel.

## 2-30. Biological Warfare Agent Delivery

The primary threat is aerosol release.

## 2-31. Environmental Detection

The NBC reconnaissance team collects samples from aerosol clouds; veterinary personnel collects specimens from animals.

## 2-32. Prevention

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

### 2-33. Biological Warfare Clinical Presentation

a. *Incubation Period.* 10 to 14 days after inhalation.

b. *Signs and Symptoms.* Fever, rigors, sweating, myalgia, headache, pleuritis, chest pain, cervical adenopathy, splenomegaly, and generalized papular/pustular eruptions.

### 2-34. Diagnosis

Methylene blue stain of exudates may reveal scant small bacilli. Chest x-ray may show miliary lesions, small multiple lung abscesses, or bronchopneumonia. *B. mallei* can be cultured from infected secretions using meat nutrients.

### 2-35. Treatment

a. *Triage Categories.* Triage categories will vary based upon the stage and severity of illness and available resources. Patients with signs and symptoms of acute pulmonary disease are classified as Immediate or Delayed category, depending on severity of presentation. Those presenting in septic shock are classified as Immediate or Expectant category, depending on available resources.

b. *Medical Management.* In medical management, therapy will vary with the type and severity of the clinical presentation.

(1) For localized disease, administer one of the following for a duration of 60 to 150 days:

- Amoxicillin/clavulanate, 60 mg/kg/day in 3 divided oral doses.
- Tetracycline, 40 mg/kg/day in 3 divided oral doses.
- Trimethoprim/sulfa (TMP, 4 mg per kg per day/sulfa, 20 mg per kg per day in

divided oral doses).

(2) For localized disease with mild toxicity, administer antibiotics as follows: Combine two of the above oral regimens for a duration of 30 days, followed by monotherapy with either amoxicillin/clavulanate or TMP/sulfa for 60 to 150 days.

(3) For extrapulmonary suppurative disease, the antibiotic therapy should be administered for 6 to 12 months. Surgical drainage of abscesses is indicated.

(4) For severe and/or septicemic disease, administer antibiotics as follows: Ceftazidime, 120 mg/kg/day in three divided doses, combined with TMP/sulfa (TMP, 8 mg per kg per day/sulfa, 40 mg per kg per day in four divided doses). Initially, administer parenteral therapy for 2 weeks, followed by oral therapy for 6 months.

(5) The addition of streptomycin is indicated if presentation (acute pneumonia) and sputum studies suggests plague.

*c. Prognosis.* The extent of infection will vary with inoculum, individual's underlying state of health, availability of protective mask or other respiratory protective devices, and other factors. Late activation or recrudescence can result years or decades later.

### **2-36. Control of Patients, Contacts, and Treatment Areas**

Apply Standard Precautions in management of patients and contacts. Glanders, melioidosis, and smallpox may present with diffuse pustular rashes; strict isolation and quarantine would be indicated until smallpox can be excluded. Contact precautions are indicated while caring for patients with skin involvement. Glanders, melioidosis, and smallpox may present as acute pulmonary disease with purulent sputum. Respiratory isolation pending exclusion of plague is prudent if sputum studies disclose gram-negative bacilli with bipolar "safety pin" appearance when using Wright's or methylene blue stains.

### **2-37. Medical Evacuation**

Patients may be evacuated using Standard Precautions following the exclusion of plague.

## **Section VI. PLAGUE**

### **2-38. General**

*a. Etiologic Agent.* *Yersinia pestis* (*Y. pestis*) is a gram-negative bacillus of the family *Enterobacteriaceae*.

*b. Reservoir.* The primary reservoir is rodents. Domestic cats and wild carnivores can also transmit plague to humans.

*c. Transmission.* In endemic or epidemic plague, the disease is transmitted via infected fleas from rodent to human, dog or cat to human, or person to person. Respiratory droplet transmission can occur person to person or cat to person. Respiratory transmission is enhanced in humid climates. Plague may also be transmitted via cat bites or scratches.

*d. Endemic Disease.*

(1) Bubonic plague features the acute onset of fever and prostration in association with acute, painful lymphadenitis in the lymph node group draining the site of the fleabite. A skin lesion at the portal of entry (site of fleabite) is seen in less than 25 percent of cases; clinically apparent lymphangitis does not occur. The disease progresses with bacteremia, resulting in metastatic infection, septic shock, and

thrombosis of small arteries, resulting in digital gangrene. Pneumonia due to hematogenous metastasis occurs in approximately 25 percent of cases. The case fatality rate for untreated bubonic plague is approximately 60 percent, but is less than 5 percent with prompt, effective therapy.

(2) Primary pneumonic plague occurs after inhalation of organisms, which may occur via aerosol transmission from a person or animal with secondary or primary pneumonic plague.

(3) Septicemic plague may evolve from any form of plague. It features the acute onset of bacteremia, septic shock, and thrombosis with or without antecedent lymphadenitis. Prognosis for pneumonic and septicemic pneumonic plague is poor; the fatality rate is 100 percent for untreated cases.

### **2-39. Biological Warfare Agent Delivery**

The primary threat is by aerosol release or by contamination of food and water.

### **2-40. Environmental Detection**

The NBC reconnaissance teams may collect the agent from an aerosol cloud. Preventive medicine/PHS/BEE personnel may collect suspect soil or water samples. Veterinary/PVNTMED/PHS personnel may collect samples from suspect contaminated food. A plague BW attack may result in simultaneous onset of disease in humans, rodent reservoirs, and possibly domestic and wild animals not usually associated with plague.

### **2-41. Prevention**

*a. Repellents.* Use of insect repellents, approved for human use, will provide a level of protection from bites by infected fleas.

*b. Immunization.* The currently available inactivated whole cell vaccine is not recommended for protection from the BW agent; it does not protect laboratory animals from aerosolized plague. However, the vaccine is effective in preventing bubonic plague among troops deployed in endemic/epidemic areas (see endemic disease, above).

*c. Pre-exposure Prophylaxis.* Administer ciprofloxacin 500 mg orally every 12 hours or doxycycline 100 mg orally every 12 hours beginning when a BW attack is imminent or suspected; discontinue if the employment of plague BW can be excluded.

*d. Post-exposure Prophylaxis.* Administer doxycycline 100 mg orally every 12 hours for one week or ciprofloxacin 500 mg orally every 12 hours for one week.

### **2-42. Biological Warfare Clinical Presentation**

*a. Incubation.* 2 to 10 days.

*b. Signs and Symptoms.* Following an aerosol release of the organisms, unprotected individuals will present with acute pneumonic plague featuring high fever, systemic toxicity, productive cough, and hemoptysis. Chest x-ray findings are discussed in paragraph 2-43. Patients may present with disseminated intravascular coagulation (DIC) with resultant thrombosis and digital gangrene. However, hemorrhagic complications of DIC in plague are rare. Further, an aerosol attack of plague could result in an epidemic of bubonic plague if rodent hosts and flea vectors are present in the vicinity of the attack.

#### **2-43. Diagnosis**

Gram stain of expectorated sputum may disclose gram-negative bacilli; Giemsa or Van Wayson stains may disclose blue-staining bacilli with a bipolar “safety pin” appearance. Organisms may be visualized on peripheral blood smears during bacteremia. Cultures of blood and respiratory secretions are indicated. Findings on a chest x-ray may include patchy peribronchial infiltrates, cavitation, consolidation, hilar adenopathy, and pleural effusions. Other findings may include leukocytosis (at times severe leukemoid reaction) and abnormal coagulation studies consistent with DIC. Differential diagnosis should include other causes of acute pneumonia.

#### **2-44. Treatment**

*a. Triage Categories.* The triage category varies with conditions and available resources. Plague pneumonia is curable if treatment is begun early; therefore, these patients are classified as Immediate. Patients presenting after 24 hours following the onset of respiratory symptoms are less likely to survive; they are classified as Expectant.

*b. Medical Management.*

(1) *Supportive care.* Supportive care should include IV hydration, supplemental oxygen, and respiratory support as indicated.

(2) *Specific therapy.* Administer one of the following:

- Streptomycin, 15 mg/kg lean body mass IM every 12 hours for 10 to 14 days.
- Gentamicin, 5 mg/kg lean body mass IV every 24 hours for 10 to 14 days.
- Gentamicin, 1.75 mg/kg lean body mass IV every 8 hours for 10 to 14 days.
- Ciprofloxacin, 400 mg IV every 12 hours. Oral therapy may be given (750 mg orally every 12 hours) after the patient is clinically improved, for completion of a 10- to 14-day course of therapy.
- Doxycycline, 200 mg IV loading dose followed by 100 mg IV every 12 hours. Oral therapy may be given (100 mg orally every 12 hours) after the patient is clinically improved, for completion of a 10- to 14-day course of therapy.

(3) *Plague meningitis*. Administer chloramphenicol 25 mg/kg IV loading dose, followed by 15 mg/kg IV every 6 hours. Oral therapy may be given after the patient is clinically improved, for completion of a 10- to 14-day course of therapy.

c. *Prognosis*. Pneumonic plague is invariably fatal if antibiotic therapy is delayed more than 1 day after the onset of symptoms.

#### **2-45. Control of Patients, Contacts, and Treatment Areas**

Pneumonic plague is a very contagious disease; control of patients, contacts, and treatment areas is critical in preventing spread of the disease. The following must be applied for all cases:

- Report case(s) to line and medical chains of command.
- Employ Standard Precautions for disease control. For suspected pneumonic plague (BW presentation), apply respiratory droplet isolation for a minimum of the first 48 hours of therapy. If plague pneumonia is confirmed, continue respiratory droplet isolation until sputum cultures are negative.
- Employ measures to minimize personnel contact with rodents (proper food storage, trash disposal, and elimination of rodent nests); enforce the use of topical insect repellents and the use of insecticides in and around troop encampments to kill fleas, thus decreasing the risk of secondary transmission. Eliminate fleas from patients and their personal effects.
- Administer post-exposure prophylaxis to immediate contacts as described paragraph 2-41 above.
- Conduct terminal disinfection of all items used in the care of patients. The standard disinfectants available at MTFs will inactivate *Y. pestis*.

#### **2-46. Medical Evacuation**

Quarantine patients. Evacuate only with other plague cases. Employ respiratory droplet precautions in addition to Standard Precautions for patients with pneumonic plague until sputum cultures are negative. Do not evacuate across international borders unless authorized by senior medical leadership (see paragraph 1-21 for additional information).

## **Section VII. Q FEVER**

#### **2-47. General**

a. *Etiologic Agent*. *Coxiella (C.) burnetii* is a rickettsial organism that is highly resistant to heat and desiccation. The organism is highly communicable via aerosol. A single viable organism is enough to cause infection in humans.

*b. Reservoir.* The reservoir is sheep, goats, cattle, dogs, cats, some wild mammals, birds, and ticks. Infected animals usually do not develop the disease, but shed large numbers of organisms ( $10^9$  organisms per gram) in placental tissues and body fluids.

*c. Transmission.* The organisms are usually transmitted via aerosols containing dust from areas contaminated by placentas, amniotic fluid, excreta from infected animals, aerosols generated by processing products of infected animals, direct contact with infected animals, and/or ingestion of unpasteurized milk. Q fever has also been transmitted by inhaling aerosols generated from manure, straw, contaminated laundry, and vehicles. The role of ticks as vectors of human disease is unclear, but they may transmit the disease to humans by dropping organisms on the body at the site of their bite.

*d. Endemic Disease.* Acute Q fever can present as an undifferentiated febrile illness, as an atypical pneumonia, or as a rapidly progressive pneumonia.

(1) The “atypical pneumonia” presentation features fever, fatigue, chills, sweats, and myalgia. Approximately 75 percent of patients will complain of severe headache. There is a relative absence of respiratory symptoms; coughing occurs in approximately 25 percent of patients with radiography confirmed pneumonia. Physical examination of the chest is usually normal; inspiratory rales may be present. Patients with the rapidly progressive pneumonic presentation may feature auscultatory findings consistent with consolidation. Q fever pneumonia can result in development of hyponatremia due to the syndrome of inappropriate antidiuretic hormone (SIADH).

(2) Neurologic complications of Q fever include aseptic meningitis or encephalitis in approximately 1 percent of cases. Other complications have included cranial nerve palsies, behavioral disturbances, cerebellar and extrapyramidal disease, and Miller Fisher syndrome. Other rare extrapulmonary complications have included hemolytic anemia and glomerulonephritis.

(3) Approximately 33 percent of Q fever cases will develop acute hepatitis (Q fever hepatitis). The acute hepatitis can present with fever and abnormal liver function tests with the absence of pulmonary symptoms, signs, or radiographic abnormalities. A liver biopsy may disclose granulomatous hepatitis with a highly suggestive histologic appearance. The granuloma will present as a dense fibrin ring surrounded by a central lipid vacuole (doughnut granuloma).

(4) Endocarditis is usually a manifestation of chronic Q fever. Patients with valvulopathies or other anatomic abnormalities of the vascular tree are at increased risk. Routine blood cultures will be negative. Fever may be absent. Typical findings include clubbing of the fingernails, hepatosplenomegaly in approximately 50 percent of cases, arterial embolic phenomena in 33 percent of cases, and purpura due to leukocytoclastic vasculitis in approximately 20 percent of cases.

## **2-48. Biological Warfare Agent Delivery**

The primary threat is by aerosol or through contamination of food.

## 2-49. Environmental Detection

The NBC reconnaissance teams collect aerosol samples for supporting laboratory analysis and confirmation. Medical personnel collect medical specimens for supporting laboratory analysis and confirmation. Veterinary/PVNTMED/PHS personnel collect suspect contaminated food samples for supporting laboratory analysis and confirmation.

## 2-50. Prevention

*a. Miscellaneous.* The military protective mask provides protection from aerosols. Only consume pasteurized dairy products and heat all foods sufficiently to destroy the organisms.

*b. Pre-exposure Prophylaxis.* A formalin-inactivated whole cell vaccine is available under IND status. A single dose of vaccine provides protection for at least five years. The vaccine is highly reactogenic in immune individuals, and can result in induration, sterile abscesses, and necrosis at the injection site. Sterile abscesses may spontaneously drain or require surgical drainage. Immunologic screening (skin testing and antibody measurements) must precede administration of the immunization. However, personnel with reaction to the screening must not be given the vaccine unless approved by a physician. Vaccine is contraindicated for individuals with positive skin tests and/or antibody titers.

### NOTE

A new vaccine prepared by chloroform-methanol extraction is being evaluated. This vaccine is safe, immunogenic in nonsensitized human volunteers, and is not reactogenic in sensitized guinea pigs.

*c. Post-exposure Chemoprophylaxis.* Chemoprophylaxis (tetracycline 500 mg orally every 6 hours for 5 days, or doxycycline 100 mg orally every 12 hours for 5 days) is effective if begun 8 to 12 days post-exposure.

### NOTE

Chemoprophylaxis is not effective if given immediately (1 to 7 days) post-exposure; it merely delays the onset of disease.

## 2-51. Biological Warfare Clinical Presentation

- a. Incubation.* 2 to 14 days (usually 7 days).
- b. Signs and Symptoms.* See endemic disease, above.



## 2-52. Diagnosis

*a.* Laboratory confirmation is accomplished by serologic testing for antibody titers. Acute Q fever results in high titers to Phase II antigen and lower antibody titers to Phase I antigen, while the antibody titers to Phase I antigen is higher during chronic Q fever. An ELISA test for IgM antibody is available at the USAMRIID and is more sensitive than the standard complement fixation test. A single high titer may be diagnostic as early as 10 to 14 days into the illness. A four-fold rise in titer in paired acute/convalescent sera is diagnostic of acute Q fever. Chronic Q fever is confirmed by complement fixation titer of 1:200 or greater to Phase I antigen. Cultures for *C. burnetii* are technically difficult, hazardous, and generally not done. *C. burnetii* can be identified on biopsy specimens (tissue) by immunofluorescent stain or electron microscopy. Nonspecific laboratory findings may include leukocytosis in one third of the patients. Mild elevations of transaminase levels (2 to 3 times the upper limit of normal) are typical. Bilirubin is usually normal.

*b.* Chest x-ray findings are abnormal in approximately one half of symptomatic cases and may include pleural effusions in up to 35 percent of cases, nonsegmental and segmented pleural based opacities, increased interstitial markings, and hilar adenopathy.

*c.* Differential diagnosis should include the diverse causes of either rapidly progressive or atypical pneumonia.

## 2-53. Decontamination

A 0.5 percent chlorine solution should be used for personnel and patient decontamination; the M291 skin decontaminating kit will not neutralize the organisms. Q fever has been transmitted from heavily contaminated unwashed laundry; therefore the laundry must be marked and managed as infectious material. Sputum and urine from patients should be autoclaved before disposal.

## 2-54. Treatment

*a. Triage Categories.* Triage categories will vary with the severity of the disease and available resources. Most patients with Q fever are placed in the Delayed category.

### *b. Medical Management.*

(1) *Acute Q fever.* While acute Q fever may run a brief, self-limited course without therapy, suspected cases of acute Q fever should be treated to reduce the risk of development of chronic disease. Therapeutics for acute Q fever are to—

- Administer doxycycline 100 mg orally every 12 hours for at least 2 days after the patient is afebrile.
- Administer tetracycline 500 mg every 6 hours for at least 2 days after the patient is afebrile.

- Consider treating patients unable to take tetracycline with ciprofloxacin and other quinolones, which are active in vitro. The duration of therapy is usually 5 to 7 days, at least 2 days after the patient is afebrile. Quinolones are not recommended for the treatment of children.

(2) *Chronic Q fever.* Therapy for Q fever endocarditis and other forms of chronic Q fever is complex, controversial, and beyond the scope of this manual. However, recommended regimens have included doxycycline combined with rifampin, ofloxacin, or TMP/sulfa and continued for at least 2 years. Antibody titers should be monitored every 6 months during therapy. Monitoring should be continued every 3 months for the first 2 years after therapy. Valve replacement is often necessary to cure Q fever endocarditis; however, this procedure should be reserved for hemodynamic indications or embolic complications.

c. *Prognosis.* Q fever usually results in a self-limited febrile illness of 2 to 14 days in duration. Previously healthy individuals would be expected to make a complete recovery. Fulminant pneumonia and chronic Q fever (including endocarditis and neurologic sequelae) are uncommon.

## 2-55. Control of Patients, Contacts, and Treatment Areas

Q fever is not communicable person to person. Observe Standard Precautions when handling patients. Unlike most other potential biological weapons, heavy environmental contamination with *C. burnetti* could pose a long-term risk due to environmental persistence. Dusts generated from the contaminated environment may continue to transmit the disease. Exposed clothing and equipment should be decontaminated.

## 2-56. Medical Evacuation

Patients may be evacuated with other classes of patients.

# Section VIII. TULAREMIA

## 2-57. General

a. *Etiologic Agent.* *Francisella tularensis* (*F. tularensis*) is an aerobic catalase-positive, gram-negative coccobacillus.

b. *Reservoir.* *F. tularensis* is maintained in numerous and diverse mammalian (rabbits, hares, rodents,) and tick reservoirs. *F. tularensis* is limited to the northern hemisphere. Type A (the predominant strain in North America) is more virulent than Type B (the predominant strain in Northern Europe).

c. *Transmission.* Transmission is by arthropod vectors (ticks and deerflies; also mosquitoes in Sweden, Finland, and the former Soviet Union), direct contact with infected animals, aerosols generated by skinning/processing infected animals, and ingestion of contaminated food or water. The organisms may also be transmitted by aerosol as a BW agent.

*d. Endemic Disease.*

(1) Clinical syndromes vary with portal of entry, inoculum, strain virulence, and the host's underlying state of health. Infection may be subclinical or fulminant. With the exception of typhoidal tularemia, the clinical syndromes are characterized by the combination of focal processes featuring ulceration at the portal of entry, and regional adenopathy involving the node groups draining the portal of entry. Following aerosol exposure, an undifferentiated febrile illness (typhoidal tularemia) or an acute pneumonia featuring fever, coughing, substernal chest tightness, and pleuritic chest pain may present. Usually, coughing is nonproductive; hemoptysis is rare. Physical findings may vary. Examination may be normal, or disclose rales, friction rubs, or findings consistent with consolidation or effusions.

(2) Pharyngeal tularemia presents as an acute pharyngitis following ingestion of contaminated food or water. The chief complaint is a severe sore throat. Physical findings include fever, exudative pharyngitis and/or tonsillitis, and possibly pharyngeal ulcers. Also, findings may include a pharyngeal membrane similar to that seen in diphtheria. Regional adenopathy may present in cervical, preauricular, and retropharyngeal node groups with occasional abscess formation.

(3) Oculoglandular disease presents following inoculation of the conjunctivae via aerosol, splashes, or direct contact (contaminated fingers). This disease presents as an acute conjunctivitis and may feature small conjunctival ulcers or papules. Complications may include corneal ulceration and dacryocystitis, but visual loss is rare. Regional adenopathy is a conspicuous feature of this illness, with preauricular or preauricular adenopathy. Severe cases of adenopathy may mimic parotiditis. Differential diagnosis should include other causes of Parinaud oculoglandular syndrome, including adenovirus infection, cat scratch disease, syphilis, herpetic infection, and pyogenic bacterial infection.

**2-58. Biological Warfare Agent Delivery**

The primary threat is by aerosol release, or by contamination of food or water supplies.

**2-59. Environmental Detection**

The NBC reconnaissance teams collect aerosol samples for supporting laboratory analysis and confirmation. Medical personnel collect medical specimens for supporting laboratory analysis and confirmation. Veterinary/PVNTMED/PHS personnel collect suspect contaminated food samples for supporting laboratory analysis and confirmation. Preventive medicine/PHS/BEE personnel collect suspect contaminated water samples for supporting laboratory analysis and confirmation.

**2-60. Prevention**

*a. Miscellaneous.* The military protective mask provides protection of the respiratory tract from exposure to aerosol organisms. All food must be thoroughly heated before consumption to kill any organisms. Water must be thoroughly disinfected before consumption.

*b. Pre-exposure Prophylaxis.*

- A live attenuated vaccine is available as an IND. It is given by scarification. The vaccine has been shown to be safe and effective in preventing laboratory-acquired tularemia and experimental infection in volunteers.

- Chemoprophylaxis given for anthrax or plague (ciprofloxacin, doxycycline) may confer protection against tularemia, based on in vitro susceptibilities.

*c. Post-exposure Prophylaxis.* Post-exposure prophylaxis following a BW attack include—

- Administer doxycycline 100 mg orally every 12 hours for 2 weeks; or tetracycline 500 mg orally every 6 hours for 2 weeks; or ciprofloxacin 500 mg orally every 12 hours for 2 weeks.

- Chemoprophylaxis is not recommended following potential natural exposures (tick bite, rabbit or other animal exposures).

**2-61. Biological Warfare Clinical Presentation**

*a. Incubation.* 1 to 21 days (usually 3 to 5 days).

*b. Signs and Symptoms.* The BW agent presentations of tularemia will be the pneumonic and typhoidal forms as discussed in paragraph 2-57 above. Oculoglandular disease could possibly occur following inoculation of the conjunctivae.

**2-62. Diagnosis**

*a.* Serologic testing is the preferred procedure for laboratory confirmation. Confirmation of diagnosis requires a four-fold increase in titer; serologies may need to be repeated at 7 to 10 day intervals. Agglutination tests and ELISA are also available. A gram stain of expectorated sputum is usually unrewarding; generally, the organism is not visualized on stains of clinical specimens. Cultures are not advised for diagnostic purposes. The organism does not grow on standard bacteriologic growth media. *F. tularensis* can be cultured on special supportive media containing cystine or another sulfhydryl source. However, cultures of the organism pose a significant occupational hazard to laboratory personnel. When cultures for *F. tularensis* are submitted, laboratory personnel must be alerted, as these cultures must be processed at Biosafety Level 3. Blood specimens may be submitted for mouse/egg inoculation.

*b.* Radiographic findings are nonspecific and may include subsegmental or lobar infiltrates, apical or miliary infiltrates, cavitation, pleural effusions, and hilar adenopathy.

**2-63. Treatment**

*a. Triage Categories.* Triage categories will vary according to the severity of the illness, available resources, and personnel. Patients presenting during the early stages of tularemia pneumonia are

classified as either Delayed or Immediate depending on the severity of illness and the requirement for respiratory support.

*b. Medical Management.* Supportive care may include respiratory support and hydration. Open lesions should be covered and topical antibiotics applied. Antibiotic therapy may be one of the following:

- Administer streptomycin 7.5 to 10 mg/kg IM every 12 hours for 10 to 14 days.
- Administer gentamicin 3 to 5 mg/kg IV daily for 10 to 14 days.
- Administer ciprofloxacin 400 mg IV every 12 hours, switch to oral ciprofloxacin (500 mg every 12 hours) after the patient is clinically improved; continue for completion of a 10- to 14-day course of therapy.
- Administer ciprofloxacin 750 mg orally every 12 hours for 10 to 14 days.

*c. Prognosis.* Inhalation tularemia can lead to fulminant pneumonia with case fatality of 30 to 60 percent without treatment.

#### **2-64. Control of Patients, Contacts, and Treatment Areas**

Apply Standard Precautions. Tularemia is not communicable person to person.

#### **2-65. Medical Evacuation**

Patients may be evacuated. Observe Standard Precautions during evacuation.

## CHAPTER 3

# VIRAL AGENTS

## Section I. INTRODUCTION

### 3-1. General

Viruses are the simplest type of microorganism and consist of a nucleocapsid protein coat containing genetic material, either ribonucleic acid (RNA) or DNA. Potential viral BW agents include smallpox, VEE, and VHF.

## Section II. SMALLPOX

### 3-2. General

*a. Etiologic Agent.* *Variola* is a member of the poxvirus family and is very contagious to humans. In addition, some animal poxviruses are virulent to humans (for example, monkeypox). Theoretically, recombinant poxviruses could be developed from animal poxviruses or vaccinia, and used as biological weapons.

*b. Reservoir.* Humans were the only natural reservoir of *variola*. *Variola* was eradicated as an endemic human pathogen, but known laboratory cultures of *variola* are maintained under security at the CDC, Atlanta, Georgia, and the State Research Center of Virology and Biotechnology, Koltsovo, Russia.

*c. Transmission.* Usually occurred by respiratory droplet transmission, following close face-to-face contact. Smallpox was also transmitted by direct contact with skin lesions or drainage, or with contaminated objects. Although uncommon, airborne transmission (long distance) also occurred.

*d. Endemic Disease.* Smallpox has been eradicated as an endemic disease. The last naturally acquired reported cases occurred in October 1977, in Somalia. However, if *variola* is delivered as a BW agent, it could result in the reemergence of smallpox. Once reestablished as an endemic disease, it could again be spread by respiratory droplet or droplet nuclei, or by contact with scabs, lesion drainage, and contaminated objects.

### 3-3. Biological Warfare Agent Delivery

The primary threat is delivery by aerosol release.

### 3-4. Environmental Detection

The NBC reconnaissance teams or other bioengineering personnel operating similar detection equipment accomplish detection.

### 3-5. Prevention

a. *Pre-exposure Prophylaxis.* There are no routine immunizations of US forces for smallpox. When the threat indicates, senior leadership may direct vaccination of personnel with vaccinia.

#### NOTE

Contraindications to pre-exposure prophylaxis include pregnancy, impaired immunity, human immunodeficiency virus (HIV) infection, eczema, severe burns, psoriasis, other chronic dermatoses, and individuals with household or other close contacts with the above conditions.

b. *Post-exposure Prophylaxis.*

(1) All individuals exposed to or suspected of being exposed to smallpox BW agents should have active or passive immunization. Contacts that are not immunized or those immunized more than 3 years prior to exposure should be given vaccinia as soon as possible (within 1 to 7 days) following exposure. Limited data obtained during the era of endemic smallpox suggested that vaccinia combined with vaccinia immunoglobulin (VIG) was slightly more effective than vaccinia alone for post-exposure immunoprophylaxis. The combination of vaccinia and VIG is very rational if post-exposure chemoprophylaxis cannot be given within 7 days of exposure.

(2) With the exception of significant immunodeficiency, there are no contraindications to vaccinia following smallpox exposure. For contacts with pregnancy or eczema at increased risk for vaccinia side effects, the combination of vaccinia and VIG 0.6 ml/kg is advised. Vaccinia immunoglobulin was administered in divided doses at multiple locations over 24 to 36 hours. Patients with HIV infection or other immunodeficiencies would be candidates for VIG alone.

(3) Possible side effects of vaccinia (vaccinia is a live virus) are the potential to cause disease in vaccinees and their contacts, especially those with conditions outlined above. Inadvertent inoculation to skin due to touching or scratching a vaccine lesion and then other areas of skin, and inadvertent inoculation of the eyes (ocular vaccinia) resulting in an intense conjunctivitis with vesicles and pustules; keratitis and corneal ulceration could result. Topical antivirals were used anecdotally to treat herpetic ocular infections (idoxuridine, vidarabine); these agents are active in vitro versus vaccinia.

(4) Generalized vaccinia is a rare idiosyncratic reaction featuring mild constitutional symptoms and a generalized vesicular rash. Vaccinia cannot be cultured from the vesicles or from the serum of patients with this condition. Pathogenesis is unknown, but is possibly due to an immunopathologic mechanism. Usually, this is a self-limited reaction and no therapy is indicated, but VIG may be indicated for severe cases.

(5) Idiosyncratic reactions of varying severity were seen that require supportive care. These included generalized urticarial exanthems, such as erythema multiforme and Stevens-Johnson syndrome.

(6) Encephalitis occurs in approximately two individuals per million receiving the vaccine. This complication produced a case fatality rate of 10 to 30 percent and neurologic sequelae in survivors. The pathogenesis is unknown but is probably due to an immunopathologic mechanism because vaccinia cannot be cultured from CSF or brain tissue of patients. Treatment is supportive.

(7) Eczema vaccinatum is a severe dermatitis featuring replication of vaccinia at sites of eczema, psoriasis, burns, or other chronic or severe cutaneous lesions. Therapy is the administration of VIG 0.6 ml/kg every 2 to 3 days IM in divided doses at multiple sites over a 24 to 36 hour period until no new lesions appear.

(8) Vaccinia necrosum occurred in immunocompromised vaccinees. This condition featured an intense local reaction at the site of the vaccination, progressing to local necrosis. The lesion can progress by local extension and metastasize to distant sites on the skin; it is potentially fatal. Therapy is the administration of VIG 0.6 ml/kg every 2 to 3 days IM in divided doses at multiple sites over a 24 to 36 hour period until definite clinical improvement is apparent.

(9) Fetal vaccinia may result from giving vaccinia to females during pregnancy. The prognosis for the fetus is poor, resulting in stillbirth.

### 3-6. Biological Warfare Clinical Presentation

a. *Incubation Period.* The incubation period is 7 to 17 days, commonly 10 to 12 days.

b. *Signs and symptoms.*

(1) Smallpox begins as a febrile prodrome of 2 to 4 days duration, featuring the acute onset of fever, rigors, malaise, headache, backache, and vomiting. Other features of the prodrome included delirium and a transient erythematous macular rash, each occurring in approximately 15 percent of patients. The characteristic exanthematous phase begins with an acute papular dermatitis on the face, hands, and forearms, then spreading to the lower extremities and the trunk. Distribution of the rash is centrifugal, with face and distal extremities involved earlier and to a greater extent than proximal extremities or trunk. The lesions progress in a synchronous manner from papule to vesicle to pustule. Scabs form in 8 to 14 days and slough off in 14 to 28 days after the onset of the rash. The sloughing leaves depressed depigmented scars. Enantheis involving the upper aerodigestive tract may also occur.

(2) Variants include flat-type smallpox, featuring severe systemic toxicity and large flat maculopapular lesions with a soft, velvety, nonindurated texture. The most severe form of smallpox is the hemorrhagic variant, featuring severe systemic toxicity, and diffuse ecchymosis and purpura. This variant is associated with a high-titer viremia and absent or negligible antibody responses; patients usually died before the characteristic papules or vesicles appeared. A relatively mild form of smallpox (*variola minor*, *alastrim*) featured little systemic toxicity and a milder exanthem and was seen in parts of southern Africa, Europe, and Latin America. It was due to a less virulent strain of *variola*.

(3) Complications of smallpox include encephalitis in 1 per 500 cases, with high rates of mortality and neurologic sequelae among survivors. Keratitis with corneal ulceration leading to blindness



occurred in 1 percent of cases. Pulmonary edema could complicate the course of hemorrhagic and flat-type variants.

### 3-7. Diagnosis

Differential diagnosis of a vesicular or pustular exanthem may include other infections (varicella, enteroviruses, rickettsialpox, septicemic melioidosis) or autoimmune diseases (dermatitis herpetiformis, bullous erythema multiforme, and so forth). Cytologic examination of specimens obtained from the bases of unroofed vesicles may disclose eosinophilic inclusions (Guarnieri bodies) which are sites of viral replication in the cytoplasm. Poxviruses may also be identified by electron microscopy of specimens obtained from skin lesions; however, these methods will not differentiate poxviruses. Clinical specimens (serum, respiratory secretions, specimens obtained from skin lesions or crusts) may be sent to the laboratory for culture. The virus may also be cultured from the blood during the prodrome. Poxviruses may be identified by differential growth characteristics in tissue culture. The use of genetic typing methods will lead to a specific diagnosis.

### 3-8. Treatment

*a. Triage Category.* The triage category varies with conditions and available resources; given the prolonged incubation, prodrome, clinical course, and lack of specific therapy, most patients should be categorized as Delayed. Contacts should be vaccinated or receive booster vaccinations as soon as possible, optimally within 24 hours.

*b. Medical Management.* Provide supportive care. There is no specific antiviral therapy available for smallpox.

*c. Prognosis.* Case fatality rate for smallpox (*variola major*) was historically 20 to 40 percent and higher during pregnancy or the neonatal period. Case fatality for the flat-type variant was approximately 95 percent in the unimmunized and 66 percent in previously immunized patients. The hemorrhagic variant was nearly always fatal. Case fatality for *variola minor* (*alastrim*) was 5 percent.

### 3-9. Control of Patients, Contacts, and Treatment Areas

*a. Patients.* Strict (standard, contact, and airborne) isolation and quarantine of all patients must be maintained until scabs have separated. The virus can be spread by air currents and can be carried outside the hospital by various materials contaminated by the patient, especially clothing and linens. Deposit all oral and nasal discharges in a paper container and burn. Sterilize (autoclave or boil) all bedclothes and other fabrics that are exposed to the patient. Spray or mop all floors, walls, and other hard surfaces in the patient isolation area with a disinfectant solution (phenolic and quaternary ammonium compounds, formalin, or a 5 percent chlorine solution). Allow the disinfectant to remain on the surfaces for at least 4 hours.

*b. Patient Contacts.*

(1) The reappearance of a single case of smallpox would be a global emergency. Immediately report all occurrences to Military Public Health.

(2) Quarantine all direct contacts with any case and maintain daily surveillance for 17 days after last known contact with a case. Vaccinate all contacts, including health care workers, if they have not been immunized or received a booster within 3 years (see post-exposure prophylaxis paragraph 3-5*b* above).

*c. At Risk Personnel.* Conduct an epidemiological investigation to identify all potentially exposed personnel. Quarantine identified personnel for the remainder of the incubation period; usually 7 to 12 days following the appearance of index cases. Give post-exposure prophylaxis as discussed in paragraph 3-5*b* above.

### 3-10. Medical Evacuation

Smallpox is an IQD. Apply strict quarantine measures. Isolate and evacuate all smallpox patients in cohorts of smallpox patients only. Do not evacuate smallpox patients across national boundaries unless approved by major command authority (see paragraph 1-21).

## Section III. VENEZUELAN EQUINE ENCEPHALITIS

### 3-11. General

*a. Etiologic Agent.* The VEE virus is an arthropodborne alphavirus.

*b. Reservoir.* Enzootic serotypes are maintained in a rodent-mosquito cycle. Enzootic strains are frequently transmitted to humans living in endemic disease areas via mosquito bites. However, enzootic strains are not virulent for horses. Epizootic serotypes are thought to arise from enzootic strains by mutation. In contrast to enzootic strains, epizootic strains are highly virulent for Equidae (horses, mules, donkeys). Horses serve as amplifying hosts of epizootic (but not enzootic) strains, providing a source of virus for mosquitoes, which transmit virus to humans. The VEE virus occurs in northern South America, Central America, and Trinidad.

*c. Transmission.* The endemic disease is transmitted by mosquitoes. Aerosol transmission has occurred in laboratory settings, but is not known to occur naturally.

*d. Endemic Disease.* The epizootic VEE virus has an incubation period of 1 to 15 days. The usual presentation is an undifferentiated febrile illness with fever, malaise, and headache. Other symptoms that may appear include myalgia (72 percent), vomiting (50 percent), drowsiness (40 percent), chills (20 percent), sore throat (20 percent), and diarrhea (20 percent). Fever can remit but recur the following day. Patients may be incapacitated by malaise and fatigue for 1 to 2 weeks. Less than 1 percent of adults will develop severe encephalitis featuring meningismus, ataxia, seizures, and coma; paralysis and neurologic sequelae may result in survivors. The case fatality rate in adults is approximately 1 percent of all cases, but may reach 10 percent with CNS involvement.

### 3-12. Biological Warfare Agent Delivery

The primary threat is delivery by aerosol release.

### 3-13. Environmental Detection

The NBC reconnaissance teams collect aerosol samples for submission to the supporting medical laboratory for analysis and field confirmation. Medical personnel will collect specimens from patients presenting at MTFs with signs and symptoms of the VEE virus (outside of its natural geographic range, it would suggest a possible BW attack or importation of infected horses or mosquito vectors) for supporting laboratory analysis and confirmation. Veterinary personnel collect samples from equines within the AO for laboratory analysis and confirmation. A natural epidemic would usually be preceded by equine disease. A BW attack will most likely result in human disease as a primary event, or the simultaneous onset of disease in humans and equines. A BW attack in an area with equines and mosquito vectors may also initiate an epizootic/epidemic.

### 3-14. Prevention

*a. Pre-exposure Prophylaxis.* Live attenuated vaccine (TC-83) is available as an IND. However, 20 percent of vaccinees do not respond and another 20 percent develop severe reactions. An inactivated vaccine (C-84) is available as an IND for TC-83 nonresponders. The C-84 vaccine has the typical disadvantages of inactivated vaccines (multiple doses and boosters are required to confer and maintain immunity). In addition, C-84 vaccine does not protect rodents against experimental aerosol challenge; human data is not available.

*b. Post-exposure Prophylaxis.* There are no post-exposure prophylaxes available.

### 3-15. Biological Warfare Clinical Presentation

*a. Incubation Period.* Incubation period is 1 to 6 days; onset is sudden.

*b. Signs and Symptoms.* See endemic disease above.

### 3-16. Diagnosis

Perform serologic tests to measure antibody titers. A single high titer IgM value 5 to 7 days after the onset of illness is supportive; a four-fold rise in antibody titer in paired acute and convalescent sera is diagnostic. Identification of the virus in clinical specimens (serum, CSF) by PCR is under investigation. Viral cultures may confirm the diagnosis if serum is sent early during the illness (a low titer viremia is present during the first 24 to 72 hours of illness); however, cultures will be negative later in the clinical course and in those who have progressed to encephalitis. Nonspecific laboratory findings include lymphopenia, and

occasionally, neutropenia and mild thrombocytopenia. Transaminase levels (aspartate aminotransferase and lactate dehydrogenase) are usually elevated and a CSF lymphocytic pleocytosis may be present.

### **3-17. Treatment**

*a. Triage Categories.* The triage categories vary according to severity of the disease and available resources. Most patients are placed in the Delayed category, given the usual clinical course and a lack of specific therapy. Patients with seizures are placed in the Immediate category for anticonvulsive therapy, airway management, and other supportive care measures.

*b. Medical Management.* There is no specific antiviral therapy. Administer anticonvulsive therapy for patients with seizures and other supportive care measures as indicated.

*c. Prognosis.* The VEE virus is an incapacitating agent. While acute morbidity is severe, most patients recover. However, animal studies demonstrate that aerosol exposure leads to viral attachment to olfactory nerve endings and direct invasion of the CNS via the olfactory nerve, resulting in a high incidence of CNS disease. This suggests that in contrast to the mosquito-borne disease, VEE resulting from a BW attack would be more likely to cause CNS involvement and could be associated with higher morbidity and mortality.

### **3-18. Control of Patients, Contacts, and Treatment Areas**

*a. Patient Management.* Apply Standard Precautions for infection control.

*b. Management of Patient Contacts.* Observe Standard Precautions. Control mosquito vectors and vaccinate horses in the vicinity. The VEE virus is not communicable person to person.

### **3-19. Medical Evacuation**

Patients may be evacuated with all other classes of patients.

## **Section IV. VIRAL HEMORRHAGIC FEVERS**

### **3-20. General**

*a. Etiologic Agent.* The VHF viruses belong to four families of lipid-enveloped viruses with single-stranded RNA genomes. The taxonomy, ecology, and epidemiology of these viruses are summarized below. Transmission of VHFs varies with the specific virus. However, all of the VHFs, with the exception of dengue, are potentially transmitted via aerosol, underscoring their possible role as BW agents. Table 3-1 provides the taxonomy of VHFs.

Table 3-1. Taxonomy of Viral Hemorrhagic Fevers

VIRUS	DISEASE	GEOGRAPHY	RESERVOIR	TRANSMISSION
<b>ARENAVIRIDAE</b>				
<b>NEW WORLD COMPLEX</b>				
JUNIN	ARGENTINE VHF	S. AMERICA	RODENT	AEROSOL, FOMITES
MACHUPO	BOLIVIAN VHF	S. AMERICA	RODENT	AEROSOL, FOMITES
GUANARITO	VENEZUELAN VHF	S. AMERICA	RODENT	AEROSOL, FOMITES
SABIA	BRAZILIAN VHF	S. AMERICA	UNKNOWN	AEROSOL, FOMITES
<b>OLD WORLD COMPLEX</b>				
LASSA BUNYAVIRIDAE	LASSA FEVER	W. AFRICA	RODENT	AEROSOL, FOMITES
<b>PHLEBOVIRUS GENUS</b>				
RIFT VALLEY	RIFT VALLEY FEVER	AFRICA	MOSQUITO	MOSQUITO, AEROSOL OR FOMITES FROM SLAUGHTERING INFECTED ANIMALS
<b>NAIROVIRUS GENUS</b>				
	CRIMEAN-CONGO VHF	AFRICA, MIDDLE EAST, E. EUROPE	TICKS	MOSQUITO, AEROSOL OR FOMITES FROM SLAUGHTERING INFECTED ANIMALS
<b>HANTAVIRUS GENUS</b>				
HANTAAN	VHF WITH RENAL SYNDROME	ASIA, EUROPE	RODENT	AEROSOL, FOMITES
DOBRAVA	VHF WITH RENAL SYNDROME	E. EUROPE	RODENT	AEROSOL, FOMITES
SEOUL	VHF WITH RENAL SYNDROME	WORLDWIDE	RODENT	AEROSOL, FOMITES
PUUMALA	NEPHROPATHIA ENDEMICA	EUROPE	RODENT	AEROSOL, FOMITES
<b>FILOVIRIDAE FAMILY</b>				
EBOLA	EBOLA VHF	AFRICA, ASIA	UNKNOWN	UNKNOWN
MARBURG	MARBURG VHF	AFRICA	UNKNOWN	UNKNOWN
<b>FLAVIVIRIDAE FAMILY</b>				
<b>MOSQUITO-BORNE</b>				
YELLOW FEVER	YELLOW FEVER	S. AMERICA, AFRICA	MOSQUITO, PRIMATE	MOSQUITO
DENGUE	DENGUE, DENGUE VHF	TROPICS AND SUBTROPICS	MOSQUITO, HUMANS	MOSQUITO
<b>TICK-BORNE</b>				
KYASANUR FOREST OMSK	KYASANUR FOREST DISEASE OMSK VHF	INDIA SIBERIA	RODENT, MONKEY RODENT	TICK TICK

*b. Endemic Disease.* Viral hemorrhagic fever is a clinical syndrome featuring fever, myalgia, malaise, and hemorrhage, and in some cases, hypotension, shock, and death. Viral pathogenesis is complex, incompletely understood, and varies among specific viruses. Some infections result in immune complex deposition which activates complement and other inflammatory cascades. This process damages vascular endothelium, results in capillary leak, and deregulates vascular smooth muscle tone. These lead to hypotension, shock, and end-organ failures. Some of these diseases activate coagulation cascades and result in DIC. Hemorrhage can also be enhanced by specific end-organ failures. For example, yellow fever can cause massive hepatic necrosis resulting in a deficiency of vitamin K-dependent clotting factors. The uremia

complicating the acute renal failure of hemorrhagic fever with renal syndrome (HFRS) leads to platelet dysfunction, further promoting hemorrhage. The final common pathway of hemorrhagic fever is damage to the vascular endothelium.

### **3-21. Biological Warfare Agent Delivery**

The primary threat is delivery by aerosol release.

### **3-22. Environmental Detection**

The NBC reconnaissance teams collect environmental samples for submission to the supporting medical laboratory for analysis. Preventive medicine/PHS/BEE personnel collect water samples for laboratory analysis. Veterinary personnel collect blood samples from animals for laboratory analysis. Medical personnel collect blood and other specimens from patients presenting with signs and symptoms for laboratory analysis.

### **3-23. Prevention**

*a. Pre-exposure Prophylaxis.* For pre-exposure prophylaxis, ensure all service members have received their yellow fever vaccinations. Investigational vaccines are available as INDs. Argentine hemorrhagic fever (AHF) attenuated vaccine has been safely used and has proven effective in preventing AHF in more than 150,000 agricultural workers in endemic areas; animal studies suggest that this vaccine also provides protection against Bolivian VHF. Two Rift Valley hemorrhagic fever vaccines (an inactivated vaccine and a live attenuated vaccine) are in development.

*b. Post-exposure Chemoprophylaxis.* As a post-exposure chemoprophylaxis, administer ribavirin, 500 mg orally every 6 hours for 7 days, for Crimean-Congo VHF (CCVHF) and Lassa fever. Ribavirin (intravenous and oral) is available under IND status and available through human use protocol only.

### **3-24. Biological Warfare Clinical Presentation**

*a. Incubation Period.* The incubation period can be days to months.

*b. Signs and Symptoms.* Initial clinical features may include flushing, conjunctival injection, possible periorbital edema, petechiae, and hypotension. Illness then progresses with prostration, fatigue, and hemorrhage. The most dreaded complications are shock, multiple organ system failure, and death.

### **3-25. Diagnosis**

Serologic methods include IgM antibody capture and ELISA techniques to detect the antigen. Tissue can be submitted for immunohistochemical staining, electron microscopy, or for genetic typing. Serum and other clinical specimens should be forwarded for viral culture under maximum containment (Biosafety Level 4).

Laboratory findings are nonspecific and variable. In general, these result in thrombocytopenia and leukopenia. Elevated liver function tests and other nonspecific laboratory findings may be present. The blood urea nitrogen (BUN) will be related to the circulatory status with the exception of HFRS in which the kidneys are target organs of the Hantaviruses. Differential diagnosis include diseases such as typhoid fever, meningococcemia, leptospirosis, malaria, vasculitic diseases, hemolytic uremic syndrome, thrombotic thrombocytopenic purpura, and the diverse etiologies of DIC.

### 3-26. Treatment

*a. Triage Categories.* The triage categories vary according to the severity of disease and available resources. Patients who are acutely ill with AHF, Bolivian VHF, Brazilian VHF, Venezuelan VHF, Lassa fever, CCVHF, or HFRS may be candidates for the Immediate category if ribavirin is available, as ribavirin may improve outcome. If ribavirin is not available, these patients are placed in the Delayed category. Other patients with hemorrhagic fevers may be classified as Delayed or Expectant categories.

*b. Medical Management.*

(1) Treatment is primarily supportive with special attention to fluid and electrolyte balance. Patients require treatment for shock, blood loss, renal failure, seizures, and coma. Treatment may include intensive care and specific interventions such as mechanical ventilation, dialysis, and neurological support. Heparin therapy may provide benefit for DIC. However, its role is controversial and should be reserved for patients with clinically significant hemorrhage and laboratory evidence of DIC. Aspirin and other medications that impair platelet function are contraindicated; as are IM injections. The use of intravascular devices must be carefully considered in the context of potential benefit versus the risk of hemorrhage. Surgical interventions should not be withheld if indicated.

(2) Specific antiviral therapy is limited. Clinical studies support the use of IV ribavirin for the treatment of Lassa fever and HFRS (Hantaan virus). The role of ribavirin therapy for CCVHF is supported by in vitro studies, although there is no clinical experience. Ribavirin (IV and oral) is available under IND status and is available through human use protocol only. For Lassa fever and CCVHF, administer a loading dose of ribavirin 30 mg/kg IV, followed by 16 mg/kg IV every 6 hours for 4 days; then 8 mg/kg IV every 8 hrs for 6 days to complete a 10-day course of therapy. For HFRS, therapy may benefit patients who have been febrile for 6 days or less. Administer a loading dose of ribavirin 33 mg/kg IV, followed by 16 mg/kg IV every 6 hours for 4 days, then 8 mg/kg IV every 8 hours for 3 days, to complete a 7 day course of therapy.

*c. Prognosis.* Prognosis varies from agent to agent; case fatality rates range from less than 10 percent (HFRS) to as high as 90 percent (Ebola). Survivors may be left with long-term sequelae (such as blindness, neurosensory hearing loss, and other neurologic, retinal, and ocular involvement).

### 3-27. Control of Patients, Contacts, and Treatment Areas

*a. Report.* Report suspected cases of VHFs outside the US to PVNTMED/PHS personnel immediately. Yellow fever is an IQD.

*b. Isolation.* The following recommendations apply to patients with suspected or proven arenavirus, filovirus, or CCVHF virus infections: these patients should be isolated in private rooms or isolation tents; if private rooms are not available, only other patients with the same disease should be in the same room; a negative air flow room should be used, if possible, if the patient has significant cough, hemorrhage, or diarrhea. Limit exposure to caregivers only; other staff members and visitors should not be allowed in the room to avoid injuries/nosocomial exposures. Caregivers should be the most skilled/experienced staff.

*c. Caregiver Protection.* The following recommendations apply to patients with suspected or proven arenavirus, filovirus, or CCVHF virus infections: all caregivers must wear gloves and gowns; anyone coming within 3 feet of the patient should also wear face shields or surgical masks and eye protection (for example, goggles or eyeglasses with side shields). When caring for patients with prominent cough, vomiting, diarrhea, or hemorrhage, caregivers should wear a HEPA filter air purifying respirator, a battery powered, air-purifying respirator, or a positive pressure supplied air respirator.

*d. Infectious Material Handling.* Sewage, bulk blood, suctioned fluids, secretions, and excretions should be autoclaved, processed in a chemical toilet, or treated with a 5 percent chlorine solution for at least 5 minutes in bedpan or commode prior to flushing.

*e. Contacts.*

(1) *Casual contacts.* There is no known risk of transmission to casual contacts, such as travelers in the same airplane.

(2) *Close contacts.* Close contacts, such as household members, physicians, nursing care, and individuals handling laboratory specimens, increase the possibility of contracting the disease. Close contacts should have their temperature recorded twice daily for 3 weeks post-exposure. Close contacts should receive post-exposure chemoprophylaxis/evaluation/treatment if fever (above 101°F) or other systemic symptoms present within 3 weeks of exposure.

(3) *High-risk contacts.* High-risk contacts include anyone who has mucous membrane or percutaneous exposures. High-risk contacts with mucous membrane exposure should copiously irrigate with water or eyewash solution for at least 15 minutes. For percutaneous exposure, individuals should frequently wash affected skin surfaces with soap and water; an antiseptic solution or handwashing agent may also be considered to provide better removal of any contamination on the exposed surfaces. High-risk contacts with exposure to Lassa fever and CCVHF should—

- Receive post-exposure chemoprophylaxis (ribavirin 500 mg orally every 6 hours for 7 days).
- Have their temperature recorded twice daily for 3 weeks post-exposure.
- Receive further evaluation/treatment if fever (greater than 101°F) or other systemic symptoms present within 3 weeks of exposure.



**3-28. Medical Evacuation**

Evacuation may result in increased morbidity and mortality for patients with VHFs; therefore, treatment at a local facility is preferred. Strict isolation as outlined in paragraph 3-27 above must be used for all patients evacuated. Obtain approval from the senior medical authority before evacuation; see paragraph 1-21 for more information.

## CHAPTER 4

# TOXINS

## Section I. INTRODUCTION

### 4-1. General

Toxins are poisonous byproducts of living organisms. They are very stable and produce severe illness when ingested, inhaled, or introduced into the body by any other means. Some toxins are susceptible to heat, while others are heat stable. Their effects on the human body range from minor illness to death.

## Section II. CLOSTRIDIUM BOTULINUM TOXIN

### 4-2. General

*a. Etiologic Agent.* Botulinum toxins are a group of seven toxins produced by *Clostridium (C.) botulinum*. The spores are ubiquitous; they germinate to give rise to vegetative bacteria that produce toxins during anaerobic incubation. Industrial-scale fermentation can produce large quantities of toxin for use as a BW agent. There are three forms of naturally occurring botulism—foodborne, infantile, and wound. Botulinum toxin is the most potent neurotoxin known; paradoxically it has been used therapeutically to treat spastic conditions (strabismus, blepharospasm, torticollis, and tetanus). Botulinum toxin consists of two polypeptide subunits (A and B chains). The B subunit binds to a receptor on the axons of motor neurons. The toxin is taken into the axon, where the A chain exerts its cytotoxic effect; it inactivates the axon, preventing release of acetylcholine and neuromuscular transmission (pre-synaptic inhibition). Recovery follows only after the neuron develops a new axon, which can take months. The presynaptic inhibition affects both autonomic (muscarinic) and motor (nicotinic) receptors.

*b. Reservoir.* The reservoir is soil, animals, and fish. The organisms can be recovered from honey and other agricultural products. High-risk foods are primarily improperly canned foods and dried meat or fish.

*c. Transmission.* Consumption of food contaminated with the *C. botulinum* toxin.

*d. Endemic Disease.*

(1) *Foodborne.* Foodborne botulism is due to ingestion of food contaminated with botulinum toxins. Inadequately heating vegetables and fruits during canning, then inadequate heating before serving is the primary mode of transmission in the US. In some foreign countries, smoked sausage, salmon, and fermented salmon eggs are the source of intoxication. In Asian countries, seafood is the primary source of intoxication.

(2) *Infantile.* Germination of spores leading to colonization and toxin production may occur in the infantile GI tract due to anatomic, physiologic, and microbiologic factors present during the first year

of life. *Clostridium botulinum* spores survive transit through the stomach in infants, relative to achlorhydria; spores can then germinate and colonize the intestinal tract in the absence of well-established GI tract microflora. Parents are advised not to feed infants honey, molasses, and other foods potentially high in *C. botulinum* spore content to prevent this disease. This form of botulism is a rare disease of adults, but may occur in cases of underlying anatomic or physiologic abnormalities of the GI, or alteration of the normal GI tract flora (such as after antibiotic exposure).

(3) *Wound*. Wound botulism is due to the germination of *C. botulinum* spores and in-situ toxin production in traumatic wounds. The spores may be introduced by organisms entering during wounding, by drug abusers through subcutaneous injection sites, and by cocaine abusers inhaling the spores into ischemic nasal ulcers and sinuses.

Botulism can feature milder presentations limited to cranial nerve palsies and mild GI symptoms related to autonomic dysfunction. Botulism should be considered in the differential diagnosis of patients presenting with symptoms of cranial nerve neuropathies, especially if numerous patients present simultaneously.

#### **4-3. Biological Warfare Agent Delivery**

The primary threat is delivery by aerosol release. Inhalation challenge does not occur naturally, but can be used in a BW attack. Aerosol dispersion has delivered lethal intoxication to experimental animals. The BW agent may also be delivered through contaminated food or water.

#### **4-4. Environmental Detection**

The NBC reconnaissance teams collect aerosol samples. Veterinary/PHS/PVNTMED personnel collect food samples for laboratory analysis. Veterinary personnel collect animal specimens for laboratory testing. Preventive medicine/PHS/BEE personnel collect water samples for laboratory testing. Patient care personnel collect medical specimens for laboratory testing.

#### **4-5. Biological Warfare Clinical Presentation**

*a. Incubation*. The incubation period for foodborne botulism is usually 24 to 36 hours. The incubation period for infantile botulism is unknown. The incubation period for wound botulism is usually 3 or more days.

*b. Signs and Symptoms*.

(1) The autonomic features of botulism are typical anticholinergic signs and symptoms: dry mouth, ileus, constipation, and urinary retention. Nausea and vomiting may occur as nonspecific sequela of ileus. Dilated pupils (mydriasis) occur in approximately 50 percent of cases.

(2) The motor complications of botulism feature a descending paralysis, usually beginning with cranial nerve palsies leading to blurred vision, diplopia, dysphonia, and dysphagia. Collapse of the upper

airway may occur due to weakness of the oropharyngeal musculature. As the descending motor weakness involves the diaphragm and accessory muscles of respiration, respiratory failure may occur.

(3) Sensory symptoms usually do not occur. Botulinum toxins do not cross the blood/brain barrier and do not cause CNS disease. However, the psychological sequelae of botulism may be severe and require specific intervention.

(4) Symptoms usually begin 12 to 36 hours following intoxication; time can vary according to the amount of toxin absorbed and could be reduced to hours following a BW attack.

#### **4-6. Prevention**

*a. Pre-exposure Prophylaxis.* A pentavalent (types A, B, C, D, and E) toxoid vaccine has been developed as a pre-exposure prophylaxis. This vaccine is safe and effective in animal studies, and has been demonstrated to be safe in human volunteers. The vaccine remains under an IND status since it is not feasible to test for efficacy in humans. Vaccine is given by deep subcutaneous injection at 0, 2, and 12 weeks, with a booster 1 year after the initial dose.

*b. Post-exposure Prophylaxis.* Currently, post-exposure prophylaxis is not available. Animal experiments demonstrate that botulinum antitoxin is effective; however, human data or practice guidelines are not available. Botulinum antitoxin should be considered in extraordinary circumstances.

#### **4-7. Diagnosis**

Botulism is primarily a clinical diagnosis. Laboratory confirmation may be obtained by the use of an ELISA test to detect toxin antigen. The assay may be used to test specimens of implicated food or water, or samples obtained from the environment. Clinical specimens submitted for study may include serum, gastric aspirates, stool, and respiratory secretions. A simple bioassay (mouse neutralization) confirms the diagnosis if an aliquot of the patient's serum produces descending paralysis when injected into a laboratory mouse. Nerve conduction studies and single-fiber electromyography (EMG) can confirm the diagnosis, although these modalities may not be readily available in a tactical setting. Edrophonium test results can be positive in botulism as well as in myasthenia gravis; therefore, this test may not be useful due to the lack of specificity. Antibody tests are not useful for botulism, as the amount of antigen required to stimulate an antibody response exceeds the lethal dose.

#### **4-8. Treatment**

*a. Triage Categories.* Triage categories will vary according to situation and available resources. Given that up to 95 percent of patients will survive with supportive care, prompt respiratory support and medical evacuation for further supportive care can be lifesaving. Patients with upper airway compromise could be placed in the Immediate category. Patients with mild or gradually progressive symptoms could be

placed in the Delayed category. Patients with respiratory failure due to neuromuscular involvement may be placed in the Immediate category if endotracheal intubation and respiratory support are available, or in the Expectant category if these are not available. The implications of a mass casualty situation create a demand for limited respiratory support resources that are ominous.

*b. Medical Management.* Supportive care includes respiratory support, hydration, bowel, bladder and skin care, nasogastric suctioning for ileus, physical therapy, and psychological support. Long-range issues include meticulous attention to the details of daily care; specifically, the prevention of decubitus ulcers, nosocomial infections, and deep venous thrombosis.

(1) Specific therapy for inhalation or foodborne/waterborne botulism consists of giving botulinum antitoxin to neutralize the circulating toxin in patients with progressive symptoms, or who have not progressed to a stable state. The standard product is a trivalent (types A, B, E) equine antiserum. The serum is available through CDC. Since this is a horse-derived product, potential complications include acute (anaphylaxis) and delayed (serum sickness) hypersensitivity reactions. A despeciated equine heptavalent antitoxin (types A, B, C, D, E, F, G) has been prepared by cleaving the Fc fragments, leaving F(ab)2 fragments. This product is available through USAMRIID as an IND. The despeciated product has been effective in animal studies. However, 4 percent of horse antigens are retained; there is still a risk of hypersensitivity reactions. Administration of either product must be given in an MTF where personnel and equipment are available to treat possible anaphylaxis. Before administering the antitoxin, perform a sensitivity skin test by intradermally injecting 0.1 ml of a 1:10 dilution of antitoxin and monitoring the patient for 20 minutes. If the injection site becomes hyperemic (greater than 0.5 centimeters [cm] in diameter), or if the patient develops fever, chills, hypotension, rash, respiratory difficulties, nausea, vomiting, or generalized pruritus, the test is considered positive. If no allergic symptoms are observed, administer the antitoxin by IV (10 cubic centimeters [cc] over 20 minutes). Repeat this dose until there is no more improvement. For patients with positive skin tests, attempt desensitization by subcutaneously administering 0.01 to 0.1 ml of antitoxin, gradually increase the dose every 20 minutes until 2.0 cc can be sustained without a marked reaction. Preferably, desensitization should be performed by an experienced allergist. Medical personnel attempting to give the antitoxin should be prepared to treat a possible anaphylactic reaction; intubation equipment, epinephrine, and IV access must be immediately available.

(2) Therapy for wound and sinusitis consists of debridement and administration of antibiotics.

#### NOTE

Aminoglycosides and clindamycin may further impair neuromuscular transmission and may lead to clinical deterioration if used for patients with botulism.

*c. Prognosis.* Botulism can result in severe morbidity. Complications include descending paralysis, with possible respiratory failure. Case fatality is approximately 60 percent without respiratory intensive care. However, with respiratory supportive care, prognosis is favorable, with case fatality rates at approximately 5 percent. Recovery may be prolonged, requiring up to three months for signs of initial

improvement and up to one year for complete symptomatic recovery. Psychological sequelae may be severe and require specific interventions.

#### **4-9. Control of Patients, Contacts, and Treatment Areas**

The patient can be evacuated. Employ Standard Precautions; botulism is not communicable person to person.

#### **4-10. Medical Evacuation**

Patients may be evacuated with other classes of patients. Observe Standard Precautions for evacuation.

### **Section III. CLOSTRIDIUM PERFRINGENS TOXINS**

#### **4-11. General**

*a. Etiologic Agent.* *Clostridium perfringens* is a common anaerobic bacillus that produces at least 12 toxins. Spores survive cooking and then germinate and multiply at storage at ambient temperature, slow cooling, or inadequate rewarming. A high inoculum (greater than 100,000 colony-forming units [CFU]/gm of food) is usually required to produce disease.

*b. Reservoir.* The reservoir is soil and the GI tract of healthy persons and animals.

*c. Transmission.* Gas gangrene results from wound contamination with soil containing spores of *C. perfringens*. Clostridial food poisoning follows ingestion of foods contaminated with soil or feces and then stored under conditions that allow replication of the organism.

*d. Endemic Disease.* The diseases produced by these toxins depend upon the site of *C. perfringens* colonization or infection and toxin production. For example, wound infection results in gas gangrene, while ingesting contaminated food results in clostridial food poisoning, or in susceptible hosts, enteritis necroticans. Clostridial food poisoning is usually a brief, self-limited disease, featuring the abrupt onset of nausea, abdominal colic, and diarrhea; vomiting and fever are rare. Individuals can develop gas gangrene by having wounds contaminated with soil containing bacterial spores. The spores germinate, resulting in bacterial toxin production. Gas gangrene (clostridial myonecrosis) features necrosis of skeletal muscle and overlying soft tissue and constitutes a surgical emergency.

#### **4-12. Biological Warfare Agent Delivery**

The primary threat is delivery of *C. perfringens* alpha toxin as an aerosol to the respiratory tract. This would result in pulmonary disease, vastly different from the naturally occurring diseases associated with *C. perfringens*. The toxin may also be delivered in combination with other toxins to produce a variety of clinical effects.

#### 4-13. Environmental Detection

The NBC reconnaissance teams collect environmental samples for submission to the supporting medical laboratory for analysis. Medical personnel collect pulmonary secretions from patients presenting with signs and symptoms for laboratory analysis.

#### 4-14. Prevention

There is no pre-exposure or post-exposure prophylaxis for *C. perfringens*.

#### 4-15. Biological Warfare Clinical Presentation

*a. Incubation.* The incubation period is 1 to 6 hours.

*b. Signs and Symptoms.* Aerosol challenges of *C. perfringens* alpha toxin produce lethal pulmonary disease in laboratory animals. The *C. perfringens* alpha toxin is a highly toxic phospholipase, which will result in severe injury to the exposed respiratory tract. An aerosol delivery can produce a severe pulmonary capillary leak, resulting in adult respiratory distress syndrome (ARDS) and respiratory failure. Absorbed toxin can lead to intravascular hemolysis, thrombocytopenia, and liver damage.

#### 4-16. Diagnosis

Acute serum and tissue specimens should be collected and transported to the designated reference laboratory for toxin immunoassay. Clinical laboratory findings could include anemia, thrombocytopenia, abnormal liver function tests, and hypoxia. The differential diagnosis should include other causes of ARDS including chemical warfare (CW) agent (phosgene or mustard) exposure, inhalation injury due to ricin or staphylococcal enterotoxin B (SEB), Hantavirus pulmonary syndrome, and other diverse etiologies of ARDS. Pulmonary disease due to SEB will be less severe; also hemolysis, thrombocytopenia, or liver damage should not occur.

#### 4-17. Treatment

*a. Triage Categories.* Triage categories will vary according to severity and stage of illness and available resources.

*b. Medical Management.* Medical management consist of supportive care. Patients may require assisted ventilation to relieve the respiratory effects. There are no specific antitoxins or antidotes available

*c. Prognosis.* Prognosis is poor.

#### 4-18. Control of Patients, Contacts, and Treatment Areas

Apply Standard Precautions in patient care. The *C. perfringens* toxin is not communicable person to person.

#### 4-19. Medical Evacuation

Patients may be evacuated. Apply Standard Precautions during evacuation.

### Section IV. RICIN

#### 4-20. General

*a. Etiologic Agent.* Ricin is a potent cytotoxin derived from the beans of the castor plant (*Ricinus communis*). Over one million tons of castor beans are processed annually in the production of castor oil, which is used for medicinal and industrial purposes including the production of aircraft and marine engine lubricants, dyes, and paints. The waste mash from this process is approximately 5 percent ricin by weight. Consequently, large quantities of ricin are easily and inexpensively produced. Ricin consists of two hemagglutinins and two toxins. These toxins are dimers consisting of cytotoxic A chains and B chains which serve as transport peptides and bind to cellular membrane receptors. Ricin toxins are potent inhibitors of DNA replication and protein synthesis. The toxin can be transmitted through contaminated food and water, percutaneously via small pellets/projectiles designed to carry toxins, or as a BW aerosol.

*b. Reservoir.* Castor beans.

*c. Transmission.* Transmission has been by inhalation of organism during industrial operations. Also, transmitted through ingestion of castor bean meal.

*d. Endemic Disease.* There is no endemic disease; however, there have been exposures in industrial operations. Clinical features vary according to the route of intoxication and toxin dose. Accidental sublethal aerosol exposures occurred during the 1940's. Patients presented with acute onset of fever, chest tightness, cough, dyspnea, nausea, and arthralgias 4 to 8 hours after exposure. The onset of profuse sweating several hours later was the sign of termination of most of the symptoms. Lethal aerosol exposures in humans have not been reported; however, large aerosol exposures in experimental animals result in necrosis of upper and lower respiratory epithelium, and perivascular and alveolar edema. Respiratory tract exposure to a large dose will produce necrosis of the entire exposed respiratory tract; pulmonary capillary leaks result in extravasation of protein-rich fluid into the alveoli, resulting in pulmonary edema, ARDS, and respiratory failure. Ingestion results in necrosis of the GI epithelium, local hemorrhage, and hepatic, splenic, and renal necrosis. Intramuscular injection results in severe local muscle necrosis and visceral organ involvement.

#### 4-21. Biological Warfare Agent Delivery

The primary threat is delivery of the BW agent by aerosol release. Ricin is less toxic than botulinum. A larger quantity is required to cover a significant area on a battlefield. This feature may limit the use of ricin as a tactical weapon; however, it can be used for small-scale operations. The agent may also be delivered through contamination of food and water supplies.



#### 4-22. Environmental Detection

The NBC reconnaissance teams collect aerosol samples for supporting laboratory identification. Preventive medicine/PHS/BEE personnel collect suspect contaminated water samples for laboratory identification. Veterinary/PVNTMED/PHS personnel collect suspect contaminated food samples. Veterinary personnel collect specimens from government-owned animals for supporting laboratory identification. Medical treatment personnel collect specimens from patients presenting with signs and symptoms for laboratory identification. The supporting laboratory performs an antigen detection (ELISA) test to identify the presence of toxins in samples or specimens.

#### 4-23. Prevention

- a. Pre-exposure prophylaxis is not available; however, candidate vaccines are under development.
- b. Post-exposure prophylaxis is not available.

#### 4-24. Biological Warfare Clinical Presentation

- a. *Incubation Period.* The incubation period is 18 to 24 hours.
- b. *Signs and Symptoms.* See endemic disease, paragraph 4-20.

#### 4-25. Diagnosis

Serum and respiratory secretions may be submitted for antigen detection (ELISA). Immunohistochemical stains of tissue may also be available. Paired acute and convalescent sera for antibody studies can be submitted from survivors. Nonspecific laboratory and radiographic findings may include neutrophilic leukocytosis, bilateral interstitial infiltrates compatible with noncardiogenic pulmonary edema. Differential diagnosis of respiratory disease would include phosgene exposure, SEB, Hantavirus pulmonary syndrome, atypical pneumonias including Q fever and tularemia, and diverse causes of ARDS.

#### 4-26. Treatment

- a. *Triage Categories.* Triage categories will vary according to severity of illness and available resources. Respiratory distress would result in placement of the patient in the Immediate category if respiratory support was available, or Expectant if respiratory support was not available. Patients with milder presentations would be candidates for the Delayed category.

- b. *Medical Management.*

- (1) Supportive care including intensive care measures, such as supplemental oxygen, endotracheal intubation and mechanical ventilation, positive end-expiratory pressure, and hemodynamic monitoring, may be required for respiratory disease.

(2) Gastrointestinal intoxication is best managed by vigorous gastric decontamination with lavage and superactivated charcoal, followed by use of cathartics such as magnesium citrate. Volume replacement of GI tract fluid loss is important.

(3) In percutaneous exposures, treatment would be primarily supportive, managing specific organ system failures.

(4) Specific therapeutic drugs are not currently available.

*c. Prognosis.* Prognosis depends on the route and intensity of exposure. Due to a lack of data, specific prognosis outcomes cannot be stated.

#### **4-27. Control of Patients, Contacts, and Treatment Areas**

Apply Standard Precautions in patient care. Ricin is not communicable person to person.

#### **4-28. Medical Evacuation**

Patients may be evacuated.

## **Section V. SAXITOXIN**

#### **4-29. General**

*a. Etiologic Agent.* Saxitoxin is the parent compound of a group of related neurotoxins produced by marine dinoflagellates of the genus *Gonyaulax*.

*b. Reservoir.* Shellfish.

*c. Transmission.* Saxitoxin is transmitted to humans by ingesting bivalve mollusks, which accumulate dinoflagellates during filter feeding.

*d. Endemic Disease.* Paralytic shellfish poisoning (PSP) is a severe, life-threatening neuromuscular condition. Saxitoxin is rapidly absorbed from the GI tract following ingestion of contaminated shellfish. Saxitoxin binds to the sodium channels of nerve and muscle tissue, preventing propagation of action potentials in excitable cells. This leads to neuromuscular dysfunction, and in severe cases, death due to respiratory paralysis and respiratory failure. In contrast to botulism, sensory and CNS symptoms are present in addition to motor symptoms. Symptoms begin as early as 10 minutes to several hours after ingestion, depending on the ingested dose and host factors. Initial symptoms include numbness and tingling of the lips, tongue, and fingertips; followed by numbness of the neck and extremities and motor

incoordination. Cranial nerve involvement can result in diplopia, speech, and swallowing difficulties. Other symptoms may include light-headedness, dizziness, weakness, confusion, memory loss, and headache. Flaccid paralysis and respiratory failure are life-threatening complications, and occur within 2 to 12 hours after ingestion. The toxin is rapidly cleared by renal excretion; however, complete neurologic recovery may require 7 to 14 days.

#### **4-30. Biological Warfare Agent Delivery**

The primary threat is delivery by aerosol release. Saxitoxin may also be delivered by projectiles or by contamination of food and water. Contamination of food and water supplies would be on a very limited basis.

#### **4-31. Environmental Detection**

The NBC reconnaissance teams collect aerosol samples for supporting laboratory identification. Preventive medicine/PHS/BEE personnel collect suspect contaminated water samples for laboratory identification. Veterinary/PVNTMED/PHS personnel collect suspect contaminated food samples. Veterinary personnel collect specimens from government-owned animals for supporting laboratory identification. Medical treatment personnel collect specimens from patients presenting with signs and symptoms for laboratory identification.

#### **4-32. Prevention**

*a. Pre-exposure Prophylaxis.* There is no pre-exposure prophylaxis available. Avoidance of potentially contaminated food and water will protect individuals from the effects of ingested toxins.

*b. Post-exposure Prophylaxis.* There is no post-exposure prophylaxis available.

#### **4-33. Biological Warfare Clinical Presentation**

*a. Incubation.* Minutes to hours.

*b. Signs and Symptoms.* Clinical features would be similar to those discussed above for endemic disease; animal experiments using aerosol challenges suggest that the clinical course following inhalation is accelerated and that death occurs within minutes following exposure.

#### **4-34. Diagnosis**

Diagnosis is confirmed by antigen (toxin) detection by ELISA test or mouse bioassay. Clinical specimens which may be submitted for toxin assay include stomach contents, serum, and in a BW context, respiratory

secretions. Specific toxins can be identified by high-pressure liquid chromatography. Routine clinical laboratory findings are not specific for saxitoxin poisoning. Cardiac conduction disturbances may develop; however, these electrocardiographic findings are nonspecific. The differential diagnosis of saxitoxin poisoning includes ciguatoxin (ciguatera) and tetrodotoxin ingestion. Ciguatoxin occurs following ingestion of large finned reef fish, and in contrast to saxitoxin, will result in more severe GI symptoms (nausea, vomiting, diarrhea), and in a peculiar reversal of temperature sensation—hot feels cold, cold feels hot.

#### **4-35. Treatment**

*a. Triage Categories.* Triage categories vary according to the severity of the disease and availability of resources. Following aerosol delivery or toxic projectile, patients may be considered candidates for the Immediate category for airway and ventilatory support, if available; or candidates for the Expectant category in remote, isolated locations.

*b. Medical Management.* Supportive care is essential. Airway management and mechanical respiratory support is required for severe intoxication. Standard management of poison ingestion, including superactivated charcoal, should be used following oral ingestion.

*c. Prognosis.* Prognosis following an aerosol challenge is poor.

#### **4-36. Control of Patients, Contacts, and Treatment Areas**

Apply Standard Precautions in patient care. Saxitoxin is not transmitted person to person.

#### **4-37. Medical Evacuation**

Patients may be evacuated. Apply Standard Precautions during evacuation.

## **Section VI. STAPHYLOCOCCAL ENTEROTOXIN B**

#### **4-38. General**

*a. Etiologic Agent.* Staphylococcal enterotoxin B is one of numerous exotoxins produced by *Staphylococcus (S.) aureus*. Up to one-half of all clinical isolates of *S. aureus* produce exotoxins; related toxins include toxic shock syndrome toxin-1 (TSST-1) and exfoliative toxins. The SEB toxin is heat-stable and is the second most common source of outbreaks of food poisoning.

*b. Reservoir.* The reservoir of *S. aureus* is humans (especially, food handlers with infected cuts on their hands, abscesses, acne eruptions, nasal discharges, or on occasion, from normal appearing skin) and contaminated milk or milk products. The SEB is usually produced in foods contaminated with *S. aureus*.

c. *Transmission.* Ingestion of food, milk, or milk products containing preformed toxin.

d. *Endemic Disease.* Staphylococcal food poisoning features the acute onset of fever, nausea, vomiting, and diarrhea within hours of intoxication. The toxin increases intestinal peristalsis; severe nausea and vomiting may be due to stimulation of the CNS. The staphylococcal enterotoxins belong to a class of potent immune stimulants known as bacterial superantigens. Superantigens bind to monocytes at major histocompatibility complex type II receptors rather than the usual antigen binding receptors. This leads to the direct stimulation of large populations of T-helper cells while bypassing the usual antigen processing and presentation. This results in a brisk cascade of pro-inflammatory cytokines and recruitment of other immune effector cells, and a relatively deficient activation of counter-regulatory negative feedback loops. This results in an intense inflammatory response that can injure host tissues.

#### **4-39. Biological Warfare Agent Delivery**

The primary threat is SEB aerosol release. The SEB may also be employed by sabotage contamination of food and/or water supplies.

#### **4-40. Environmental Detection**

The NBC reconnaissance teams collect aerosol samples for supporting laboratory identification. Preventive medicine/PHS/BEE personnel collect suspect contaminated water samples for laboratory identification. Veterinary/PVNTMED/PHS personnel collect suspect contaminated food samples. Veterinary personnel collect specimens from government-owned animals for supporting laboratory identification. Medical treatment personnel collect specimens from patients presenting with signs and symptoms for laboratory identification. The supporting laboratory performs toxin assay of epidemiologically implicated food or water. The laboratory can also perform toxin assay of environmental samples following an aerosol attack.

#### **4-41. Prevention**

a. *Pre-exposure Prophylaxis.* Currently, there is no pre-exposure prophylaxis available. Protecting food and water supplies from contamination and avoiding potentially contaminated food and water will protect individuals from the effects of ingested toxins.

b. *Post-exposure Prophylaxis.* Currently post-exposure prophylaxis is not available; however, passive immunization (immunoglobulin) can attenuate experimental disease in experimental animals if given within 4 to 8 hours post-exposure. There are no human data or practice guidelines.

#### **4-42. Biological Warfare Clinical Presentation**

a. *Incubation.* Variable. 4 to 10 hours for GI illness.

*b. Signs and Symptoms.* Illness due to poisoning of food or water supplies will present as acute GI illness (see endemic disease, paragraph 4-38). Illness due to inhalation will result in respiratory tract disease not encountered in the endemic disease. This is due to the activation of pro-inflammatory cytochrome cascades in the lungs, leading to pulmonary capillary leak and pulmonary edema. Symptoms include fever, headache, myalgia, nonproductive cough, and in severe cases, dyspnea. Gastrointestinal symptoms may also occur due to inadvertent swallowing of SEB delivered via aerosol and deposited in the upper aero-digestive tract, or coughed following mucociliary clearance. Severe cases may result in acute pulmonary edema and respiratory failure.

#### **4-43. Diagnosis**

Diagnosis includes performing toxin assay (antigen detection) of implicated food or water and on environmental samples collected following a suspect BW attack. Clinical specimens that could be sent for toxin assay include serum and respiratory secretions. However, the toxin may not be detectable before the onset of symptoms. Acute and convalescent sera for antibody tests will confirm the diagnosis. Nonspecific findings may include leukocytosis, elevated sedimentation rate, and in severe cases, chest x-ray abnormalities featuring pulmonary edema. Differential diagnosis include pneumonia due to viruses, mycoplasmas, *Chlamydia pneumoniae*, *Coxiella burnetii*, Hantavirus pulmonary syndrome, CW agent inhalation injury (mustard, phosgene), and in severe cases, other diverse causes of noncardiogenic pulmonary edema and ARDS.

#### **4-44. Treatment**

*a. Triage Categories.* Triage categories will vary with conditions and available resources. Patients with acute respiratory distress should be placed in the Immediate category to obtain respiratory support. Patients without respiratory distress should be placed in the Delayed category.

*b. Medical Management.* Medical management is primarily supportive care; symptomatic relief may be provided by the use of acetaminophen and cough suppressants. Severe cases will require intensive care including respiratory support, hemodynamic monitoring, and possibly diuretics and vasopressors.

*c. Prognosis.* Staphylococcal enterotoxin B is considered an incapacitating agent; most patients may be expected to make a full recovery, although most patients will be unfit for duty for 1 to 2 weeks. Patients with pulmonary edema and respiratory failure will be at risk for mortality.

#### **4-45. Control of Patients, Contacts, and Treatment Areas**

Apply Standard Precautions in patient care. Staphylococcal enterotoxin B is not communicable person to person.

#### **4-46. Medical Evacuation**

Patients may be evacuated. Observe Standard Precautions in patient movement.

## Section VII. TRICHOTHECENE MYCOTOXINS

### 4-47. General

*a. Etiologic Agent.* Trichothecene (T2) mycotoxins are a diverse group of over 40 compounds produced by molds of the genus *Fusarium*. These toxins inhibit protein and DNA synthesis, mitochondrial respiration, and alter cell membrane structure and function. Naturally occurring mycotoxicosis occurs in livestock following ingestion of grains contaminated with molds.

*b. Reservoir.* Moldy grain.

*c. Transmission.* Ingestion of moldy grains.

*d. Endemic Disease.* While there have been no laboratory-confirmed cases of human disease due to T2 mycotoxins, these toxins are thought to have caused an epidemic of foodborne illness (alimentary toxic aleukia) in Russia during World War II due to the ingestion of foods prepared from moldy grain.

### 4-48. Biological Warfare Agent Delivery

The toxin may be delivered by aerosol release or through contamination of food and water supplies. These toxins are the agents allegedly delivered via aerosol during the “Yellow Rain” attacks in Afghanistan and Southeast Asia during the 1970s and 1980s. The T2 mycotoxins are the only potential BW agents that can harm and be absorbed through intact skin.

### 4-49. Environmental Detection

The NBC reconnaissance teams collect aerosol samples for supporting laboratory identification. Preventive medicine/PHS/BEE personnel collect suspect contaminated water samples for laboratory identification. Veterinary/PVNTMED/PHS personnel collect suspect contaminated food samples. Veterinary personnel collect specimens from government-owned animals for supporting laboratory identification. Medical treatment personnel collect specimens from patients presenting with signs and symptoms for laboratory identification. The supporting laboratory performs toxin assay of epidemiologically implicated food or water. The laboratory can also perform gas-liquid and high-pressure liquid chromatography of environmental samples.

### 4-50. Prevention

*a. Pre-exposure Prophylaxis.* As a pre-exposure prophylaxis, the use of topical antivesicant cream or ointment may provide limited protection of skin surfaces. Food and water contaminated with mycotoxins must not be consumed.

*b. Post-exposure Prophylaxis.* There is no post-exposure prophylaxis.

#### **4-51. Biological Warfare Clinical Presentation**

*a. Incubation.* The incubation period is minutes after exposure.

*b. Signs and Symptoms.* The BW disease presentation will vary according to the portal of entry and delivered dose. Mycotoxins are highly cytotoxic and may be viewed as “radiomimetic” agents, or having effects similar to vesicants, especially mustard agents. Delivery to the skin may cause a burning skin pain, redness, tenderness, blistering, and progression to skin necrosis with eschar formation and sloughing. Respiratory exposure may result in nasal itching with pain, rhinorrhea, sneezing, epistaxis, dyspnea, wheezing, and cough. Exposure of the conjunctivae and other mucosal surfaces may result in local burning pain and redness, followed by necrosis. Gastrointestinal exposure would be expected to result in nausea, vomiting, crampy abdominal pain, and watery or bloody diarrhea. Systemic absorption may follow delivery via any route and would result in late toxicity of decreased blood cell counts, predisposing to bleeding and sepsis.

#### **4-52. Diagnosis**

Serum and urine should be sent for antigen detection. The parent toxin and metabolites (50 to 75 percent) are eliminated in urine and feces within 24 hours; however, metabolites can be detected as late as 28 days after exposure.

#### **4-53. Treatment**

*a. Triage Categories.* The triage category varies with the stage and severity of illness and available resources.

*b. Medical Management.* Following oral ingestion, standard therapy for poison ingestion including the use of superactivated charcoal is indicated. Other measures of supportive care depend upon the organ system involved (for examples, respiratory support for respiratory involvement and standard burn care for cutaneous involvement). All medical interventions are supportive; there are no antidotes or other specific therapies available.

*c. Prognosis.* Prognosis following the development of symptoms is poor.

#### **4-54. Control of Patients, Contacts, and Treatment Areas**

Apply Standard Precautions in patient care. Mycotoxins are not transmitted person to person.

#### **4-55. Medical Evacuation**

Patients may be evacuated. Observe Standard Precautions during evacuation.



APPENDIX A

**RECOGNITION OF A  
BIOLOGICAL WARFARE AGENT CASUALTY**

**A-1. General**

*a.* Medical personnel must be familiar with the signs and symptoms of BW agent casualties. With current technology, it is likely that a BW attack will be completed before the local commander, or his medical advisor, is aware that it has taken place. The medical officer must attempt to distinguish between an epidemic of natural origin and a BW attack.

*b.* Medical and tactical intelligence channels should communicate with each other as early as possible. Threat information on potential enemy force use of BW weapons/agents is important for planning and executing HSS operations. Once BW agents have been used, identification of agents will be important to medical intelligence channels for operational purposes.

*c.* Medical units should rely on information not only from detectors and intelligence sources, but also from the casualties themselves. This applies particularly to BW weapons/agents since at present there are no rapid methods of detection or identification. Some of the problems in the recognition and diagnosis of casualties suffering from the effects of BW operations are discussed here. Medical personnel must remember that the signs and symptoms of most BW agents are identical to or similar to those of endemic and epidemic diseases. The nature and timing of symptoms will vary with the route of exposure. Although most BW agents require days to manifest, some agents produce their effects in minutes to a few hours. It is important that the fullest and earliest information be given to medical units when the enemy has used BW weapons/agents. This information is used to facilitate the diagnosis of individual cases, to initiate immediate treatment, and to permit the arrangement for the reception of casualties.

**A-2. Types of Casualties**

On the BW battlefield, the following types of casualties may be seen:

*a. Conventional Casualties.*

(1) Conventional casualties with no BW injury and with no contamination of their clothing and equipment.

(2) Conventional casualties with no BW injury but with contamination of their clothing and equipment.

*b. Direct Biological Warfare Casualties.*

(1) Biological warfare agent casualties with no other injury.

(2) Mixed casualties with conventional and BW injuries. Since BW munitions often include burst charges, such injuries may occur as part of a BW agent attack. They may also be present when the

BW injury and conventional injury occur at different times. Other types of mixed casualties may be from nuclear or chemical weapons used as well as the biological weapons. Also, mixed casualties may result when biological injuries are combined with natural illnesses (infectious disease still accounts for the majority of casualties in conventional warfare).

*c. Indirect Biological Warfare Casualties.*

(1) Casualties suffering combat stress reaction occur often in warfare, but may be more frequent where NBC threats exist. The service member will have the additional stress of isolation from wearing the chemical protective ensemble; additional fatigue when wearing the protective garments; and fear of NBC agents. See FM 8-51, FM 22-51, and MCRP 6-11c for additional information on combat stress control.

(2) Some BW agent treatments can have undesirable side effects when taken inappropriately, or in large enough quantities. Antibiotics kill desirable bacteria in the digestive tract, causing abdominal pain and frequent bowel movements. Medical personnel must be alert for their appearance.

(3) Wearing the protective ensemble makes dissipation of excess body heat more difficult. Wearing the mask also makes water intake difficult. Both will increase the probability of heat injury (heat exhaustion or heat stroke).

(4) Indirect BW casualties will most likely be the largest group requiring treatment.

**A-3. Recognize Biological Casualties**

*a.* It is unlikely that BW agents will produce single casualties under field conditions. Also, a BW attack should be suspected with any sudden increase in the numbers of unexplained casualties presenting with the same signs and symptoms. If BW operations are unlikely, and if relatively few service members are affected, an endemic or epidemic disease may be more probable (for example, *Salmonella* food poisoning). If the number of cases continue to present over an extended period, as opposed to a large number presenting in one or two days, a naturally occurring epidemic is suspected.

*b.* Under operational conditions, the psychological effects may complicate the medical situation. To determine if a BW agent has caused the casualty, the medical officer should ask questions along the following lines:

- Was the casualty wearing full MOPP at the time of the exposure?
- Was there any aircraft or artillery bombardment in the area at the time of the attack?
- Was there anyone in the area dispersing a suspicious spray or vapor from portable or vehicle-mounted devices?
- Were there any suspicious persons around the unit water supply or in the unit food service area?

- Was there any evidence of spray, liquid droplets, or suspicious persons in the area?
  - Was anyone else affected and if so, what effects?
- c. To recognize a BW attack, the identity of the agent must be determined.
- (1) The medical officer should consider the following:
- Groups of patients from a specific unit/area presenting with the same illness signs and symptoms in a short period of time (hours to days).
  - Signs and symptoms not associated with any known endemic diseases in the AO.
- (2) Also, question the patient about the delay or rapidity of the onset of symptoms. Was there any delay between exposure or contamination and the onset of effects? If so, how long was the delay?
- Did the effects persist after adjustment of the protective mask?
  - Has the casualty used any self-injection device or did anyone else use any injection devices on the casualty? If so, did the symptoms improve or deteriorate?
  - Is the casualty's behavior normal?
- d. To assess the dose of the agent received by the patient, determine the following:
- Was the casualty exercising or at rest?
  - Was the casualty in the open or under cover?
  - How long was the suspect BW agent inhaled?
  - How long was the interval between suspected contamination and decontamination?

APPENDIX B

**MEDICAL MANAGEMENT AND TREATMENT  
IN BIOLOGICAL WARFARE OPERATIONS**

**Section I. US ARMY MEDICAL TREATMENT FACILITIES**

**B-1. General**

All US Army MTFs must be prepared to receive mass casualties caused by exposure to BW agents. A mass casualty situation exists when the number and type of casualties exceed the local medical support capabilities for their care. If the unit follows conventional operational standing operating procedures, an overwhelming backlog of work will rapidly accumulate. Such backlogs can result in unnecessary loss of life and limb with suffering. Therefore, all HSS planners must prepare plans for mass casualty situations and all units must be trained and equipped for these plans. The unit must be ready to operate with minimal confusion. Medical units must provide medical treatment to these casualties and supervise their decontamination. Normally, individual service members are responsible for their own decontamination. For casualties who are injured and unable to decontaminate themselves, this process has to be performed by buddy aid, by unit personnel at a decontamination site, or at an MTF by nonmedical personnel from the supported units.

*a.* At US Army Levels I and II (unit, division, and nondivisional) units, the supported unit commander must provide at least 8 nonmedical personnel to perform patient decontamination. At US Army Levels III and IV (corps and echelons above corps) hospitals, a 20-man patient decontamination augmentation team or 20 nonmedical personnel must be provided to perform patient decontamination. The base cluster commander or units within the geographical area of the hospital must provide the 20 nonmedical personnel.

*b.* Medical personnel must supervise patient decontamination personnel to ensure patient conditions are not aggravated by decontamination process. Supervising medical personnel must make the final determination on the completeness of patient decontamination.

*c.* If the supported units do not have the necessary resources to provide nonmedical personnel, the units (not the medical services) must address this issue with higher headquarters.

**B-2. Objectives of Health Service Support in Biological Warfare Operations**

The objectives of HSS in BW operations are to—

- a.* Return to duty the maximum number of personnel as soon as possible.
- b.* Manage casualties so that BW agent injuries are minimized and any other injuries or illnesses are not aggravated.
- c.* Protect persons handling contaminated casualties or working in contaminated areas.
- d.* Avoid spreading contamination in ambulances, other evacuation vehicles and aircraft, MTFs, and adjoining areas.

*e.* Continue the MTF's operations to maintain normal services unrelated to the medical treatment of BW agent illnesses and injuries.

### **B-3. Planning for the Management and Treatment of Biologically Contaminated Casualties**

The initial management and treatment of casualties contaminated with a BW agent will vary with the tactical situation and the nature of the contaminant. Therefore, each MTF must have a plan and put it into effect immediately, then modify it to meet each specific situation. Patient decontamination sites are collocated with an MTF. This ensures that medical supervision of patient decontamination is available. Specifics on management of BW-contaminated patients at the MTF are found in FM 8-10-7. Each MTF has identical medical equipment sets (MES) for chemical agent patient decontamination and treatment. The numbers of each type of MES vary, depending on the level of care. For example, the battalion aid station (BAS) has one chemical agent patient decontamination MES and two chemical agent patient treatment MES. The patient decontamination MES provides sufficient supplies to decontaminate 60 patients. Each chemical agent patient treatment MES provides sufficient medical supplies to treat 30 patients. The chemical agent patient treatment MES contains the patient protective wraps (PPWs) that are needed to transport decontaminated litter patients to the next level MTF. Each MTF must be prepared to treat—

- Biological warfare agent casualties generated within the geographical area of the MTF.
- Patients received from a forward and, in some cases, a lateral MTF.
- Patients suffering from a combination of injuries/illnesses (such as BW and conventional, BW and chemical agent, and BW and endemic disease.)
- Patient suffering from battle injuries and DNBI that have not been exposed to any NBC agents.
- Enemy prisoners of war, detained persons, and noncombatants, when directed.

### **B-4. Emergency Medical Treatment of Biologically Contaminated Casualties**

*a.* Biological warfare agent casualties received at an MTF may also have traumatic wounds or illnesses due to other causes. Management of these patients must minimize the BW agent injuries without aggravating their traumatic wounds or illnesses.

*b.* Triage of arriving casualties is extremely important. A decision is made whether EMT or decontamination of the casualty requires priority. Airway management and/or control of hemorrhage may be equal to or more urgent than treatment for BW agent poisoning. Therefore, EMT measures may have to be performed in rapid sequence with decontamination or by simultaneous team actions.

*c.* For contaminated casualties who have traumatic injuries or other illnesses, decontamination should be accomplished as soon as the situation permits. Lifesaving measures for a traumatic injury or some illnesses must be given priority over immediate decontamination, although the delay may increase the BW agent illness or injury.

*d.* When a contaminated casualty has another injury or illness resulting in respiratory difficulty, hemorrhage, or shock, the order of priority for emergency action is as follows:

- (1) Control respiratory failure (provide assisted ventilation) and/or massive hemorrhage.
- (2) Decontaminate the casualty.
- (3) Administer additional EMT for shock, wounds, and illnesses so severe that delay may be life or limb threatening.
- (4) Evacuate the casualty as soon as possible, if necessary.

#### **B-5. Patient Decontamination Methods**

*a.* Patient decontamination serves two purposes—

- (1) It prevents the patient's system from absorbing additional contaminants.
- (2) It also protects medical personnel treating the patient and other patients from contamination. Accumulated contamination in the MTF is a serious threat to medical personnel and patients. Accumulated contamination may also impose a serious medical logistical burden on the unit. The effectiveness of decontamination is strongly influenced by the time lapse between initial contamination and decontamination. In many cases, the patient may have absorbed dangerous quantities of a contaminant before arriving at the MTF.

*b.* Each service member is trained in immediate decontamination procedures and is equipped to do so. However, any patient arriving at an MTF from a BW-contaminated area is considered contaminated, unless there is positive proof to the contrary.

*c.* A decontamination area is established on the downwind side of the MTF. It is provided with overhead protection such as plastic sheeting, trailer covers, ponchos, tarpaulins, or tents. Only those patients requiring treatment at a forward MTF will have their protective overgarments and other clothing removed. Needless removal of protective clothing only increases the patient's vulnerability to liquid agent exposure which results in increased injury. Also, forward MTFs do not have replacement protective overgarments. Any ambulatory patient decontaminated by clothing removal becomes a litter patient; he must be placed in a PPW for protection from BW agents during evacuation. Patients not requiring treatment at a forward MTF, but requiring evacuation to the next level MTF must have their MOPP gear and equipment spot decontaminated. Spot decontamination will remove gross contamination, reducing the hazard to the casualty and evacuation personnel.

*d.* Every person entering the decontamination area (including patients) must be wearing a protective mask or have other respiratory tract protection in place. Most contaminants are removed by carefully removing all clothing.

**WARNING**

**Do not remove the patient's protective mask. Remove the mask hood, overgarments, booties and boots, the BDU, and undergarments. For step-by-step procedures in performing patient decontamination, see FM 8-10-7.**

*e.* After patients have been decontaminated, exercise rigid control to prevent exposing their unprotected skin to a liquid BW agent. After treatment in the clean treatment area or collective protection shelter (CPS), the patient is placed in a PPW (to protect them during evacuation) and taken to the evacuation point to await evacuation. Medical personnel must monitor patients at the evacuation point to ensure that their condition remains stable; if their condition changes, additional treatment may have to be provided before evacuation.

*f.* Ambulatory patients may be able to decontaminate themselves and assist with the decontamination of other ambulatory patients. Their overgarments are not removed unless they must enter the clean treatment area or CPS for treatment. For patients not entering the clean treatment area or CPS, spot decontaminate the overgarment to remove gross contamination. When possible, have them proceed as groups of two or three to facilitate control. Ambulatory patients require constant observation and periodic assistance during the decontamination process. The aidman at the decontamination point removes all bandages from patients that will be treated at the MTF. Bandages are not replaced unless needed to control bleeding. After decontamination, each patient goes through the shuffle pit to the clean treatment area where wounds are treated and if possible, protective covering is restored. Restore protective covering by taping holes or tears in the protective overgarment. Patients are then returned to duty or go to the evacuation point, as their medical conditions dictate. Ambulatory patients with injuries that do not require immediate attention but require treatment at a higher level MTF are evacuated in their MOPP ensemble. For example, a patient with a broken arm has a stabilizing splint on. This individual does not require treatment at the BAS; however, his MOPP gear must be spot decontaminated to remove gross contamination before evacuation to the Level II MTF.

**NOTE**

At forward MTFs (Levels I and II), only patients that cannot survive evacuation to the next level MTF will be completely decontaminated (have their clothing removed) and treated at the lower level of care facility. Patients that are stable but require evacuation to a higher level MTF should have their overgarments spot decontaminated before evacuation. The patients must be completely decontaminated at the MTF where essential medical care is provided.

## **B-6. Logistics**

*a.* Provisions must be made to ensure that medical personnel are supplied and equipped to manage and treat contaminated casualties. Also, supplies and equipment must be provided for the protection of personnel manning the contaminated areas. Medical supplies are stored or stocked in a manner that reduces potential loss from BW contamination.

*b.* Patient protective wraps must be available for casualties whose injuries require decontamination (clothing removal) for treatment in the clean treatment area. After treatment, decontaminated patients must be placed in PPWs before they are moved to the evacuation point (paragraph B-5*e* above).

## **B-7. Training**

Commanders must ensure that medical personnel and decontamination team members (provided by the supported unit) are trained to manage, decontaminate, and treat BW agent casualties. Personnel must be trained to protect themselves from BW agent injuries. In addition, provisions must be made for practice exercises to enable them to accomplish their responsibilities with speed and accuracy. Example: Decontaminating a casualty with speed is achieved through practice. Training emphasis should be placed on—

- Employing individual protection.
- Practicing immediate decontamination procedures.
- Providing EMT.
- Performing casualty decontamination.
- Evacuating decontaminated casualties.
- Evacuating contaminated casualties.
- Sorting and receiving contaminated casualties into a system designed for the treatment of both contaminated and uncontaminated casualties.
- Techniques for patient lifting and litter transfer.
- Using the chemical agent monitor (CAM) and chemical agent detection paper to monitor for and detect chemical agents, if employment in conjunction with BW agents is suspected.

## **B-8. Casualty Evacuation**

*a.* Contaminated casualties should be decontaminated as close to the areas where they were contaminated as possible. Their MOPP gear and clothing should not be removed until they arrive at an MTF. Evacuation by ground ambulance must not be delayed for completion of decontamination. Upon arrival at the MTF where treatment will be provided, all contaminated clothing and equipment (except the protective



mask) are removed and the skin and protective mask are decontaminated; spot decontaminate the skin. Decontaminated patients continue to be a hazard to persons handling, treating, or transporting them. Therefore, appropriate precautions for the suspected disease must be applied. After decontamination at the field MTF, the patient is placed in the clean holding area to await admission into the CPS or clean treatment area. They must be protected from recontamination. Patients will keep their protective mask on until they are in the clean treatment area (away from the hotline) or are in the air lock of the CPS (see FM 8-10-7).

(1) Once treated, the patient is placed in a PPW before movement to the evacuation pickup point. The PPW protects the individual from further contamination. Individuals inside the PPW no longer have to wear the protective mask and are evacuated as clean. A plastic window in the PPW permits patient observation. A patient in a PPW and left in a sunny area is subject to heat build up. The protective mask remains with the patient during evacuation even though it may not be worn.

(2) If a BW attack occurs, medical units in the evacuation system can expect to receive contaminated casualties because of the need for hasty evacuation. Therefore, extreme care must be taken to avoid spreading the contamination.

*b.* Before contaminated casualties are evacuated by Army aircraft or landing craft, they should be decontaminated. Otherwise, the BW agent may endanger the crew and other personnel, as ventilation is poor in aircraft compartments and other enclosed spaces. If casualties cannot be decontaminated before evacuation, they should be evacuated by ground ambulance. These casualties should wear their protective masks. The hazards of the BW agent to other persons can be further minimized by—

- Preparing each litter by placing an impermeable cover over it and an open blanket on top of the cover.
- Placing the casualties on the prepared litters and folding the sides of the blankets over them. Although this measure helps protect other persons, it increases the casualties' exposure to the contaminant and increases the possibility of heat injuries.
- Providing as much ventilation during transport as the weather and other conditions permit.
- Removing the impermeable covers and blankets with the casualties when they are removed from the vehicles. Litters that have not been protected with impermeable covers must be handled as contaminated.

*c.* Patients being evacuated by USAF AE aircraft should be decontaminated prior to evacuation. See FM 8-10-6 and FM 8-10-7 for procedures on patient evacuation by USAF aircraft.

## **Section II. US AIR FORCE MEDICAL TREATMENT FACILITIES**

### **B-9. General**

- a.* The USAF recognizes five levels of care.

### **B-6**

(1) Level I includes self-aid and buddy care, examination and emergency lifesaving measures such as maintenance of airway, control of bleeding, prevention and control of shock, and prevention of further injury. Medical treatment is administered by independent duty medical personnel.

(2) Level II care is administered at the Air Transportable Clinic which assumes AE availability. Patients are stabilized for AE. There is limited outpatient clinical services, initial trauma response, and no patient holding capability.

(3) Level III care is provided by the Air Transportable Hospital (ATH). There are 10-bed, 25-bed, and 50-bed ATH packages. Normally, individual service members who were exposed to a BW agent and are in need of medical care are assisted by the WMDT in the decontamination process. For casualties who are injured and unable to decontaminate themselves, this process has to be performed by the WMDT. (Public health technicians on the WMDTs also have a secondary mission to provide technical guidance on food decontamination.)

(4) Level IV care provides definitive therapy for patients in the recovery phase. If rehabilitation cannot be accomplished within a pre-determined holding period, patients are evacuated to Level V.

(5) Level V care is convalescent, restorative, and rehabilitative. Level V care is normally provided by military, Department of Veterans Affairs, or civilian hospitals in CONUS.

*b.* Military personnel exposed to sufficient BW agents without personal protective equipment and without immunity or prophylaxis will become medical casualties when 75 percent incapacitated. Commanders must be aware that military personnel who become BW medical casualties will require medical treatment for more than 7 days and it is unlikely that they will be recovered to 75 percent capacity to permit return to duty until after a lengthy convalescent period. In-theater commanders must make arrangements for medical evacuation of BW casualties and arrangement for replacement personnel. Continental US commanders must prepare for at least a 10-day forecast of patient loads from theater commanders and identify resources for treatment and recovery of BW patients. Special resources and transportation requirements will be required for casualties exposed to IQDs; see paragraph 1-21.

## **B-10. Detection of Biological Agents**

*a.* For information on the employment, physical properties, infectivity, detection, and control of biological agents, see AFJMAN 32-4009 and AFVA 32-4011. Basically, protection consists of denying access of the agent to the respiratory and digestive systems and immunization of individuals. Skin and wound contamination is of secondary importance.

*b.* If a real-time field detection/identification capability is not present, recognition of BW agents must be based on epidemiology and symptoms. Once illness begins to appear, the presence of an airborne BW agent should be relatively obvious because of the large numbers of casualties and the absence of a common exposure source such as food or water. However, food and/or water may also serve as a vehicle of transmission. If the situation is not readily apparent, the attack will not have been effective. Some indications of an attack are—

## FM 8-284/NAVMED P-5042/AFMAN (I) 44-156/MCRP 4-11.1C

- Point-source epidemiology with a record number of sick and dying patients presenting within a short period of time (within 12 to 48 hours).
- Very high attack rates (60 to 90 percent of personnel are affected/symptomatic).
- A high incidence of pulmonary involvement signaling an aerosol route of infection. This would apply to such agents as plague, tularemia, anthrax, and Q fever where the usual form of infection is not pulmonary.
- “Impossible epidemiology.” If CCVHF occurred in Alaska or New York, or VEE in England, a man-made epidemic would be extremely likely.
- Record fatality rates would be expected for many agents, since a large number of victims would receive doses of organisms far beyond what could possibly occur in nature. This is especially true of an aerosol attack.
- Localized areas of disease epidemics might occur in an area or sector downwind from the point of attack.
- Multiple infections at a single site with unusual pathogens.
- Increased numbers of dead animals of all species, such as rats for plague, or horses with equine encephalitis viruses.
- Protection of those working in indoor environments or environments with filtered air at the time of the attack.
- The near simultaneous outbreak of similar or different epidemics at the same site or at different sites in a TO or at military installations around the world.
- Direct evidence of an attack, such as finding unexploded munitions or a contaminated exploded munitions; admission by hostile forces or terrorists that BW weapons are being used; witnessing an attack; or intelligence information reporting use of BW agents by hostile forces from covert agents working within those hostile forces.

### **B-11. Identification**

The MTF should attempt to identify the agent using whatever laboratory resources are available. The MTF should collect and transport appropriate environmental samples and biological specimens to more capable medical laboratory facilities, such as the Forward Naval Laboratory or the Area Medical Laboratory.

### **B-12. Decontamination**

Normally, only life-saving medical treatment can be provided prior to decontamination, as described in AFJMAN 44-149. Decontamination of casualties is normally done by the 19-member WMDT (Unit Type

Code [UTC] FFGLB) using the equipment package UTC FFGLA. Decontamination is performed prior to the delivery of definitive care in MTFs. Supplies are sufficient to perform complete body skin decontamination of 500 casualties, but should be reviewed and modified to support local wartime tasking and types of decontamination (DECON) facilities. For example the DECON facility can be connected to the chemically hardened ATH via air locks at one end of the emergency room/triage area. Decontamination is performed to arrest the action of the contaminant on the patient and prevent further contamination of patients, medical personnel (who may work without protective equipment to maintain full patient care capabilities) and medical assets. Decontamination does not imply absolute removal of contaminants. The outer layer of clothing is removed and contaminated skin is washed with germicidal soap or 0.5 percent hypochlorite and warm water. The clothing removal step in the decontamination process offers the greatest opportunity for contaminant removal. Removal of the BDO normally decontaminates approximately 90 to 94 percent of the BW agent. If removal of the BDO adequately decontaminates the patient, the rest of the clothing is not removed. Masks are not removed from patients until they have been transferred out of the liquid and vapor hazard areas. Exception: The mask can be removed from the patient for emergency airway management or resuscitation by the EMT trained personnel assigned to the WMDT. The resuscitation device, individual chemical (RDIC) must be used to prevent exposing the patient to secondary aerosolization hazards. (See FM 8-10-7 and USAF WMDT CONOPS for complete details on patient decontamination.)

## **Section III. US NAVY MEDICAL TREATMENT FACILITIES**

### **B-13. General**

For purposes of this publication, US Navy Level I MTFs include battle dressing stations and medical departments of US naval vessels, and BASs in support of the Fleet Marine Forces, regardless of the presence of a physician. Where this manual differs from Navy and Marine Corps doctrine, such doctrine shall have precedence.

*a.* Although the decontamination of naval personnel is considered a nonmedical function, it is accepted that the potential scenario exists in which contaminated personnel might arrive at an MTF. Therefore, all arriving casualties should be considered contaminated until proven otherwise, and all levels should be prepared to receive such casualties.

*b.* Because of the variation in supported units, readers are referred to unit and higher level medical policy in determining assignment of necessary decontamination personnel.

*c.* No casualty will be denied medical treatment to the degree necessary, given overall medical condition, local resources, other casualty demands, availability of evacuation, and proximity to higher levels of care, solely due to casualty contamination. This is not to be construed, however, as to preclude triaging a contaminated patient to the Expectant category. Such Expectant category patients should still be provided minimal care, comfort, pain relief, and other measures as available.

GLOSSARY

**Section I. ABBREVIATIONS AND ACRONYMS**

**ABCA** American, British, Canadian, and Australian

**ACTD** Advanced Concept Technology Demonstration

**AE** aeromedical evacuation (USAF)

**AFMAN (I)** United States Air Force Manual (Interservice)

**AFVA** Air Force Visual Aid

**AHF** Argentine hemorrhagic fever

**AIT** aeromedical isolation team

**AMEDDC&S** Army Medical Department Center and School

**AO** area of operation

**ARDS** adult respiratory distress syndrome

**ATH** air transportable hospital

*B. Burkholderia*

**BAS** battalion aid station

**BDO** battle dress overgarment

**BDU** battle dress uniform

**BEE** bioenvironmental engineering

**BIDS** Biological Integrated Detection System

**BUN** blood urea nitrogen

**BW** biological warfare

**BWC** Biological Weapons Convention

*C. Clostridium; Coxiella*

**C** Celsius

**FM 8-284/NAVMED P-5042/AFMAN (I) 44-156/MCRP 4-11.1C**

**CAM** chemical agent monitor

**cc** cubic centimeter(s)

**CCVHF** Crimean-Congo Viral Hemorrhagic Fever

**CDC** Centers for Disease Control and Prevention

**CFU** colony-forming units

**CINC** Commander in Chief

**cm** centimeter(s)

**CNS** central nervous system

**CONOPS** concept of operations

**CONUS** continental United States

**CPS** collective protection shelter

**CSF** cerebrospinal fluid

**CT** computed tomography

**CW** chemical warfare

**DA** Department of the Army

**DD** Department of Defense

**DECON** decontamination

**DIC** disseminated intravascular coagulation

**DNA** deoxyribonucleic acid

**DNBI** disease and nonbattle injury

**DOD** Department of Defense

**ELISA** enzyme-linked immunosorbent assay

**EMG** electromyography

**Glossary-2**

**EMT** emergency medical treatment

*F. Francisella*

**F** Fahrenheit

**FDA** Food and Drug Administration

**FM** field manual

**GI** gastrointestinal

**gm** gram(s)

**GU** genitourinary

**HEPA** high efficiency particulate air

**HFRS** hemorrhagic fever with renal syndrome

**HIV** human immunodeficiency virus

**HSS** health service support

**IATA** International Air Transportation Association

**IgG** immunoglobulin class G

**IgM** immunoglobulin class M

**IM** intramuscular(ly)

**IND** investigational new drug

**IQD** internationally quarantinable disease

**IV** intravenous

**JBPDS** Joint Biological Point Detection System

**JPO-BIO** Joint Program Office for Biological Defense

**JSLIST** Joint service lightweight integrated suit technology

**kg** kilogram(s)

**FM 8-284/NAVMED P-5042/AFMAN (I) 44-156/MCRP 4-11.1C**

**km** kilometer(s)

**LRBSDS** Long-Range Biological Standoff Detection System

**MCRP** Marine Corps Reference Publication

**MES** medical equipment sets

**mg** milligram(s)

**ml** milliliter(s)

**MOPP** mission-oriented protective posture

**MRI** magnetic resonance imaging

**MTF** medical treatment facility

**NATO** North Atlantic Treaty Organization

**NAVMED P** US Navy Medical Publication

**NBC** nuclear, biological, and chemical

**PCR** polymerase chain reaction

**PHS** public health service

**PPW** patient protective wrap

**PSP** paralytic shellfish poisoning

**PVNTMED** preventive medicine

**Q fever** Query fever

**QSTAG** Quadripartite Standardization Agreement

**RDIC** resuscitation device, individual chemical

**RNA** ribonucleic acid

*S. Staphylococcus*

**S2** Intelligence Officer (US Army)

**Glossary-4**



**SAT** serum-agglutinating titers

**SEB** staphylococcal enterotoxin B

**SIADH** syndrome of inappropriate antidiuretic hormone

**SRBSDS** Short-Range Biological Standoff Detection System

**STANAG** Standardization Agreement

**T2** trichothecene

**TMP** trimethoprim

**TO** theater of operations

**TSST-1** toxic shock syndrome toxin-1

**μ** microns

**US** United States

**USAF** United States Air Force

**USAMRIID** United States Army Medical Research Institute for Infectious Diseases

**USTRANSCOM** United States Transportation Command

**UTC** unit type code (USAF)

**VEE** Venezuelan equine encephalitis

**VHF** viral hemorrhagic fevers

**VIG** vaccinia immunoglobulin

**WHO** World Health Organization

**WMD** weapons of mass destruction

**WMDT** wartime medical decontamination team

***Y. Yersinia***

## Section II. DEFINITIONS

**active immunization** The administration of a vaccine to stimulate the host immune system to develop immunity (protection) against a specific pathogen or toxin.

**Airborne Precautions** Standard Precautions plus: Placing the patient in a private room that has negative air pressure, at least six air changes/hour, and appropriate filtration of air before it is discharged from the room. Use of respiratory protection when entering the room. Limiting movement and transport of the patient. Using a mask on the patient if he needs to be moved.

**bacterial agent** A live pathogenic organism that can cause disease, illness, or death.

**biological contamination** The presence of an infectious agent on a body surface or on an environmental surface.

**biological warfare agent** A biological warfare agent is a pathogen (microorganism capable of causing disease) or toxin derived from a living organism that is deliberately used to produce disease or death in humans, animals, or plants.

**chemoprophylaxis** The administration of an antibiotic agent to prevent an infection, or to prevent an incubating infection from progressing to disease, or to eliminate a carrier state to prevent transmission and disease in others.

**Contact Precautions** Standard Precautions plus: Placing the patient in a private room or with someone with the same infection, if possible. Using gloves when entering the room. Changing gloves after contact with infective material. Using 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. Limiting the movement or transport of the patient from the room. Ensuring that patient care items, bedside equipment, and frequently touched surfaces receive daily cleaning. Dedicating use of noncritical patient-care equipment to a single patient, or cohort of patients with the same pathogen. If not feasible, adequate disinfection between patients is necessary.

**Droplet Precautions** Standard Precautions plus: Placing the patient in a private room or with someone with the same infection. If not feasible, maintaining at least 3 feet between patients. Using a mask when working within 3 feet of the patient. Limiting movement and transport of the patient. Using a mask on the patient if he needs to be moved.

**endemic** A disease that is present in a human population, or in an animal population that is transmittable to humans, but has a very low morbidity rate.

**enzootic** A disease that is present in an animal population at all times, but has a low morbidity rate.

**epidemic** A disease that is only present for a limited time in a human population or animal population that is transmittable to humans, and has a very high morbidity rate.

**epizootic** A disease that is only present in an animal population for limited periods, but has a high morbidity rate.

**etiologic** Cause of the disease/illness.

**inoculum** The amount of microorganisms introduced into a host.

**passive immunization** The administration of pre-formed antibodies to confer immunity to a specific pathogen or toxin.

**sample** Material collected from a source other than an animal or man for laboratory analysis (such as water sample or soil sample).

**specimen** Material collected from a man or animal for laboratory analysis (such as tissue or blood specimen).

**Standard Precautions** Handwashing after patient contact. Using gloves when touching blood, body fluids, secretions, excretions, and contaminated items. Using mask, eye protection, and gown during procedures likely to generate splashes or sprays of blood, body fluids, secretions, or excretions. Handling contaminated patient-care equipment and linens in a manner that prevents the transfer of microorganisms to people or equipment. Practicing care when handling sharps and using a mouthpiece or other ventilation device as an alternative to mouth-to-mouth resuscitation, when practical. Placing the patient in a private room if they contaminate the environment, when feasible.

**toxin agents** Poisonous by-products of living organisms used to cause disease, illness or death in susceptible individuals.

**viral agents** A group of viruses that have been selected as BW agents because of their ability to produce disease, illness, and death in susceptible individuals.

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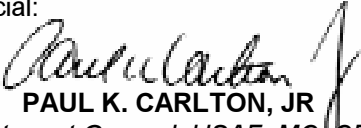
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